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ORIGINAL RESEARCH

Main Clinical and Laboratory Features of Children with Bacterial Meningitis: Experience from a Tertiary Paediatric Centre in Central Vietnam

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Objective: Our study aimed to summarize symptoms and laboratory findings of bacterial meningitis at a Vietnam tertiary care hospital.

Methods: We performed a retrospective study and enrolled 33 children diagnosed with bacterial meningitis admitted at the Pediatric Center, Hue Central Hospital, between January 2019 and July 2021.

Results: Only 24.2% (8 out of 33) cases can determine etiology of bacterial meningitis. *Streptococcus pneumonia* was the most common pathogen. The mortality in this study was 12.1%. The most commn symptoms were fever (93.9%) and vomiting (60.6%). Loss of consciousness and poor appetite were predominant among patients who died (75%); seizures and local paralysis accounted for a half. For cerebrospinal fluid (CSF), the cloudy or turbid color was the most common in bacterial meningitis (54.5%), CSF leucocytes in a half of patients were greater than 500 cells/mm^3 (48.5%). CSF white blood cells count was higher among children who died.

Conclusion: *Streptococcus pneumonia* was the most common pathogen. Fever, vomiting, loss of consciousness, local paralysis, and increased leucocytes, neutrophils of CSF were more common in severe cases.

Keywords: bacterial meningitis, *S. pneumonia*, Vietnam, cerebrospinal fluid

Introduction

Meningitis is an infection of the membranes that surround the brain and spinal cord. It has been a major global challenge of public health.[1] In general, World Health Organization (WHO) indicated that the incidence of meningitis was approximately 700,000 cases for all ages in 2004.[2] Notably, 70% of these cases came from Africa and South-East Asia.[2] According to a systematic analysis for the Global Burden of Disease Study 2019 in Lancet, meningitis ranked sixth among the top causes of burden in children.[3] Bacterial meningitis (pyogenic meningitis) is a kind of meningitis that occurs because of a bacterial infection. It is one of the Central Nervous System infections most common in children.[4,5] Although most patients recover from pyogenic meningitis, it can lead to serious long-term sequelae and is life-threatening without treatment.[6,7] With the use of vaccines and antibiotics, the efficacy of therapy improves, but pyogenic meningitis is still a substantial cause of childhood morbidity and mortality in the world.[8,9] Currently, the diagnosis of pyogenic meningitis mainly depends on cerebrospinal fluid (CSF) analysis and culture because the clinical presentation is unspecified and various. Untreated or delayed treatment of bacterial meningitis can cause complications or become highly fatal. Hence, it is important to learn common manifestations and changes of the laboratory at local health care facilities to aid physicians in determining and taking a timely intervention. From 1995–2002, Haemophilus influenzae type b (Hib) was the most frequent etiology of bacterial meningitis in Vietnamese hospitalized children.[10,11] An estimation in 2002 showed the total Hib meningitis incidence went around 12/100.000 in children ≤ 5 years.[11] The

result of lastest study in Vietnam from 2007–2010 indicated that Hib remained most common pathogen among children.[11] Up to now, after 10 years, few updated information on epidemiology of bacterial meningitis was available. Therefore, our study aimed to summarize symptoms and laboratory findings of bacterial meningitis at a Vietnamese tertiary care hospital. This can improve the care and treatment of children with bacterial meningitis.

Methods

Study Design and Setting

A retrospective review was carried out from medical records with bacterial meningitis between January 2019 and July 2021 at the Pediatric Center, Hue Central Hospital, a tertiary hospital in Vietnam. This center was a leading pediatric-specialized facility playing a crucial role in providing child health care in a vast area of central Vietnam. The study was conducted from August to December 2021.

Eligible Population

We included medical records of all child patients aged 1 month to 15 years admitted at the Pediatric Center, Hue Central Hospital over a 2-years study period. In this study, a BM case was defined if they had at least one of the following inclusion criteria:[11–13] 1) appearance of bacteria in cerebrospinal fluid (CSF) by culture; 2) color of CSF with turbid or cloudy like pus; 3) laboratory results of CSF examination: leukocytes >100 cells/mm3, or leukocytes range from 10–100 cell/mm3 accompanied by the increase of protein (>1 g/l) or decrease of glucose (<2.22 mmol/l). Meningitis caused by different causes (virus, fungi, tuberculosis, parasite, etc.) was excluded. Anemia was diagnosed based on WHO guidelines.[14] The cerebrospinal fluid (CSF) culture with standard culture methods was performed to confirm appearance of bacteria. Positive cultures was identified using Optochin susceptibility with VITEK 2 automated microbial identification system (bioMérieux Inc., France). The CSF of all eligible patients was cultured. Because of unavailable real-time polymerase chain reaction (PCR) or Gram stain in the laboratory, the study only included culture method.

Data Collection

At first, a list of patients with meningitis was preliminarily involved by ICD code (G00) from the hospital's electronic database, then a storage unique identifier of paper medical records were collected.[15] Secondly, paper medical records were identified and screened according to the case definition. For eligible one, study data were collected through a standardized form developed by a senior investigator in the assistant of senior pediatrists. Then, data were engaged in information processed using Microsoft Office Excel 2019. Two independent researchers were chosen to extract items from paper medical records to a standardized form. The discussion was undertaken to solve any discrepancies between these two by the senior researchers. We manually collected demographic characteristics, clinical features, and laboratory findings. The clinical data comprised: sex, age, symptoms at admission (chief complaint) and during admission (symptoms), and sequelae. Information regarding the laboratory of blood and CSF was evaluated as well. For alive patients, the sequelae were recorded at moment when the patient discharged.

Statistical Analysis

This study used descriptive statistics as counts and percentages (%) for categorical variables or median and interquartile range (IQR) for continuous variables. Pearson's Chi-squared test or Fisher's exact test (if existing the expected cell counts with less than 5) was applied for categorical variables. Differences among values of continuous variables were determined using Student's *t*-test or Mann–Whitney *U*-test. A significance level of 0.05 was used for all statistical tests. Statistical analysis was performed using R Statistical Program version 4.0.4.

Results

During two years, there were 43 patients with diagnosis of bacterial meningitis, only 33 eligible cases were included. We classified participants into two groups: alive and dead. Table 1 describes the demographic features of participants. Most cases of bacterial meningitis occurred in male children, (60.6%), aged 1–5 years (60.6%), rural areas (72.7%). The

Table 1 The Demographic Characteristic of Study Participants

Variables	Total (n=33)	Outcome		P value
		Alive (n=29)	Death (n=4)	
Age group				>0.05
<1	3 (9.1%)	2 (6.9%)	1 (25%)	
1–5	20 (60.6%)	17 (58.6%)	3 (75%)	
>5	10 (30.3%)	10 (34.5%)	0 (0%)	
Gender				>0.05
Female	13 (39.4%)	12 (41.4%)	1 (25%)	
Male	20 (60.6%)	17 (58.6%)	3 (75%)	
Location				>0.05
Rural	24 (72.7%)	22 (75.9%)	2 (50%)	
Urban	9 (27.3%)	7 (24.1%)	2 (50%)	
Chief complaint at admission				
Headache	8 (24.2%)	7 (24.1%)	1 (25%)	>0.05
Fever	26 (78.8%)	23 (79.3%)	3 (75%)	>0.05
Vomit	13 (39.4%)	11 (37.9%)	2 (50%)	>0.05
Seizures	12 (36.4%)	11 (37.9%)	1 (25%)	>0.05
Symptoms during admission				
Fever	31 (93.9%)	27 (93.1%)	4 (100%)	>0.05
Headache	10 (30.3%)	9 (31%)	1 (25%)	>0.05
Vomit	20 (60.6%)	18 (62.1%)	2 (50%)	>0.05
Large fontanelle	7 (21.2%)	6 (20.7%)	1 (25%)	>0.05
Neck stiffness	14 (42.4%)	12 (41.4%)	2 (50%)	>0.05
Loss of consciousness	5 (15.2%)	3 (10.3%)	2 (50%)	<0.05
Diarrhea	7 (21.2%)	5 (17.2%)	2 (50%)	>0.05
Constipation	5 (15.2%)	5 (17.2%)	0 (0%)	>0.05
Poor appetite	16 (48.5%)	13 (44.8%)	3 (75%)	>0.05
Seizures	14 (42.4%)	12 (41.4%)	2 (50%)	>0.05
Local paralysis	5 (15.2%)	3 (10.3%)	2 (50%)	<0.05
Bacterial confirmation	8 (24.2%)	7 (24.1%)	1 (25%)	>0.05
Streptococcus pneumonia	6 (75%)	5 (17.2%)	1 (100%)	
Escherichia coli	1 (12.5%)	1 (100%)	0 (0%)	
Pseudomonas aeruginosa	1 (12.5%)	1 (100%)	0 (0%)	
Duration of admission*	18 (13–25)	18 (14–25)	11 (9.8–17.8)	>0.05
<7 days	1 (3%)	1 (3.5%)	0 (0%)	
7–14 days	11 (33.3%)	8 (27.6%)	3 (75%)	
>14 days	21 (63.6%)	20 (69%)	1 (25%)	
Sequelae (n=31)	4 (12.9%)	4 (13.8%)	-	

Note: *Data are median (IQR).

mortality was 12.1% (4 of 33). Notably only 24.2% (8 out of 33) cases could find etiologic agent of bacterial meningitis. There were 6 cases with *Streptococcus pneumonia* which was the most common pathogen. Others were *Escherichia coli* and *Pseudomonas aeruginosa*. Among children who died, only 1 case was confirmed organism with *Streptococcus pneumonia*.

At admission, fever, vomit, and seizures were common chief complaints with the percentage of 78.8%, 39.4%, and 36.4%, respectively. Vomit occurred in half of the deceased patients. The most popular symptoms during admission included fever (93.9%) and vomiting (60.6%). Poor appetite, seizures, and neck stiffness accounted for about 45 to 50%. Half of the patients in the death group got diarrhea, while no one had constipation. Loss of consciousness and poor appetite were predominant among deceased patients (75%); seizures and local paralysis accounted for a half. On the

contrary, those symptoms were unpopular among alive patients. There was an association between the loss of consciousness, local paralysis, and survival status. Four patients developed sequelae. The treatment course of deceased patients was shorter than that of alive patients, but it was not significant. Children with meningitis were often admitted greater than 2 weeks with 63.6%. Patients usually died within 7–14 days.

Laboratory findings are presented in Table 2. For CSF, the result showed that the cloudy or turbid color was the most common, followed by yellow. CSF leucocytes in a half of patients were greater than 500 cells/mm³ (48.5%). All deceased patients had leucocytes > 500 cells/ mm3. White blood cells (WBC) neutrophil (NEU) in CSF of the death group were higher than its alive group, and the difference was statistically significant. Only 10 cases (30%) decreased CSF glucose while CSF protein increased in most patients (97%). The protein and glucose level in CSF among deceased cases was higher than alive cases, but it was not significant. Nearly 2 of 3 children with meningitis had decreased WBC,

Table 2 Laboratory Findings of Blood and Cerebrospinal Fluid (CSF)

Variables	Total (N=33)	Outcome		P value
		Alive (n=29)	Death (n=4)	
Blood				
WBC (10⁹/L)*	15.3 (9.4–19.4)	15.3 (9.4–19.4)	17.8 (12.8–22.6)	>0.05
Increase (>12 × 10⁹/ L)	6 (18.2%)	6 (20.7%)	0 (0%)	
Decrease (<8 × 10⁹/ L)	20 (60.6%)	17 (58.6%)	3 (75%)	
NEU (10⁹/L)*	9.2 (5.7–13)	9.2 (5.4–13)	9.4 (7.9–12.5)	>0.05
Increase (>70%)	16 (48.5%)	15 (51.7%)	1 (25%)	
Platelet (10⁹/L)*	298 (218–392)	298 (205–392)	338.5 (282.8–449.2)	>0.05
Increase (>300 × 10⁹/ L)	16 (48.5%)	14 (48.3%)	2 (50%)	
Decrease (<150 × 10⁹/ L)	3 (9.1%)	3 (10.3%)	0 (0%)	
CRP (mg/L)*	56.5 (10–169.4)	57 (11.2–176.7)	7 (2.8–38.6)	>0.05
Increase (>10 mg/ L)	24 (72.7%)	22 (75.9%)	2 (50%)	
Glucose (mmol/L)*	5.3 (4.2–6.6)	5.3 (4.2–6.6)	5.2 (4.1–8.3)	>0.05
Increase (> 7.5 mmol/L)	5 (15.2%)	4 (13.8%)	1 (25%)	
Na+ (mmol/L)*	130 (129–134)	130 (129–134)	128 (125–131.7)	>0.05
Decrease (<135 mmol/L)	26 (78.8%)	22 (75.9%)	4 (100%)	
K+ (mmol/L)*	3.8 (3.6–4.2)	3.8 (3.6–4.2)	3.8 (3.7–3.8)	>0.05
Increase (>5 mmol/L)	1 (3%)	1 (3.5%)	0 (0%)	
Decrease (<3.5 mmol/L)	5 (15.2%)	5 (17.2%)	0 (0%)	
Cl-(mmol/L)*	98 (94–101)	98 (94–101)	97.5 (94–100.1)	>0.05
Increase (>105 mmol/L)	0	0	0	
Decrease (<95 mmol/L)	10 (30.3%)	9 (31%)	1 (25%)	
Cerebrospinal fluid				
Color				>0.05
Cloudy	18 (54.5%)	13 (44.9%)	3 (75%)	
Yellow	7 (21.2%)	6 (20.7%)	1 (25%)	
Pink	2 (6.1%)	4 (13.8%)	0 (0%)	
Transparent	6 (18.2%)	6 (20.7%)	0 (0%)	
WBC (cells/mm³)*	480 (154–1750)	450 (135–1130)	2170 (1610–2800)	<0.05
5–100	6 (18.2%)	6 (20.7%)	0 (0%)	
100–500	11 (33.3%)	11 (37.9%)	0 (0%)	
>500	16 (48.5%)	12 (41.4%)	4 (100%)	
NEU (cells/mm³)*	198 (59.5–744)	164.5 (59.5–744)	466 (166.5–1062)	<0.05
Glucose (mmol/L)*	2.6 (1.7–3.7)	2.6 (1.5–3.7)	4.6 (2.7–7.6)	>0.05
Decrease (<2.2 mmol/L)	10 (30.3%)	10 (34.5%)	0 (0%)	
Protein (g/L)*	1.5 (0.8–3.5)	1.5 (0.9–3.4)	3 (0.7–6)	>0.05
Increase (≥ 0.45 g/L)	32 (97.0%)	28 (96.6%)	4 (100%)	

Note: *Data are median (IQR).
Abbreviations: WBC, white blood cells; NEU, neutrophils; CRP, C-reactive protein.

and a half had increased NEU. No cases with decreased NEU were recorded. The prevalence of anemia took account around 1 of 3. More than 70% of patients elevated CRP, only 15% showed increased blood glucose. Approximately 80% had a low level of sodium, around 30% had a low concentration of chloride, and an abnormal of potassium was unpopular.

Discussion

The study describes clinical and laboratory features of bacterial meningitis in a Vietnam tertiary care hospital. Until now, bacterial meningitis has been a significant cause of childhood morbidity and mortality worldwide, especially in low- and middle-income countries. During 2019–2021, our study detected 33 cases with pyogenic meningitis. *Streptococcus pneumonia* was the most common pathogen in children, similar to the previous report in 1998–2007 at USA, and Netherland.[16,17] But it was different to reports at Vietnam in 1995–1996 and in 1998–2010 when Haemophilus influenzae type b (Hib) was the most frequent cause.[10,11,18] Our study showed the etiology of bacterial meningitis in Vietnamese children might vary. It was likely to derive from Hib conjugate vaccine which has just been introduced to the Vietnamese National Expanded Program on Immunization (NEPI) in 2010. The situation was similar to developed countries approaching early introduction of Hib conjugate vaccine.[17,19] Until now, childhood pneumococcal vaccinations are not routine in Vietnam, so it was considered that pneumococcal vaccinations should be included national or local program on immunization to against *Streptococcus pneumonia*. The mortality rate was similar to the average rate of the world,[20] but it was higher than reports from Kosovo or South Korea.[21,22] The reason could be a difference in economy and care service among countries. The incidence of bacterial meningitis in the rural regions was higher than that in the urban regions. There have been inconsistent to previous reports of incidence of bacterial meningitis.[23–25] For Vietnamese context, it would be reasonable to consider the impact of various risk factors to this difference: low socioeconomic status, education level, overcrowding, smoking, social gathering, and healthcare.[26,27] The microbial confirmation in CSF were uncommon, which presented the importance of empiric treatment in pyogenic meningitis as soon as possible, and the diagnosis must be comprehensively analyzed with support from laboratory tests.[28–30] The typical symptoms, including fever and vomit, were the same as the previous report in China.[5] This study had higher seizure incidence than another report in Iran, but was similar in Taiwan.[31,32] Among children who died, the main symptoms were vomit, diarrhea, poor appetite, loss of consciousness, seizures, and local paralysis. Those should be noticed in diagnosis and prognosis for children with pyogenic meningitis. Regarding the CSF examination, WBC, NEU, and elevated protein need to follow strictly because they were common in severe patients.

The limitation in our study included unavailable PCR (Polymerase Chain Reaction) testing and unavailable blood culture, limited time of study, and small sample size. Besides, the survey was conducted at a referral hospital in Vietnam so the findings might not generalize to other locations. The further study with larger sample and longer period is important to understand epidemiology of bacterial meningitis among children in Vietnam.

Conclusion

In our study, microbial evidence in children bacterial meningitis were uncommon. *Streptococcus pneumonia* was the most popular pathogen among children. Fever, vomiting were often symptoms. Loss of consciousness, local paralysis, and CSF WBC, CSF NEU were common for severe cases.

Ethical Consideration

The study was assessed and accepted by the Institutional Review Board of Hue Central Hospital in compliance with the Declaration of Helsinki. The personal information of patient (name, phone number, address) was not collected. Others data was anonymized and maintained with confidentiality.

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Disclosure

The authors report no conflicts of interest in this work.

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