Received: 1 June 2023 | Revised: 25 September 2023 | Accepted: 27 September 2023

DOI: 10.1111/apa.16991

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

ORIGINAL ARTICLE

Finnish paediatric study found a low incidence of bacterial meningitis from 2011 to 2018 but a substantial proportion of nosocomial meningitis

Sakke Niemelä[1] | Laura Lempinen[2] | Eliisa Löyttyniemi[3] | Juha O. Grönroos[4] | Raakel Luoto[5] | Ville Peltola[5] | Jussi Jero[6]

[1]Department of Otorhinolaryngology, Turku University Hospital, University of Turku, Turku, Finland

[2]Department of Radiology, HUS Medical Imaging Center, Helsinki University Central Hospital, University of Helsinki, Helsinki, Finland

[3]Department of Biostatistics, Turku University Hospital, University of Turku, Turku, Finland

[4]Department of Clinical Microbiology, Turku University Hospital, University of Turku, Turku, Finland

[5]Department of Paediatrics and Adolescent Medicine, Turku University Hospital, University of Turku, Turku, Finland

[6]Department of Otorhinolaryngology, Head and Neck Surgery, Helsinki University Hospital, University of Helsinki, Helsinki, Finland

Correspondence
Sakke Niemelä, Department of Otorhinolaryngology, Turku University Hospital, University of Turku, Savitehtaankatu 5, 20540 Turku, Finland.
Email: sasani@utu.fi

Abstract

Aim: This study examined the predisposing factors, clinical picture, bacterial aetiology and clinical outcomes of infants and children with bacterial meningitis (BM).

Methods: The medical records of patients under 16 years of age, treated by Turku University Hospital, Finland, from 2011 to 2018, were screened for meningitis using the International Classification of Diseases, Tenth Revision codes. Patients were included if bacteria were detected in cerebrospinal fluid (CSF) or other predefined laboratory variables indicated BM, despite CSF testing negative for bacteria. The Glasgow Outcome Scale (GOS) was used to determine outcomes.

Results: We identified 37 children with BM: 22 infants aged 0–89 days and 15 children aged 90 days to 15 years. The overall incidence was approximately 5.7/100 000/year. Nosocomial meningitis was documented in 51%. Bacterial growth was detected in the CSF or blood cultures of the majority of patients (57%). *Escherichia coli* (14%), group B streptococcus (11%) and *Streptococcus pneumoniae* (8%) were the most common pathogens. There were 14% of patients with unfavourable outcomes, namely GOS scores of 1–4, but no deaths.

Conclusion: The incidence of paediatric BM was low during the study period, but the proportion of nosocomial meningitis was substantial. The frequency of unfavourable long-term outcomes was relatively low.

KEYWORDS
bacterial meningitis, Glasgow Outcome Scale, group B streptococcus, nosocomial infection, *Streptococcus pneumoniae*

Abbreviations: BM, bacterial meningitis; CSF, cerebrospinal fluid; GBS, group B streptococcus; GOS, Glasgow Outcome Scale; Hib, *Haemophilus influenzae* type b; ICD-10, International Classification of Diseases, Tenth Revision; PCR, polymerase chain reaction.

1 | INTRODUCTION

Bacterial meningitis (BM) is the tenth most common cause of death in children under 5 years of age in the world and causes significant morbidity and mortality worldwide.[1,2] Group B streptococcus (GBS) and *Escherichia coli* have dominated the bacterial aetiology in infants from 0 to 89 days of age. Since universal vaccinations, *Streptococcus pneumoniae* and *Neisseria meningitidis* have been the most important causative agents in children and adolescents over that age. *Haemophilus influenzae* type b (Hib) was also on that list before BM immunisation.[1,2]

The incidence of BM has decreased substantially in areas with high vaccination coverage against *S. pneumoniae*, *N. meningitidis* and Hib. In the Netherlands, the implementation of Hib vaccination has reduced the incidence of BM caused by *H. influenzae* from 1.44 to 0.04 episodes per 100 000 population per year.[2] In the USA, the Hib conjugate vaccine was associated with a 55% reduction in bacterial meningitis in the early 1990s and the 7-valent pneumococcal conjugate vaccine was associated with a 59% reduction in pneumococcal meningitis in children.[3,4] The implementation of the meningococcal group C vaccination has also been effective in the Netherlands. It decreased the incidence of *N. meningitidis* meningitis from 2.87 to 0.20 per 100 000 individuals between 1989–1993 and 2014–2019.[2] Neonatal BM is more difficult to prevent, because maternal intrapartum antibiotic prophylaxis does not protect children from late-onset GBS disease.[5]

Meningitis survivors risk neurological sequelae, such as hearing loss, cerebral palsy and mental retardation.[6] Although hearing loss can spontaneously improve, studies have reported that it was permanent in around 30% of pneumococcal meningitis survivors.[7,8] Prematurity, male gender and seizures are predictors of unfavourable outcomes in neonates.[9] Data about the prognosis of BM in high-income countries has been scarce and continuously affected by changing epidemiology and improvements in diagnostics and treatment.

Our aim was to describe the epidemiology of paediatric BM patients treated at Turku University Hospital, Finland, from 2011 to 2018. We also evaluated the predisposing factors, aetiology, clinical manifestations and treatment of BM, together with indicators of unfavourable outcomes.

Key notes

- We examined bacterial meningitis (BM) in 22 infants aged 0–89 days and 15 children aged 90 days to 15 years.
- Bacterial growth was detected in the cerebrospinal fluid or blood cultures of 57% and *Escherichia coli* (14%), group B streptococcus (11%) and *Streptococcus pneumoniae* (8%) were the most common pathogens.
- There were 14% with unfavourable outcomes, defined as Glasgow Outcome Scale scores of 1–4, but no deaths.

2 | METHODS

2.1 | Study design

Turku University Hospital is a tertiary referral centre in the Hospital District of Southwest Finland, which also receives patients from Western Finland. At the time of the study, its catchment area was approximately 480 000 people, including 75 000 children below 16 years of age, and some 4000 live births per year. We performed a database search of patients under 16 years of age who were hospitalised between 1 January 2011 and 31 December 2018 using the International Classification of Diseases, Tenth Revision (ICD-10) codes for meningitis: A87.9, B94.80, G00.9, G01*A32.1, G01*A39.0, G01*A69.2, G05.2*B83.2, A17.0, A32.1, A87, B01.0+, B02.1, B05.1+, B37.5, B38.4+, B45.1, B94.80, G00, G01, G02, G03, G05. The children's medical records were reviewed. Meningitis caused by non-bacterial pathogens, such as viruses, fungi or parasites were excluded and so were neuroborreliosis cases. We included cases with positive cerebrospinal fluid (CSF) cultures or polymerase chain reaction (PCR) results with an ICD-10 code for meningitis. Previous research has found that a substantial proportion of BM cases were culture-negative, because of pre-diagnostic antibiotic therapy or other causes.[10] Therefore, we also included CSF culture-negative patients with clinical symptoms of BM and CSF pleocytosis ($>30\times10^6$/L). They also had to have at least one of the following laboratory findings: a positive blood bacterial culture, a high CSF protein level (>1000 mg/L) or elevated plasma C-reactive protein (>50 mg/L). The inclusion criteria for neonatal early-onset BM cases, defined as 0–6 days of age, were clinical symptoms of BM and a CSF leucocyte count of $>30\times10^6$/L. In CSF *Staphylococcus epidermidis* was considered to be a causative agent of BM if the patient was having BM symptoms and there was simultaneous CSF pleocytosis.

Of the 149 children with an ICD-10 code for meningitis, 37 had a confirmed case of BM and were included in the study. The ICD-10 codes for meningitis included viral, aseptic and bacterial meningitis. The patients who were excluded had a confirmed or probable case of viral or aseptic meningitis or they did not fill the inclusion criteria for BM. The patients were then classified into two age groups: infants from 0 to 89 days of age and children and adolescents from 90 days to 15 years of age. Nosocomial BM was defined as early-onset meningitis, meningitis acquired during the patient's hospital stay or meningitis after a neurosurgical operation, which occurred <30 days after discharge. All other patients were defined as having community-acquired BM.

Since 2010, the Finnish national vaccination programme has offered children the 10-valent pneumococcal conjugate vaccine at 3, 5 and 12 months. This covers *S. pneumoniae* serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Hib vaccines have been given at the same ages since 1993. Meningococcal vaccines are not included in the Finnish national vaccination programme for children.

The microbiological laboratory methods are described in Appendix S1.

2.2 | Outcomes

We evaluated the outcomes with the five-point Glasgow Outcome Scale (GOS), based on the information in the patient's medical records.[11] The scale comprises death (one point), vegetative state (two points), severe disability (three points), moderate disability (four points) and mild or no disability (five points). The outcomes were evaluated at discharge and 8 months after discharge. An unfavourable outcome was defined as a score from 1 to 4. When we determined the GOS scores, we considered the age of the patient and the disability was assessed in relation to their age-appropriate behaviour.

Hearing was tested with an appropriate method, either a brainstem auditory evoked response, an audiogram, otoacoustic emissions or mechanical source of voice. Hearing deficiency was defined by a better ear hearing level of 20 dB or above.

2.3 | Statistical analysis

The incidence of BM was calculated by dividing the number of patients in the Hospital District by the number of study years and the population below 16 years of age. The incidence in infants was obtained by dividing the annual number of infant cases by the number of live births.

The age groups were compared with the Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical variables. Associations between two categorical variables were tested with Fisher's exact test. Furthermore, a separate log-binomial model was performed with unfavourable outcomes, defined as GOS scores 1–4, for each factor as a univariate approach. We were not able to perform a multivariate analysis because of the low number of children with an unfavourable outcome. Two-tailed p values of <0.05 were regarded as statistically significant. The data analysis was generated using SAS for Windows, Version 9.4 (SAS Institute Inc).

2.4 | Ethics

The study received institutional approval and was not subject to the Ethics Committee approval.

3 | RESULTS

3.1 | Incidence, demographics and causative agents

We identified 37 children (54% male) with BM treated at Turku University Hospital between 2011 and 2018. There were 22 infants aged 0–89 days and 15 children or adolescents aged 90 days to 15 years (Figure 1).

Three of the patients had been transferred from other hospitals in Finland. The incidence was approximately 5.7/100 000/year based on the 34 children living in the Hospital District. The estimated incidence among infants was 0.7/1000 live births. The median age of the 37 children was 1 month, with an interquartile range of 9 days to 3 years and 9 months. The majority (51%) of the BM cases were nosocomial (Table 1).

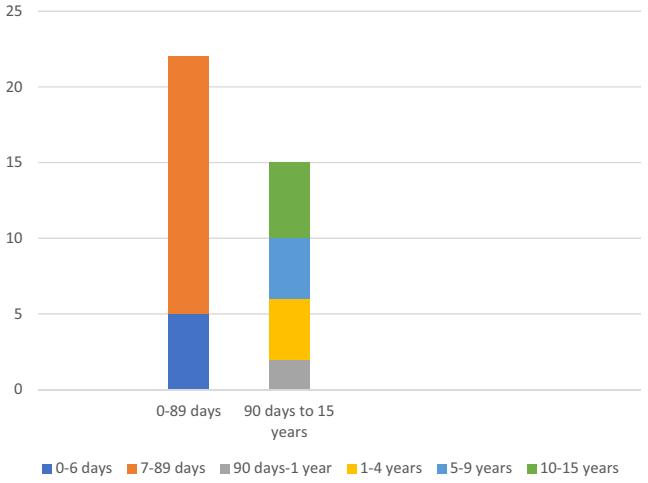

FIGURE 1 Age distribution of the 37 patients.

Pathogens were detected in either the CSF or blood of 57% of the patients (Table 2). The CSF culture was positive for bacteria in 41% of cases and the PCR of the CSF was positive in one culture-negative case (Figure 2). A blood culture detected a pathogen in five cases when the CSF culture was negative. GBS (11%), *S. pneumoniae* (8%) and *E. coli* (5%) were the most frequent pathogens in the CSF cultures. All the causative pathogens are shown in Figure 2. The CSF culture was positive in 15% of the 20 patients who received antibiotics before their lumbar puncture and in 71% of the 17 patients who only received antibiotics after the lumbar puncture ($p = 0.001$).

3.1.1 | Background characteristics

Most (55%) of the 22 infants (59% male) aged 0–89 days of age (Table 1) were born preterm before 37 + 0 weeks of gestation: 14% before 28 + 0 and 18% between 28 + 0 and 31 + 6 weeks. Four mothers were carrying GBS. The data on BM by age group are presented in Table 3.

Two of the 15 children (47% male) aged 90 days to 15 years (Table 1) had both otitis media and mastoiditis. Pneumonia, pyelonephritis, a brain abscess and a dental infection were each detected in one patient prior to or simultaneously with, BM. The subgroups of BM by age group are presented in Table 3.

3.1.2 | Clinical characteristics, causative agents and treatment

The clinical characteristics of the infants aged 0–89 days are presented in Table 1. The most common pathogens cultured from either

TABLE 1 Comparison of the clinical findings, laboratory values and outcomes of 37 children with bacterial meningitis (BM), by age.

Variable	Children aged 0–89 days *n* = 22 *n/N* (%) or median	Children aged 90 days to 15 years *n* = 15 *n/N* (%) or median	All children *n* = 37 *n/N* (%) or median	*p*-Value	Proportion difference (%) and 95% confidence interval
Type of bacterial meningitis					
Community-acquired	9 (41)	9 (60)	18 (49)	0.32	19 (−13 to 51)
Previous surgery	3 (14)	7 (47)	10 (27)	0.056	33 (4 to 62)
Neurosurgical BM	3 (14)	4 (27)	7 (19)	0.41	13 (−14 to 40)
Nosocomial	13 (59)	6 (40)	19 (51)	0.32	−19 (−51 to 13)
Clinical findings at presentation					
Pre-diagnostic antibiotics	15 (68)	5 (33)	20 (54)	0.050	−35 (−66 to −4)
Neurological symptoms[a]	3 (14)	5 (33)	8 (22)	0.41	13 (−14 to 40)
Decreased general condition	19 (86)	12 (80)	31 (84)	0.67	−6 (−31 to 18)
Irritability	18 (82)	6 (40)	24 (65)	0.015	−42 (−71 to −12)
Fever	9 (41)	14 (93)	23 (62)	0.002	52 (28 to 77)
Decreased consciousness	11 (50)	5 (33)	16 (43)	0.50	−17 (−48 to 15)
Vomiting	Not available	12 (80)	12 (32)	0.0001	Not available
Neck stiffness	0	9 (60)	9 (24)	0.0001	60 (35 to 85)
Headache	Not available	8 (53)	8 (22)	0.0001	Not available
Petechiae	0	3 (20)	3 (8)	0.059	20 (0 to 40)
Seizures	1 (5)	2 (13)	3 (8)	0.55	9 (−10 to 28)
Confusion	0	2 (13)	2 (5)	0.16	13 (−4 to 31)
Facial paresis	0	1 (7)	1 (3)	0.41	7 (−6 to 19)
Pupil-asymmetry	1 (5)	0	1 (3)	1.0	−5 (−13 to 4)
Bulging fontanel	1 (5)	0	1 (3)	1.0	−5 (−13 to 4)
Laboratory and imaging results (interquartile range)					
C-reactive protein (mg/L)	19.5 (4.8–75)	85 (28–133)	45 (5–86)	0.033	−61 (−124 to-31)
Leucocyte count in blood ($\times 10^9$/L)	9.2 (4.5–12.5)	14.9 (8.3–22)	9.6 (6.8–16.6)	0.016	−6 (−13 to 1)
Leukocyte count in CSF ($\times 10^6$/L)	360 (45–1848)	1600 (414–2430)	738 (92–2220)	0.052	1230 (−2102 to-10)
Granulocyte percentage in CSF (%)	44 (0–78)	79 (66–96)	75 (10–85)	0.016	−29 (−75 to −4)
Glucose levels in CSF (mmol/L)	2.1 (1.2–3)	3.2 (1–3.4)	2.3 (1.1–3.4)	0.22	−1 (−2 to 1)
Lactate levels in CSF (mmol/L)	3.4 (2.6–3.9)	6.3 (3.1–8.7)	3.5 (2.9–7.0)	0.040	−3 (−5 to 0)
Protein levels in CSF (mg/L)	1784 (1063–2645)	1105 (566–1791)	1277 (702–2569)	0.092	555 (119 to 1524)
Head magnetic resonance imaging performed	5 (23)	7 (47)	12 (32)	0.16	24 (−7 to 55)
Imaging findings consistent with BM	2 (9)	5 (33)	7 (19)	0.095	24 (−7 to 55)

TABLE 1 (Continued)

Variable	Children aged 0–89 days $n = 22$ n/N (%) or median	Children aged 90 days to 15 years $n = 15$ n/N (%) or median	All children $n = 37$ n/N (%) or median	p-Value	Proportion difference (%) and 95% confidence interval
CSF culture positive	7 (32)	8 (53)	15 (41)	0.31	22 (−10 to 53)
Blood culture positive	10 (45)	4 (27)	14 (38)	0.31	−19 (−49 to 12)
Treatment and outcome					
Hospital stay in days (median): 1st to 3rd quartile	21 (14–51)	7 (5–14)	15 (7–33)	0.0015	14 (7 to 17)
Intravenous antibiotic therapy in days (median): 1st to 3rd quartile	14 (12–21)	11 (7–25)	14 (10–21)	0.50	3 (−3 to 8)
Unfavourable outcome at discharge	6 (27)	3 (20)	9 (24)	0.71	−7 (−35 to 20)
Unfavourable outcome at 8 months control	3 (14)	2 (13)	5 (14)	1.0	0 (−23 to 22)
Hearing tests performed	18 (82)	10 (67)	28 (76)	0.71	−11 (−40 to 19)
Permanent hearing deficiency	1 (5)	1 (7)	2 (5)	1.0	−2 (−17 to 13)

[a]Neurological symptoms were defined as seizures, confusion, facial paresis, pupil-asymmetry and bulging fontanel.

Abbreviations: BM, bacterial meningitis; CSF, cerebrospinal fluid.

CSF or blood were *E. coli* (18%), GBS (18%) and *Staphylococcus aureus* (9%). Two infants of 0–6 days of age had GBS and so did two infants of 7–89 days of age. All the detected pathogens are presented in Figure 2. Multi-drug resistance, which was defined as resistance to three or more relevant antibiotics, was seen in two bacterial isolates: *S. epidermidis* and *Staphylococcus hominis*. One CSF sample was positive with PCR for *Sphingomonas species* when the CSF culture was negative.

The most frequently used antibiotics were ampicillin (55%), cefotaxime (41%) and gentamycin (27%). Multimodal antibiotic therapy was used to treat 77% of the patients with BM and this ranged from three to seven different antibiotics. There were no cases where the cultured bacteria that caused BM were resistant to the empirically initiated antibacterial treatment. Two patients underwent neurosurgery: one had a brain haemorrhage and one had hydrocephalus. Two patients needed invasive respiratory support.

The clinical characteristics of the children aged 90 days to 15 years are presented in Table 1. The most common pathogen, cultured from either their CSF or blood, was *S. pneumoniae* (20%). *Escherichia coli*, *Staphylococcus capitis* and *N. meningitidis* were all detected once. There was one CSF sample with two cultured bacteria. All the pathogens detected are presented in Figure 2.

Pre-diagnostic antibiotics were administered to 33% of the patients. The most frequently used antibiotics after BM diagnoses were ceftriaxone (87%) and vancomycin (33%). Multimodal antibiotic therapy was used to treat 53% of the patients with BM and this ranged from three to seven different antibiotics. Corticosteroid treatment was given to 60% of the patients as well as antibiotics. Three patients needed neurosurgery and ear-related operations. Six patients received oral antibiotics after discharge and the duration ranged from 7 to 14 days.

3.1.3 | Outcome

The majority (82%) of the infants who were 0–89 days of age underwent hearing tests, using a brainstem auditory evoked response (89%) or otoacoustic emissions and a mechanical source voice (11%). Permanent hearing deficiency was documented in one patient and two received a ventriculoperitoneal shunt. One patient was diagnosed with epilepsy. Six patients had an unfavourable outcome at discharge: four had a GOS score of three and two had a GOS score of four. Three of the patients with a GOS score of three had an unfavourable outcome 8 months after discharge. There were no deaths.

More than two-thirds (67%) of the children aged 90 days to 15 years had hearing tests, using an audiogram (70%), a brainstem auditory evoked response (20%) or otoacoustic emissions (10%). One had a permanent hearing deficiency and another had a ventriculoperitoneal shunt. Other negative outcomes were visual difficulties in one patient and a change in personality in another. Three patients had an unfavourable outcome at discharge: one had a GOS score of three and two had a score of four. The two patients with a

TABLE 2 Bacteria detected in cerebrospinal fluid (CSF) or blood culture by age groups.

Pathogens in CSF or blood culture	Infants aged 0–89 days *n* = 22 *n/N* (%)	Children aged 90 days to 15 years *n* = 15 *n/N* (%)	All children *n* = 37 *n/N* (%)
Escherichia coli	4 (18)	1 (7)	5 (14)
Group B streptococcus	4 (18)	0	4 (11)
Streptococcus pneumoniae	0	3 (20)	3 (8)
Staphylococcus aureus	2 (9)	0	2 (5)
Neisseria meningitidis	0	1 (7)	1 (3)
Staphylococcus epidermidis	1 (5)	0	1 (3)
Staphylococcus capitis	0	1 (7)	1 (3)
Actinomyces sp.	0	1 (7)	1 (3)
Staphylococcus hominis	1 (5)	0	1 (3)
Anaerobic gram-positive cocci	0	1 (7)	1 (3)

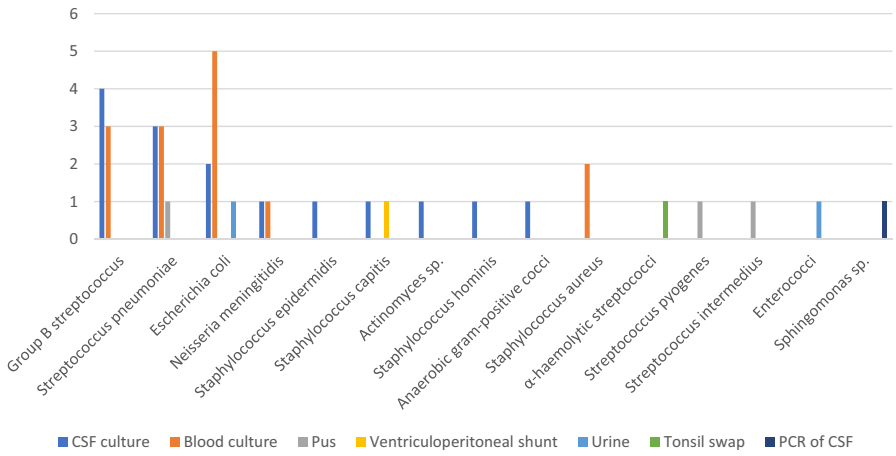

FIGURE 2 Numbers of bacterial detections by culture of cerebrospinal fluid (CSF), blood, pus, ventriculoperitoneal shunt, urine or tonsil swap specimen or by polymerase chain reaction of CSF.

TABLE 3 Subgroups of bacterial meningitis by age groups.

	n (%)
Children aged 0–89 days (*n* = 22)	
Early-onset (0–6 days)	5 (23)
Late-onset (7–89 days)	17 (77)
Late-onset community-acquired	6 (27)
Late-onset nosocomial (not neurosurgical)	8 (36)
Neurosurgical postoperative	3 (14)
Children aged 90 days to 15 years (*n* = 15)	
Community-acquired	9 (60)
Nosocomial (not neurosurgical)	2 (13)
Neurosurgical postoperative	4 (27)

GOS score of four had unfavourable outcomes 8 months after discharge. There were no deaths.

The univariate analysis showed that a positive CSF culture was associated with an unfavourable outcome at discharge ($p = 0.02$), but not 8 months after discharge ($p = 0.1$; Appendix S1). Nosocomial meningitis ($p = 0.007$) and preterm birth ($p = 0.04$) were associated with an unfavourable outcome 8 months after discharge.

4 | DISCUSSION

The incidence of paediatric BM was low in Southwestern Finland during 2011–2018. In particular, community-acquired BM was rare in children aged 90 days to 15 years, but the proportion of infants aged 0–89 days with nosocomial BM was prominent. A large number of cases continued to have negative CSF and blood bacterial cultures. The outcomes in both age groups were generally good.

Between 2010 and 2015 the incidence rates of BM in Northern Sweden were 1.9–3.4/100 000 in infants and children.[12] The incidence was highest among infants and lowest among adolescents and was approximately the same level as in our study (5.7/100 000/year). The global incidence of BM in children has decreased and a major reason for this progress has been the increased use of vaccines against the predominant pathogens. Differences in the diagnostics, recording and definitions of BM have hampered the assessment of the true incidence of BM and comparisons between studies. The pre-diagnostic administration of antibiotics was frequent in our study population and bacterial PCR tests on CSF specimens were infrequently carried out. To avoid missing cases due to this, we also included culture-negative cases based on the relevant ICD-10 codes, clinical presentation and laboratory findings.

Streptococcus pneumoniae is a dominant pathogen that causes BM in childhood. For example, this was reported by a study from the United States that covered the period 1998–2007, which found that *S. pneumoniae* causes over a third of all BM in infants and children.[13] However, we only detected three cases of pneumococcal meningitis in children from 90 days to 15 years of age. The 10-valent pneumococcal conjugate vaccine was added to the Finnish national vaccination programme in 2010, just before the current study began. This was followed by a rapid decrease in the incidence of pneumococcal meningitis in children in Finland: 54% in children aged 5–17 years and 64% in children aged 0–4 years of age.[14] Replacement by non-vaccine serotypes has been seen mainly in older adults.[14] Although meningococcal vaccines are not included in the Finnish national vaccination programme for children, only one case of *N. meningitidis* BM was found in this study. Other studies have indicated that meningococcal diseases are more common in some other European countries than in Finland. For example, one Icelandic study reported that *N. meningitidis* was the most common causative pathogen of BM.[15] No cases of BM due to Hib were documented in our study, as it has disappeared due to the high coverage of vaccinations.[16]

Our study showed the incidence of BM in infants 0–89 days of age was high compared to children aged 0–60 days in another study.[13] Our incidence rate of 0.7 per 1000 live births was in line with the estimated incidences of neonatal BM of 0.3 per 1000 live births in high-income countries and up to 3–6 per 1000 live births in low-income and middle-income countries.[17] As expected, GBS and *E. coli* were the dominant pathogens in infants. It is worth noting that no BM cases caused by *Listeria monocytogenes* were detected. Maternal GBS prophylaxis with antibiotics has been reported to be efficient against early-onset disease, but not against late-onset disease.[18] Maternal GBS vaccines are urgently needed to prevent late-onset GBS disease.[5] Neonatal nosocomial infections can, to some extent, be prevented by breastfeeding, probiotics and strict infection prevention programmes in neonatal units.[19] The rapid initiation of antibiotic treatment for any suspicion of sepsis may prevent the infection developing into BM.[20] Despite these measures, newborn infants, particularly those born prematurely, are susceptible to invasive bacterial infections, due to their immature and inexperienced innate and adaptive immune systems. Preterm infants also have inadequate protection against infectious agents through maternal immunity. Our findings demonstrated this, as 55% of the infants were born prematurely and 14% of them before 28 + 0 and 18% between 28 + 0 and 31 + 6 weeks of gestation. Moreover, the innate cytokine response against pathogens in a neonate can be inadequate or, conversely, overwhelming and has been associated with increased disease severity.[21]

We found that 41% of the CSF cultures were positive and that negative cultures were associated with administering antibiotics before a lumbar puncture. Pre-diagnostic antibiotics were used for 54% of the patients in our study, compared to 35%–46% in other studies.[22] Certain bacteria can be completely sterilised in CSF within 2 h of parenteral antibiotics[6] and an interval of over 6 h between administering antibiotics and a lumbar puncture can reduce culture positivity from 100% to 40%.[23] Using PCR testing as well as culturing bacteria in CSF resulted in a more sensitive and rapid yield, compared to just the using cultures.[24] PCR was not routinely used during our study period, but these data do support its use.

We found a lower rate of permanent hearing deficiency (5%) than previously reported (22%–30%).[7] This may have been due to the success of pneumococcal vaccines, by decreasing the proportion pneumococcal BM, as *S. pneumoniae* is a key pathogen that causes hearing loss after BM.[7] The overall functional outcome was unfavourable in 14% of the children, in accordance with previous studies (10%–18%).[25,26] In our study, nosocomial meningitis and preterm birth were correlated with unfavourable outcomes 8 months after discharge. However, these findings should be interpreted with caution, because unfavourable outcomes only occurred in a small number of subjects and the results were based on univariate analyses. Despite this, our study highlighted the increased role of nosocomial BM and its potential to cause long-term morbidity. It also supported earlier evidence that prematurity can predict unfavourable outcomes.[27] There were no deaths in our study, but a larger study population would have provided a more reliable estimate of the mortality rate. Global mortality due to childhood BM has been reported to range from 2% to 33%.[28,29]

Our study had some limitations. It was a single-centre study with a small number of patients, but the design enabled uniform and detailed data collection. Nevertheless, there was a risk of inaccuracies in the retrospectively documented clinical data. The study population was heterogenic, which meant we had very small subgroups of patients, but our findings do provide an overview of paediatric BM in our area. Using the GOS with small infants and children may present challenges and it may also be difficult to differentiate moderate disability from mild disability using medical records. However, we believe that our main finding of generally good outcomes after BM was reliably determined by using the GOS scale. The patients included in this study may not represent the whole population of children in Finland. We were unable to exclude the possibility of neurosurgery itself being the cause of complications or an unfavourable outcome in some patients. Furthermore, we had no long-term follow-up data, or information on quality of life after BM, which has been reported to be impaired.[30]

5 | CONCLUSION

This study found a low incidence of BM in infants and children in Southwest Finland between 2011 and 2018. GBS and *E. coli* were the dominant bacteria in children of 0–89 days of age. The proportion of nosocomial BM was high. The likelihood of an unfavourable outcome was relatively low and there were no deaths. The changing epidemiology of BM should be considered when developing further strategies to improve prevention and treatment.

AUTHOR CONTRIBUTIONS

Sakke Niemelä: Conceptualization; data curation; formal analysis; investigation; methodology; resources; validation; visualization; writing – original draft; writing – review and editing. **Laura Lempinen:** Conceptualization; formal analysis; methodology; resources; validation; visualization; writing – review and editing. **Eliisa Löyttyniemi:** Data curation; formal analysis; software; writing – review and editing. **Juha O. Grönroos:** Methodology; validation; writing – review and editing. **Raakel Luoto:** Conceptualization; data curation; investigation; methodology; validation; writing – original draft; writing – review and editing. **Ville Peltola:** Conceptualization; data curation; methodology; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing. **Jussi Jero:** Conceptualization; data curation; methodology; project administration; supervision; validation; visualization; writing – original draft.

ACKNOWLEDGEMENTS

We thank Elizabeth Nyman for language consultations and Emmi Alimattila for technical support.

FUNDING INFORMATION

This study did not receive any specific funding.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

ORCID

Sakke Niemelä https://orcid.org/0000-0002-8479-9096

REFERENCES

1. Mijovic H, Sadarangani M. To LP or not to LP? Identifying the etiology of pediatric meningitis. Pediatr Infect Dis J. 2019;38:S39-42.
2. Koelman DLH, van Kassel MN, Bijlsma MW, Brouwer MC, van de Beek D, van der Ende A. Changing epidemiology of bacterial meningitis since introduction of conjugate vaccines: 3 decades of national meningitis surveillance in the Netherlands. Clin Infect Dis. 2021;73:e1099-107.
3. Schlech WF, Ward JI, Band JD, et al. Bacterial meningitis in the United States, 1978 through 1981: the national bacterial meningitis surveillance study. JAMA. 1985;253:1749-54.
4. Whitney CG, Farley MM, Hadler J, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N Engl J Med. 2003;348:1737-46.
5. Delara M, Vadlamudi NK, Sadarangani M. Strategies to prevent early and late-onset group B streptococcal infection via interventions in pregnancy. Pathogens. 2023;12:229.
6. Kim KS. Acute bacterial meningitis in infants and children. Lancet Infect Dis. 2010;10:32-42.
7. Arditi M, Mason EO Jr, Bradley JS, et al. Three-year multicenter surveillance of pneumococcal meningitis in children: clinical characteristics, and outcome related to penicillin susceptibility and dexamethasone use. Pediatrics. 1998;102:1087-97.
8. Lucas MJ, Brouwer MC, van de Beek D. Neurological sequelae of bacterial meningitis. J Infect. 2016;73:18-27.
9. Haffner DN, Machie M, Hone E, Said RR, Maitre NL. Predictors of neurodevelopmental impairment after neonatal bacterial meningitis. J Child Neurol. 2021;36:968-73.
10. Corless CE, Guiver M, Borrow R, Edwards-Jones V, Fox AJ, Kaczmarski EB. Simultaneous detection of *Neisseria meningitidis*, *Haemophilus influenzae*, and *Streptococcus pneumoniae* in suspected cases of meningitis and septicemia using real-time PCR. J Clin Microbiol. 2001;39:1553-8.
11. Beers SR, Wisniewski SR, Garcia-Filion P, et al. Validity of a pediatric version of the Glasgow Outcome Scale-extended. J Neurotrauma. 2012;29:1126-39.
12. Johansson Kostenniemi U, Norman D, Sellin M, Silfverdal SA. Sustained reductions of invasive infectious disease following general infant *Haemophilus influenzae* type b and pneumococcal vaccination in a Swedish Arctic region. Acta Paediatr. 2019;108:1871-8.
13. Thigpen MC, Whitney CG, Messonnier NE, et al. Bacterial meningitis in the United States, 1998–2007. N Engl J Med. 2011;364:2016-25.
14. Polkowska A, Rinta-Kokko H, Toropainen M, Palmu AA, Nuorti JP. Long-term population effects of infant 10-valent pneumococcal conjugate vaccination on pneumococcal meningitis in Finland. Vaccine. 2021;39:3216-24.
15. Snaebjarnardóttir K, Erlendsdóttir H, Reynisson IK, et al. Bacterial meningitis in children in Iceland, 1975–2010: a nationwide epidemiological study. Scand J Infect Dis. 2013;45:819-24.
16. Peltola H, Kilpi T, Anttila M. Rapid disappearance of *Haemophilus influenzae* type b meningitis after routine childhood immunisation with conjugate vaccines. Lancet. 1992;340:592-4.
17. Ku LC, Boggess KA, Cohen-Wolkowiez M. Bacterial meningitis in infants. Clin Perinatol. 2015;42:29-45.
18. Nusman CM, Snoek L, van Leeuwen LM, et al. Group B streptococcus early-onset disease: new preventive and diagnostic tools to decrease the burden of antibiotic use. Antibiotics (Basel). 2023;12:489.
19. Deshmukh M, Patole S. Prophylactic probiotic supplementation for preterm neonates – a systematic review and meta-analysis of non-randomized studies. Adv Nutr. 2021;12:1411-23.
20. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2017;390:1770-80.
21. Yu JC, Khodadadi H, Malik A, et al. Innate immunity of neonates and infants. Front Immunol. 2018;9:1759.
22. Peltola H, Roine I, Kallio M, Pelkonen T. Unusual gram-negative bacteria cause more severe bacterial meningitis than the three classical agents in children. Acta Paediatr. 2022;111:1404-11.
23. Stevens JP, Lively A, Jerris R, Yildirim I, Lantis P. Recognition and outcomes of pneumococcal meningitis in 2 tertiary pediatric hospitals since the introduction of the 13-valent pneumococcal conjugate vaccine. Pediatr Emerg Care. 2022;38:e354-9.
24. Leber AL, Everhart K, Balada-Llasat J-M, et al. Multicenter evaluation of BioFire FilmArray meningitis/encephalitis panel for detection of bacteria, viruses, and yeast in cerebrospinal fluid specimens. J Clin Microbiol. 2016;54:2251-61.
25. Svendsen MB, Ring Kofoed I, Nielsen H, Schønheyder HC, Bodilsen J. Neurological sequelae remain frequent after bacterial meningitis in children. Acta Paediatr. 2020;109:361-7.
26. Baraff LJ, Lee SI, Schriger DL. Outcomes of bacterial meningitis in children: a meta-analysis. Pediatr Infect Dis J. 1993;12:389-94.
27. Ouchenir L, Renaud C, Khan S, et al. The epidemiology, management, and outcomes of bacterial meningitis in infants. Pediatrics. 2017;140:e20170476.
28. Jung YJ. Short information: bacterial meningitis in very low birthweight infants in Korea from 2013–2016. Pediatr Int. 2022;64:e15057.

29. Lovera D, Amarilla S, Araya S, et al. Risk factors for death and severe neurological sequelae in childhood bacterial meningitis. Pediatr Emerg Care. 2022;38:637-43.
30. Rugemalira E, Karppinen M, Savonius O, et al. Health-related quality of life after childhood bacterial meningitis. Pediatr Infect Dis J. 2021;40:987-92.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Niemelä S, Lempinen L, Löyttyniemi E, Grönroos JO, Luoto R, Peltola V, et al. Finnish paediatric study found a low incidence of bacterial meningitis from 2011 to 2018 but a substantial proportion of nosocomial meningitis. Acta Paediatr. 2023;00:1–9. https://doi.org/10.1111/apa.16991