Original Article

Acute Bacterial Meningitis at Nakhon Pathom Hospital: Clinical Characteristics and Predictors of Mortality

Sireethorn Nimitvilai MD[1], Sumet Banlengchit MD[1], Duangpol Srimanee MD[1], Saharat Jarupongprapa MD[1]

[1] Department of Internal Medicine, Nakhon Pathom Hospital, Nakhon Pathom, Thailand

Background: Acute bacterial meningitis [ABM] is a medical emergency associated with high morbidity and mortality.

Objective: To describe the clinical features, causative organisms, and predictors of death among patients presented with community-acquired ABM.

Materials and Methods: The present retrospective study was conducted at Nakhon Pathom Hospital, a 722-bed tertiary care hospital in Thailand between July 2013 and August 2017. The data on demography, clinical presentation, and outcome were collected. Factors associated with death were analyzed.

Results: During the study period, there were 55 patients. median age was 45 (range 19 to 89) years and 38 (69%) were male. Median duration of symptom before hospitalization were two days (range 1 to 6). The most common presenting symptoms were fever (98%), headache (94%), and decreased level of consciousness (75%). The classic triad of fever, headache, and neck stiffness was documented in 53%. Computed tomography scan of brain was abnormal among 57% of 35 patients. Bacteria was isolated in CSF or blood in 40 patients (73%). The most common isolates were *S. agalactiae* (17 cases), *S. pneumoniae* (4 cases), and *Streptococcus* group D (4 cases). All isolates of *S. agalactiae* and *S. pneumoniae* were penicillin sensitive. The in-hospital mortality was 20%. Factors associated with death were age more than 65 years (44% versus 13%, $p = 0.047$), low cerebrospinal fluid [CSF] white blood cell [WBC] (178 versus 439 cells/mm^3, $p = 0.009$), and the presence of hydrocephalus on imaging (67% versus 9%, $p = 0.045$). The time interval between patients' presentation and appropriate antibiotics administration differed significantly for patients who survived and died (22 versus 0.5 hour, $p = 0.016$).

Conclusion: ABM remains associated with high mortality. Age, CSF WBC, hydrocephalus, and delay antibiotics therapy were associated with outcome.

Keywords: Acute bacterial meningitis, Predictors of dead, Epidemiology

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Acute bacterial meningitis [ABM] is a life-threatening infection. Early recognition and appropriate therapy are associated with outcome[1]. Selection of antibiotics depends on the common pathogens in previous studies. *Streptococcus pneumoniae* and *Neisseria meningitidis* are the leading causes of bacterial meningitis in developed countries[2,3]. *S. suis* and *S. pneumoniae* are prominent in Vietnam[4]. However, the epidemiology of bacteria causing adult ABM in Thailand and their antimicrobial susceptibility pattern have been poorly studied[5,6]. The objective of the present study was to describe clinical manifestations, causative pathogens, and predictors of mortality among patients presented with community-acquired ABM.

Correspondence to:

Nimitvilai S. Department of Internal Medicine, Nakhon Pathom Hospital, Nakhon Pathom 73000, Thailand.
Phone: +66-34-254154, Fax: +66-34-340157
Email: sireethorn200@gmail.com

Materials and Methods

The present study was a retrospective descriptive design. All adult patients older than 15 years of age presented with community-acquired ABM at Nakhon Pathom Hospital, Nakhon Pathom, Thailand between July 1, 2013 and August 31, 2017 were enrolled. The diagnosis of community-acquired ABM was based on a compatible clinical picture (acute onset of fever, headache, neck stiffness, and/or impaired consciousness) plus one of the following 1) positive cerebrospinal fluid [CSF] culture, 2) positive blood culture, 3) positive CSF Gram stain and/or antigen test, or 4) CSF neutrophilic pleocytosis defined as white blood cell [WBC] more than 100 cells/mm^3 of which more than 50% were neutrophils with decreased glucose level, and increased protein concentration. Medical records of patients were retrospectively identified by extensively searching the disease codes based on the International Classification of Diseases-10

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[ICD-10] and all microbiological data. The data on demography, clinical manifestations, cranial imaging, CSF finding, microbiology, antimicrobial susceptibility testing, and outcomes were collected. Factors associated with death were analyzed.

The SPSS software version 17.0 was used for the statistical analyses. The continuous variables were compared using the Student's t-test and the Chi-square or Fisher's exact test were used to compare the categorical variables. All *p*-values were two-tailed with those of less than 0.05 were considered statistically significant.

Results

During the study period, there were 55 patients, 38 (69%) were male and 17 (31%) were female. The mean age was 47 (range 19 to 89) years. Age distribution were as follows, 21 patients (38%) 19 to 40 years old, 32 patients (58%) 40 to 80 years old, and 2 patients (4%) 81 to 89 years old. Twenty-two (40%) patients had underlying illnesses including hypertension (16%), diabetes mellitus (9%), HIV infection (7%), chronic alcoholic drinking (7%), liver cirrhosis, and malignancy (1% each).

The door-to-appropriate antibiotic time was available in 34 cases. The median was 16.5 hours (range 0 to 144). Door-to-appropriate antibiotic time was within one hour in 18 cases (53%), within six hours in three cases (9%), 6 to 24 hours in nine cases (26%), and more than 24 hours in four cases (12%).

Clinical presentations

Median duration of symptoms before hospitalization were two days (range 1 to 6). Most patients (90%) had onset of symptoms within three days prior to admission. Clinical manifestations included fever (98%), headache (94%), alteration of consciousness (75%), stiffness of neck (60%), nausea vomiting (48%), seizure (24%), and focal neurological deficit 13%). Half of patients (53%) presented with classic triad of fever, headache, and neck stiffness (Table 1).

Laboratory findings

Computed tomography scan of brain was abnormal among 57% of 35 patients. These included basal meningeal enhancement (43%), cerebral infarction (17%), and hydrocephalus (14%) (Table 2).

Lumbar puncture was performed on all patients. Twenty-six (76%) patients received antibiotics before lumbar puncture. The mean time from antibiotics prescribed to the procedure was 21 hours (range 0 to 144). Eighty-two percent of samples had more than 100 WBC/mm^3 (median 429, range 1 to 99,000 cells/mm^3). One-fourth of CSF showed a neutrophil predominance of more than 80% (median 53, range 0 to 98%). Median CSF protein and sugar were 198

Table 1. Clinical characteristics of patients (n = 55)

Variables	n (%)
Age (year), mean ± SD	47±18
Gender (male)	38 (69)
Underlying illnesses	22 (40)
Hypertension	9
Diabetes mellitus	5
HIV infection	4
Chronic alcoholic drinking	4
Liver cirrhosis	1
Malignancy	1
Duration of symptoms (days), median (range)	2 (1 to 6)
Symptoms and signs	
Fever	47/48 (98)
Headache	33/35 (94)
Alteration of consciousness	36/48 (75)
Neck stiffness	27/45 (60)
Nausea vomiting	22/46 (48)
Seizure	11/46 (24)
Focal neurological deficit	6/45 (13)
Triad	20/38 (53)

Table 2. Laboratory findings of patients

Variables	n (%)
CSF findings	
CSF WBC (cells/mm^3), median (range)	429 (1 to 99,000)
CSF PMN (%), median (range)	53 (0 to 98)
CSF protein (mg/dl), median (range)	198 (54 to 749)
CSF sugar (mg/dl), median (range)	40 (0 to 133)
CSF Gram stain	4/28 (14)
Positive culture	
CSF	17/55 (31)
Blood	28/55 (51)
Positive CSF culture	17/55 (31)
S. agalactiae	7/55 (13)
S. pneumoniae	2/55 (4)
Group D *Streptococcus*	2/55 (4)
S. suis	1/55 (2)
Other *Streptococcus*	4/55 (7)
Other bacteria	1/55 (2)
Positive blood culture	28/55 (51)
S. agalactiae	13/55 (24)
S. pneumoniae	3/55 (5)
Group D *Streptococcus*	2/55 (4)
Other *Streptococcus*	5/55 (9)
Other bacteria	5/55 (9)
Abnormal cranial imaging	20/35 (57)
Leptomeningeal enhancement	15/35 (43)
Hydrocephalus	5/35 (14)

CSF = cerebrospinal fluid; WBC = white blood cell; PMN = polymorphonuclear neutrophil

(range 54 to 749) mg/dl and 40 (range 0 to 133) mg/dl, respectively. Only four of 28 patients had positive CSF Gram stain. Latex agglutination was performed in 14 patients, the results were positive in two patients.

Bacteria were isolated in 40 patients (73%). Of these, the organism was isolated in CSF only in 12 patients, in blood only in 23 patients, and in both CSF and blood in five patients. The most common isolates were *S. agalactiae* (17 cases, 31%), *S. pneumoniae* (4 cases, 7%), and *Streptococcus* group D (4 cases, 7%) (Figure 1). Only one patient had *S. suis* meningitis. However, *N. meningitidis*, *Hemophilus influenzae*, and *Listeria monocytogenes* were not found in the present study. All isolates of *S. agalactiae* and *S. pneumoniae* were penicillin sensitive.

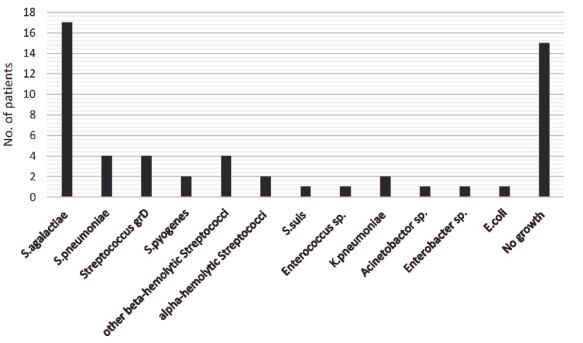

Figure 1. Causative pathogens of community-acquired ABM.

Mortality

Nine patients died, causing an overall mortality rate of 20%. Factors associated with death were elderly, low CSF WBC (178 versus 439 cells/mm^3, $p = 0.009$) and the presence of hydrocephalus (67% versus 9%, $p = 0.045$) (Table 3). The present study did not detect any statistically significant association between clinical presentations, CSF protein, and CSF sugar to risk of death.

Discussion

S. agalactiae is the leading etiologic agent of ABM in the present study. It accounts for about one-third of cases, which is similar to report from a recent study[7]. This organism is generally known to cause invasive disease in neonates and pregnant women. However, infection in adults has become frequently reported[8,9].

Surprisingly, *S. pneumoniae* was found in only 7% of cases. It is one of fastidious organisms that are difficult to isolate on culture[10]. Latex agglutination test [LAT] directly detect pneumococcal antigen and can be more valuable than culture among partially treated ABM cases, however, this test has been done in few cases.

The authors did not identify *N. meningitidis* and *L. monocytogenes*. Although they are common in Western countries, there are rare in Thailand[11,12].

Table 3. Factors associated with outcome

	Alive (n = 46)	Dead (n = 9)	*p*-value
Age more than 65 years, n (%)	6/46 (13)	4/9 (44)	0.047
Clinical presentation, n (%)			
Headache	28/30 (93)	5/5 (100)	0.66
Alteration of consciousness	29/40 (73)	7/8 (88)	0.23
Neck stiffness	24/37 (65)	3/8 (38)	0.4
Nausea vomiting	20/38 (53)	2/8 (25)	0.25
Seizure	8/38 (21)	3/8 (38)	0.24
Focal neurological deficit	4/38 (11)	2/7 (29)	0.23
Triad	17/30 (57)	3/8 (38)	0.37
Positive blood and/or CSF C/S, n (%)	31 (67)	9 (100)	0.05
Positive CSF C/S, n (%)	13 (28)	4 (44)	0.43
Positive blood C/S, n (%)	23 (50)	5 (56)	1
CSF findings, median (range)			
CSF WBC (cells/mm^3)	439 (25 to 8,617)	178 (1 to 99,000)	0.009
CSF PMN (%)	56 (2 to 98)	40 (0 to 86)	0.96
CSF protein (mg/dl)	215 (54 to 749)	133 (78 to 704)	0.63
CSF sugar (mg/dl)	40 (1 to 133)	48 (0 to 70)	0.52
Abnormal cranial imaging, n (%)	17/32 (53)	3/3 (100)	0.24
Leptomeningeal enhancement	13/32 (41)	2/3 (67)	0.57
Hydrocephalus	3/32 (9)	2/3 (67)	0.045
Time presentation to appropriate ATB (hour), median (range)	0.5 (0 to 144)	22 (0 to 120)	0.02

CSF = cerebrospinal fluid; WBC = white blood cell; PMN = polymorphonuclear neutrophil

The detection of bacterial pathogen from CSF culture in the present study was relatively low. Only 17 CSF sample had positive result. This could be explained by the fact that most patients (76%) received parenteral antibiotics prior to lumbar puncture.

The overall mortality of 20% was observed, which is similar to other studies[5,7]. A higher mortality was seen in elderly, those with low CSF WBC, and having hydrocephalus. Other studies described these associations[2,13,14]. Convulsion, low CSF glucose, and high CSF protein were associated with poor outcome in the previous reports[1,15]. However, the author did not find these association.

Timely and appropriate antimicrobial therapy is important for treatment of patients with severe infections. In the previous study, a delay of more than six hours in administration of antibiotics after admission cause a greater risk of death from meningitis[16]. Only 62% of patients received appropriate antibiotics within six hours. In-hospital mortality was 5% for patients receiving timely antibiotics within six hours, and 31% for patients receiving delayed antibiotics.

Conclusion

S. agalactiae is the common bacteria causing ABM in the present study. Age, CSF WBC, and presence of hydrocephalus were associated with poor outcome. Delayed in effective antibiotic therapy was common in the present study and associated with risk of death.

What is already known on this topic?

S. agalactiae is common whereas *N. meningitidis* and *L. monocytogenes* are rare among causative pathogens of community-acquired ABM in Thailand. Factors associated with mortality were elderly, low CSF WBC, presence of hydrocephalus, and delayed antibiotics therapy.

What this study adds?

There are a few studies of community-acquired ABM in Thailand. *S. suis* and *S. pneumoniae* are common in previous reports, however, uncommon in the present study. Knowing the causative organisms are useful to choose appropriate antimicrobial therapy for the patients.

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Potential conflicts of interest

The authors declare no conflict of interest.

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