



# Applying the bacterial meningitis score in children with cerebrospinal fluid pleocytosis: a single center's experience

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**Purpose:** The widespread introduction of bacterial conjugate vaccines has decreased the risk of cerebrospinal fluid (CSF) pleocytosis due to bacterial meningitis (BM) in children. However, most patients with CSF pleocytosis are hospitalized and treated with parenteral antibiotics for several days. The bacterial meningitis score (BMS) is a validated multivariate model derived from a pediatric population in the postconjugate vaccine era and has been evaluated in several studies. In the present study, we examined the usefulness of BMS in South Korean patients.

**Methods:** This study included 1,063 patients with CSF pleocytosis aged between 2 months and 18 years. The BMS was calculated for all patients, and the sensitivity and negative predictive value (NPV) of the test were evaluated.

**Results:** Of 1,063 patients, 1,059 (99.6%) had aseptic meningitis (AM). Only four patients (0.4%) had BM. The majority of patients (98%) had a BMS of  $\leq 1$ , indicating a diagnosis of AM. The BMS was 0 in 635 patients (60%) and 1 in 405 patients (38%). All four BM patients had a BMS of  $\geq 4$ .

**Conclusion:** To our knowledge, this is the first study to investigate the diagnostic strength of the BMS in South Korea. In our study, the BMS showed 100% sensitivity and 100% NPV. Therefore, we believe that the BMS is a good clinical prediction rule to identify children with CSF pleocytosis who are at a risk of BM.

**Key words:** Aseptic meningitis, Bacterial meningitis, Clinical prediction rule

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## Introduction

The majority of children with cerebrospinal fluid (CSF) pleocytosis are diagnosed with aseptic meningitis (AM)<sup>1,2</sup> and only ~50% are proven to be of bacterial origin<sup>1,3-5</sup>. There are effective vaccines against the three major bacterial pathogens responsible for bacterial meningitis (BM)<sup>2,6-8</sup>, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*<sup>9-13</sup>. The prevalence of BM has dramatically decreased in regions with high vaccination administration<sup>1,2,4-8,10-17</sup>.

Nevertheless, BM is still an important cause of morbidity and mortality in pediatric patients. In its initial stage, it is difficult to distinguish BM from AM, because the clinical presentations and laboratory results overlap. Additionally, it is difficult to understand or assess the clinical features that infants or children are actually experiencing.

Given the similar presentations between BM and AM, most pediatricians empirically treat with parenteral antibiotics for two to three days until negative culture results rule out BM<sup>4,18</sup>. In most cases, this means that patients are treated with antibiotics and are

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hospitalized unnecessarily. This overuse of medicine not only increases the risks of patients developing adverse effects to treatment and acquiring nosocomial infections, but also is wasteful in terms of medical cost. Unfortunately, there is not currently a single clinical symptom or laboratory finding that distinguishes BM from AM. Many researchers have investigated several clinical prediction rules (CPRs) to discriminate these two etiologies. The bacterial meningitis score (BMS)<sup>1,5)</sup>, introduced by Nigrovic et al.<sup>1)</sup>, is the first validated model that was derived from a pediatric population in the postconjugate vaccination era and has been applied to the largest number of pediatric patients worldwide<sup>1,3,4,19-23)</sup>. A meta-analysis was also carried out in 2012<sup>5)</sup>. The BMS has been used as a guide in the Emergency Department to help exclude BM. The purpose of this study was to explore the usefulness of BMS in South Korean patients, and to introduce BMS as a CPR.

## Materials and methods

### 1. Patients

A total of 1,363 patients who received a diagnosis including the term 'meningitis' or 'encephalitis' between the ages of two months and 18 years from January 2006 to December 2012 at Severance Hospital, Seoul, South Korea were included in this study. Three hundred patients were excluded with regard to the following criteria: CSF pleocytosis with cell count <10 cells/mm<sup>3</sup> (n=143), CSF red blood cell (RBC) count of ≥10,000 cells/mm<sup>3</sup> (n=44), a diagnosis that was more likely encephalitis than meningitis (n=42), positive CSF culture results with suspicion of contamination (n=8), critical illness or immunosuppressed patients (n=7), central nervous system (CNS) device or recent neurosurgery (n=8), presence of other bacterial infections (n=48). A total of 1,063 patients were ultimately included.

### 2. Definition

'Meningitis' was defined either as CSF pleocytosis (CSF WBC ≥10 cells/mm<sup>3</sup>) or as a positive CSF culture. Patients were defined as having BM if the CSF culture was positive for a bacterial pathogen or if patients had CSF pleocytosis with a positive CSF latex agglutination test for *S. pneumoniae*, *Neisseria meningitidis*, *H. influenzae* type b, or group B streptococcus. Patients were categorized as having AM if both the CSF culture and the CSF latex agglutination test were negative.

### 3. Bacterial meningitis score

The variables in the BMS include a positive CSF Gram stain, CSF absolute neutrophil count (ANC) ≥1,000 cells/mm<sup>3</sup>, CSF protein ≥80 mg/dL, peripheral blood ANC ≥10,000 cells/mm<sup>3</sup>, and a history of seizure with the illness. A positive CSF Gram stain

**Table 1.** Bacterial meningitis score (BMS)<sup>1)</sup>

BMS predictor	Criteria
CSF Gram stain (2 points)	Positive result
CSF ANC	≥1,000 cells/mm <sup>3</sup>
CSF protein	≥80 mg/dL
Peripheral blood ANC	≥10,000 cells/mm <sup>3</sup>
Seizure	Onset at or before presentation

CSF, cerebrospinal fluid; ANC, absolute neutrophil count.

corresponds to 2 points and the other criteria correspond to 1 point each; therefore, the BMS ranges from 0 to 6 points (Table 1). Children who scored 0 were classified as having 'very low risk' and those with a score above 0 were classified as 'not low risk' for BM.

### 4. Exclusion criteria

This study excluded patients who had CSF pleocytosis WBC <10 cells/mm<sup>3</sup>, CSF RBC of ≥10,000 cells/mm<sup>3</sup>, a diagnosis that was more likely encephalitis than was meningitis, positive CSF culture results with signs of contamination (e.g., *Staphylococcus epidermidis*), critical illness or immunosuppression (intensive care unit care status, altered mental status, clinical sepsis, or chemotherapy), CNS device or recent neurosurgery, and other bacterial infections.

### 5. Statistical methods

Statistical analyses were performed with the IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA). Group differences and associations between categorical variables were assessed using nonparametric statistical tests such as the Mann-Whitney *U* test and Fisher exact test, as appropriated. Bayes' Theorem was used to calculate positive predictive value and negative predictive value (NPV).

## Results

### 1. Characteristics of patients

A total of 1,063 children were investigated. There was no mortality. The clinical features are shown in Table 2. The mean patient age was 5.9±3.7 years and 669 patients (63%) were male. The mean hospital stay was 4.4±4.1 days (with a maximum of 77 days). Only 12 patients (1%) had a history of seizure associated with the illness. Four children (0.4%) were diagnosed with BM due to *S. pneumoniae* (two patients), or *H. influenzae* (two patients).

BM and AM groups are compared in Table 2. The median hospital stay of BM patients was 47 days and that of AM was 4 days. Most AM patients (82%) were admitted during the

**Table 2.** Demographic data and laboratory findings (n=1,063)

Characteristic	Bacterial meningitis (n=4)	Aseptic meningitis (n=1,059)	P value
Age (yr)	0.9 (0.5–11.7)	5.3 (3.8–7.7)	0.243
Presentation during enteroviral season*, n (%)	4 (100)	873 (82.4)	0.410
Peripheral blood WBC count (cells/mm <sup>3</sup> )	17,680.0 (8,782.5–23,307.5)	11,570.0 (9,070.0–14,520.0)	0.165
Peripheral blood ANC (cells/mm <sup>3</sup> )	12,145.0 (5,762.5–16,090.0)	8,340.0 (5,620.0–11,570.0)	0.255
CSF WBC (cells/mm <sup>3</sup> )	8,306.0 (790.5–17,687.5)	100.0 (40.0–243.0)	0.001
CSF ANC (cells/mm <sup>3</sup> )	7,889.3 (714.0–17,401.9)	19.7 (4.0–69.0)	0.001
CSF glucose (mg/dL)	8.0 (0.0–43.75)	66.0 (60.0–72.0)	0.001
CSF protein (mg/dL)	329.0 (237.3–605.3)	29.0 (21.0–41.0)	0.001
Positive CSF Gram stain, n (%)	4 (100)	0 (0)	<0.001
Hospitalized period (day)	47.0 (19.0–75.0)	4.0 (3.0–5.0)	<0.001

Values are presented as median (interquartile range [25%–75%]) unless otherwise indicated.

P value, by Mann-Whitney U test and Fisher exact test.

\*Enteroviral season, from June 1 to October 31

WBC, white blood cell; ANC, absolute neutrophil count; CSF, cerebrospinal fluid.

**Table 3.** Characteristics of the four bacterial meningitis patients

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4
BMS	6	6	6	4
Bacterial pathogen	<i>H. influenzae</i>	<i>H. influenzae</i>	<i>S. pneumoniae</i>	<i>S. pneumoniae</i>
CSF Gram stain	Gram-negative bacilli	Gram-negative bacilli	Gram-positive cocci in pairs	Gram-positive cocci in pairs
Seizure	Yes	Yes	Yes	Yes
Peripheral blood WBC count (cells/mm <sup>3</sup> )	20,750	24,160	14,610	6,840
Peripheral blood ANC (cells/mm <sup>3</sup> )	17,350	11,980	12,310	3,690
CSF WBC (cells/mm <sup>3</sup> )	14,500	2,112	18,750	350
CSF ANC (cells/mm <sup>3</sup> )	13,920	1,859	18,562	333
CSF protein (mg/dL)	213	348	691	310
CSF glucose (mg/dL)	0	99	0	16
C-reactive protein (mg/L)*	232.6	243.1	60.2	307.6
Hospitalized period (day)	17	25	69	77

BMS, bacterial meningitis score; *H. influenzae*, *Haemophilus influenzae*; *S. pneumoniae*, *Streptococcus pneumoniae*; CSF, cerebrospinal fluid; WBC, white blood cell; ANC, absolute neutrophil count.

\*Normal range of C-reactive protein: 0-8 mg/L.

enteroviral season, which lasts from June 1 to October 31. There were significant differences in CSF WBC, ANC, glucose, and protein between the two groups. Only four patients had a positive CSF Gram stain, and these patients were proven to have BM. The clinical features of the four BM patients are shown in Table 3. These patients not only had high BMS scores, but also had histories of seizure with the illness.

## 2. Performance of the BMS

The BMS of all patients are analyzed in Table 4. Scores included a BMS of 0 in 635 patients, and a BMS of 1 in 405. Thus, 98% of the patients scored 1 point or lower and were diagnosed with AM. Twenty-three patients (2%) scored 2 points or higher with BMS, and had risk of BM. Among the BM patients, one patient scored 4 points, while the three others had a BMS of 6.

We found that all four BM patients in our study had a BMS >0, suggesting that 'BMS >0' distinguishes BM from AM with 100% sensitivity. The patients who had a BMS of 0 were all diagnosed with AM. Thus, the NPV of BMS of 0 to predict AM is also 100% (635 out of 635 patients).

## Discussion

The BMS is clinically applicable and readily available for distinguishing AM from BM when a patient first presents. Most methods of distinguishing AM from BM which include CSF lactate, serum procalcitonin or CSF polymerase chain reaction for enteroviruses are disadvantageous of low sensitivity and NPV<sup>24-33</sup>. Similar to previous studies, we found that ~90% of patients

**Table 4.** Analysis of bacterial meningitis score

BMS	No. of patients (%)	Details
0	635 (59.7)	
1	405 (38.1)	PB ANC, 354 patients; CSF protein, 42 patients Seizure, 7 patients; CSF ANC, 2 patients
2	17 (1.6)	PB ANC + CSF ANC: 9 patients PB ANC + CSF protein: 7 patients PB ANC + seizure: 1 patient
3	2 (0.2)	PB ANC + CSF ANC + CSF protein
4	1 (0.1)	CSF protein + CSF Gram stain + seizure
6	3 (0.3)	All predictors are satisfied
Total	1,063 (100)	

BMS, bacterial meningitis score; PB, peripheral blood; ANC, absolute neutrophil count; CSF, cerebrospinal fluid.

with CSF pleocytosis are admitted to the hospital for parenteral antibiotic treatment for several days<sup>1,3,4,19-23</sup>. Most of these admissions are unnecessary.

In the first study on 1,063 South Korean patients, we found that BMS has 100% sensitivity and 100% NPV in ruling out BM. There was no misdiagnosis of BM as AM. Therefore, BMS is expected to be a good CPR. However, it should be used as an adjunct to one's clinical reasoning, not purely as a clinical decision making tool. The BMS should not be applied to ill-appearing children, infants younger than two months of age (who have increased risk of BM and/or invasive bacterial infections), and patients whose clinical features are suggestive of other forms of CNS infection (such as herpes simplex virus, tuberculous meningitis, or viral encephalitis)<sup>1,4</sup>. Therefore BMS as a CPR should be used in concert with careful clinical assessment of the patient.

As seen in Table 4, twenty-three patients (2%) were scored 2 points or higher with BMS, and had risk of BM. One point was given for an increased peripheral blood ANC. Thus it is hard to tell increased peripheral blood ANC contribute to discriminating BM as criteria of BMS in this study.

Out of 1,063 patients, 99.6% of patients had AM and 0.4% had BM. There are several possible explanations for the much lower rate of BM as compared to AM in this study. The rate of conjugate vaccination in South Korea is higher than it was previously. Vaccinations against *S. pneumoniae* and *H. influenzae* had increased from 40% to 74% and from 82% to 88% between 2005 and 2010, respectively<sup>34</sup>. Thus, in the era of widespread conjugate vaccines, the incidence of BM is expected to decrease. Another reason for the lower rate of BM is the possibility that patients had taken oral antibiotics before lumbar puncture<sup>35</sup>. The laboratory findings and markers of CNS inflammation in BM patients were consistently different from those of AM patients. However, given that there were only four patients with BM, this study cannot fully represent

all of the clinical features and laboratory findings in BM.

We found that the BMS performs with a high degree of diagnostic accuracy. Pediatricians can therefore use the BMS to discriminate AM from BM when patients present with suggestive features of meningitis. Multicenter studies are needed to further validate the effectiveness of the BMS.

## Conflict of interest

No potential conflict of interest relevant to this article was reported.

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