Clinical Feature & Outcome in Adults with Acute Bacterial Meningitis: A 2 Year Retrospective Study in Sunpasitthiprasong Hospital

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Background: Acute bacterial meningitis is one of the neurological emergency condition, which caused high morbidity and mortality rate if not appropriately treated. Its clinical features include acute onset of headache, fever, nuchal rigidity, impaired mental status. However, only half of the cases present with classic triad of fever, nuchal rigidity and impaired mental status. The clinical features, laboratory features, outcome of acute bacterial meningitis are never studied in Sunpasitthiprasong Hospital. The objective of this study is to describe clinical features, laboratory features, outcome of acute bacterial meningitis patients admitted in our hospital and to study factors, which related to the outcome.

Methods : Medical records of acute bacterial meningitis patients who admitted during January 2013 to December 2014 were searched according to ICD-10 in Sunpasitthiprasong hospital electronic database. We included all patients who are aged more than 15 years-old, diagnosed with acute bacterial meningitis. Demographic data, clinical features, underlying diseases, imaging studies, cerebrospinal fluid study and microbiology profile, blood culture, plasma glucose, complications and outcome of patients at discharge were collected. Data were analyzed by using Med-Calc version 16.2 and SPSS version 23.0.

Results : 123 patients were diagnosed acute bacterial meningitis. 83 patients were male (67.5%) and ratio of male and female

was 2.08. Mean age of studied patient was 50.98±18.62 years old. About 66.7% (82 patients) presented with headache. 56.9 % (70 patients) presented with fever. 65.9 % (81 patients) presented with nuchal rigidity. In addition, 51.2% (63 patients) presented with impaired mental status. However, only 12.2% (15 patients) present with all four of above symptoms. According to brain imaging data, only 10.6 % (13 patients) has abnormalities specific with meningitis. CSF analysis was done in 119 patients (96.7%). Increase opening pressure (>20) was found 42.9 % (51 patients). Elevated CSF white blood cell count was observed in 68.9 % (82 patients), with neutrophil predominated in 48 patients (40.3 %). Elevated CSF protein was observed in almost all patients (92.4 %, 110 patients). Low CSF/plasma glucose ratio was observed in 80 patients (67.2 %). CSF culture was positive in 9 patients (7.6 %). Poor outcome, determined by not improve at discharge and death, in this study is 17.9% (22 patients). Almost all of our patients had recovery from the disease (82.1%). Only 10 patients were death in hospital (8.1%). Residual neurological deficit was found in 23 patients (18.7%). Factors predicted poor outcome are elderly age (defined as age >65 years old) OR 7.14 (95% CI 2.63 to 19.34) p=0.001, altered mental status as presenting symptom OR 4.5 (95% CI 1.44 to 14.66) p=0.01 and neutrophil more than 80% in CSF white blood cell OR 6.65 (95% CI 1.33 to 33.24) p=0.02. However, prior antibiotic administration was not significant for good or poor prognostic factor.

Conclusion: Majority of acute bacterial meningitis patients in our study presented with at least two of major symptoms. Factors predicted poor clinical outcome included elderly, impaired mental status and more than 80% of neutrophil in CSF white blood cell.

Keyword: Bacterial meningitis, clinical features, laboratory features, outcome, Sunpasitthiprasong hospital

Background:

Acute bacterial meningitis is inflammation of meninges caused by bacteria, developing within hours to days.[1,2] It is a medical emergency condition characterized by headache, fever, neck stiffness and alteration of mental status. Only 44 percent of cases were characterized by the classic triad of fever, neck stiffness, and impaired mental status.[3] It causes significant morbidity

and mortality if left untreated or improper treated.[4-6] Incidence in western countries between 2006 to 2007 is 1.38/100,000 people/year and case-fatality rate is 14.3%[7] There are few studies of acute bacterial meningitis in Thailand. However, clinical features, laboratory features, outcome of acute bacterial meningitis are never studied in Sunpasitthiprasong Hospital. The objective of this study is to determine clinical features, laboratory features, outcome of acute bacterial meningitis patients admitted in our hospital and to study factors that related to the outcome.

Methods :

Medical records of acute bacterial meningitis patients who admitted during January 2013 to December 2014 were searched according to ICD-10 in Sunpasitthiprasong hospital electronic database. We included all patients who are aged more than 15 years-old, and diagnosed with acute bacterial meningitis. Demographic data, clinical features (headache, fever, neck stiffness and alteration of mental status), underlying diseases including altered immune status, imaging studies, cerebrospinal fluid (CSF) study and microbiology profile, blood culture, plasma glu-

cose, complications and outcome of patients at discharge were collected. Patients aged more than 65 years old were classified as elderly. Patients with immunosuppressive therapy, diabetes mellitus and HIV infection were classified as immunocompromised host.[7]

Imaging studies include brain computed tomography (CT) and chest radiograph. Abnormalities specific to bacterial meningitis in CT scan of brain include hydrocephalus, cerebral edema, meningeal enhancement, cerebral infarction, subdural effusion, lesions consistent with septic emboli, venous sinus thrombosis and subdural empyema.[5] Abnormalities of chest radiograph were lesion that consistent with bacterial pneumonia. Abnormalities of CSF studies includes cell number and differential count, glucose, protein, gram stain, culture for bacterial, and counter immunoelectrophoresis (CIE). Data of prior antibiotics use were also collected.

Neurological complications and discharge outcome were recorded. Chi-square tests were used to compare categorical outcomes. Odds ratios and 95 percent confidence intervals were used to predict association between clinical parameter and unfavorable outcome. Data were analyzed

by using MedCalc version 16.2 and SPSS version 23.0.

Results :

123 patients were diagnosed acute bacterial meningitis. 83 patients were male (67.5%) and ratio of male and female was 2.08. Mean age of studied patients was 50.98±18.62 years old (range 16-87 years old). Demographic and clinical data were summarized in Table 1.

Table 1 Demographic and clinical data of acute bacterial meningitis patients

	Number of case (N=123)	Percentage
Gender		
Male	83	67.5
Female	40	32.**5**
Age (years)		
>65	30	24.4
<65	93	75.6
Predisposing conditions		
None	76	61.8
Diabetes mellitus	13	10.6
HIV infection	2	1.6
Immunosuppressive therapy	4	3.3
Others	28	22.8

Our study found that about 66.7 % (82 patients) presented with headache. 56.9 % (70 patients) presented with fever. 65.9 % (81 patients) presented with nuchal rigidity. Moreover, 51.2% (63 patients) presented with impaired mental status. 86.2% (106 patients) presented with at least 2 of the above symptoms. However, only 12.2% (15 patients) present with all of the above symptoms. Presenting symptoms of acute bacterial meningitis are presented in Table 2.

Table 2 Presenting symptoms of acute bacterial meningitis patients

	Number of case (N=123)	Percentage
Headache		
Yes	82	66.7
No	41	33.3
Fever		
Yes	70	56.9
No	53	43.1
Stiff neck		
Yes	81	65.9
No	42	34.1
Altered mental status		
Yes	63	51.2
No	60	48.8
At least 2 of above symptoms		
Yes	106	106
No	17	17
All above 4 symptoms		
Yes	15	12.2
No	108	87.8

According to brain imaging data, only 10.6 % (13 patients) had abnormalities specific with meningitis. 6 patients (4.9%) had hydrocephalus. 2 patients (1.6%) had leptomeningeal enhancement. 1 patient (0.8%) had subdural collection. 2 patients (1.6%) had brain edema and 2 patients (1.6%) had ring-enhanced lesion. Normal CT scan were 84 patients (68.3 %). Missing data of CT Brain were 21.1 % (26 patients) Abnormalities of chest radiograph included lesion consistent with bacterial pneumonia 0.8% (1 patient). Others non-specific abnormalities such as pulmonary congestion, cardiomegaly, emphysematous lung 18.7% (23 patients). Normal chest radiograph were

43.1% (53 patients). Missing data of chest radiograph were 37.4% (46 patients). CT scan and chest radiograph features of acute bacterial meningitis are shown in Table 3 and Table 4 respectively.

Table 3 CT brain finding of acute bacterial meningitis patients

	Number of case (N=123)	Percentage
Lesion specific with bacterial meningitis (total)	13	10.6
• Hydrocephalus	6	4.9
• Leptomeningeal enhancement	2	1.63
• Subdural collection	1	0.8
• Brain edema	2	1.63
• Ring-enhanced lesion	2	1.63
Non-specific abnormality finding	0	0
Normal CT findings	84	68.3
Not done	26	21.1

Table 4 Chest radiograph features of acute bacterial meningitis

	Number of case (N=123)	Percentage
Pneumonia	1	0.8
Non-specific abnormality finding	23	18.7
Normal chest finding	53	43.1
Not done	46	37.4

CSF was obtained in (96.7%) 119 patients. Four patients (3.3%) failed to do lumbar puncture. Increase opening pressure (>20) was found 42.9% (51 patients). Elevated CSF white blood cell count was observed in 68.9% (82 patients), with neutrophil predominated in 48 patients (40.3%). Elevated CSF protein was observed in almost

all patients (92.4%, 110 patients). Low CSF/ plasma glucose ratio was observed in 80 patients (67.2%). CSF culture was positive in 9 of 119 patients (7.3%). Among 4 of 9 positive CSF culture were identified as Streptococcus group B. The others 5 of 9 were identified Streptococcus pneumoniae, Streptococcus group D, Streptococcus spp., Klebsiella pneumoniae, and Staphylococcus coagulase negative respectively. CSF features of acute bacterial meningitis are shown in Table 5 and Table 6 respectively.

Table 5 CSF features of acute bacterial meningitis patients

	Number of case (N=119)	Percentage
Open pressure (mmH$_2$O)		
• ≤20	68	57.1
• >20-40	46	38.7
• >40	5	4.2
WBC count (cell/ml)		
• ≤100	37	31.1
• >100-1000	57	47.9
• >1000-5000	17	14.3
• >5000	8	6.7
Neutrophil (percentage)		
• ≤20	32	26.9
• >20-80	39	32.8
• >80	48	40.3
CSF protein (mg%)		
• ≤45	9	7.6
• >45-200	53	44.5
• >200	57	47.9
CSF glucose (≤40 mg%)		
Yes	58	48.7
No	61	51.3
CSF/serum glucose ratio ≤0.5		
Yes	80	67.2
No	39	32.8

Table 6 CSF microbiology of acute bacterial meningitis

	Number of case (N=119)	Percentage
CSF gram stain		
• Found organism	4	3.4
• Not found organism	115	96.6
CSF culture		
• Positive	9	7.6
• No growth	110	92.4
CIE (N=17)		
• Positive	3	17.6
• Negative	14	82.4

In 19 patients (15.4 %) were hemoculture positive. 7 patients (5.7%) were identified Streptococcus group B, 3 patients (2.4%) were identified Streptococcus group A, 2 patients(1.6%) were identified Streptococcus pneumoniae, 3 patients (2.4%) were identified Streptococcus spp., 2 patients (1.6%) were identified Escherichia coli and the others 2 were reported Pseudomonas spp. (0.8%) and gram positive bacilli (0.8%) respectively. 55 patients (44.7%) had received antibiotics before arrived our hospital. Antibiotics used in all of 55 patients were ceftriaxone which had been administered from rural hospital. Data of hemoculture and prior antibiotics use are shown in Table 7.

Table 7 CSF Data of hemoculture and prior antibiotics use

	Number of case (N=123)	Percentage
Hemoculture		
Positive	19	15.4
No growth	104	84.6
Prior antibiotics use		
Yes	55	44.7
No	68	55.3

Poor outcome, determined by not improvement at discharge and death, in this study was 17.9% (22 patients). Almost all of our patients had improvement and recovery from the disease (82.1%). Only 10 patients were death in hospital (8.1%). Residual neurological deficit was found in 23 patients (18.7%). Factors predicted poor outcome were elderly age (defined as age >65 years old) OR 7.14 (95% CI 2.64 to 19.34) p=0.0001, altered mental status as presenting symptom OR 4.5 (95% CI 1.44 to 14.66) p=0.01 and neutrophil more than 80% in CSF white blood cell OR 6.65 (95% CI 1.33 to 33.24) p=0.02. However, prior antibiotic administration was not significant for good or poor prognostic factor. Analysis of factors associated with poor outcome and neurological complications are shown in Table 8 and Table 9 respectively.

Table 8 Multivariate analysis of factors associated with poor outcome of acute bacterial meningitis

Characteristic No./No. evaluated (%)	Poor outcome (N = 22)	Good outcome (N = 101)	Odds ratio (95%CI)	P Value
Elderly (age>65)	13/22 (59.1%)	17/101 (16.8%)	7.14 (2.64 - 19.34)	0.0001
Male gender	14/22 (63.6%)	69/101 (68.3%)	0.81 (0.31 - 2.13)	0.67
Clinical presentation				
▪ Headache	6/22 (27.3%)	76/101 (75.2%)	0.12 (0.04 - 0.35)	0.0001
▪ Fever	10/22 (45.5%)	60/101 (59.4%)	0.57 (0.23 - 1.44)	0.23
▪ Stiff neck	15/22 (68.2%)	66/101 (65.3%)	1.14 (0.42 - 3.05)	0.80
▪ Altered mental status	18/22 (81.8%)	45/101 (44.6%)	4.6 (1.44 - 14.66)	0.01
Predisposing conditions				
▪ DM	2/17 (11.8%)	1/72 (1.4%)	1.35 (0.27 - 6.76)	0.71
▪ HIV	0/15 (0%)	2/63 (3.2%)	0.79 (0.04 - 17.39)	0.88
▪ Immunosuppressive therapy	1/16 (6.25%)	3/64 (4.7%)	1.36 (0.13- 13.97)	0.80
Specific abnormalities on CT brain	13/16 (81.25%)	52/68 (76.5%)	1.33 (0.34 - 5.27)	0.68
CSF inflammatory index				
▪ Open pressure >20-40 vs.≤20	8/13 (61.5%)	38/67 (56.7%)	1.22 (0.36 - 4.13)	0.75
▪ Open pressure >40 vs. ≤20	0/5 (0%)	5/34 (14.7%)	0.49 (0.02 - 10.14)	0.64
▪ WBC count >100-1000 vs. ≤100	9/17 (52.9%)	48/77 (62.3%)	0.68 (0.24 - 1.96)	0.47
▪ WBC count >1000-5000 vs. ≤100	2/10 (20%)	15/44 (34.1%)	0.48 (0.09 - 2.57)	0.39
▪ WBC count >5000 vs. ≤100	1/9 (11.1%)	7/36 (19.4%)	0.52 (0.06 - 4.85)	0.56

Table 8 (continued.)

Characteristic	Poor Outcome (N = 22)	Good Outcome (N = 101)	Odds Ratio (95%CI)	P Value
▪ %Neutrophil >20-80 vs. ≤20	4/8 (50%)	35/62 (56.5%)	0.77(0.18 - 3.37)	0.73
▪ %Neutrophil >80 vs. ≤20	12/16 (75%)	36/63 (57.1%)	2.25(0.65 - 7.75)	0.20
▪ CSF protein >45-200 vs. ≤45	6/8 (75%)	47/54 (87%)	0.45(0.07 - 2.67)	0.38
▪ CSF protein >200 vs. ≤45	12/14 (85.7%)	45/52 (86.5%)	0.93(0.17- 5.09)	0.94
▪ Low CSF glucose (≤40)	10/20 (50%)	48/98 (49%)	1.04(0.40 - 2.73)	0.93
▪ CSF/serum glucose ratio ≤0.5	11/19 (57.9%)	69/89 (77.5%)	0.40(0.14 - 1.13)	0.08
Positive CSF gram stain	2/20 (10%)	2/93 (2.2%)	5.06(0.67 -38.27)	0.12
Positive CSF culture	2/20 (10%)	7/91 (7.7%)	1.33(0.26 - 6.96)	0.73
CIE	1/2 (50%)	2/15 (13.3%)	6.5(0.28- 151.13)	0.24
Pneumonia on chest radiograph	0/10 (0%)	1/44 (2.3%)	1.38(0.05- 36.37)	0.85
Positive hemoculture	3/21 (14.3%)	16/88 (18.2%)	0.75(0.20 - 2.86)	0.67
Prior antibiotics	7/22 (31.8%)	48/101 (47.5%)	0.52(0.19 - 1.37)	0.18

Table 9 Multivariate analysis of factors associated with neurological complications of acute bacterial meningitis

Characteristic No./No.evaluated (%)	Neurological complications (N = 23)	No complications (N = 64)	Odds ratio (95%CI)	P Value
Elderly (age>65)	9/23 (39.1%)	13/64 (20.3%)	2.52(0.9 - 7.1)	0.08
Male gender	14/23 (60.9%)	43/64 (67.2%)	0.76(0.28 - 2.04)	0.59
Clinical presentation				
▪ Headache	9/23 (39.1%)	53/64 (82.8%)	0.13(0.05 - 0.38)	0.0002
▪ Fever	15/23 (65.2%)	41/64 (64.1%)	1.05(0.39 - 2.85)	0.92
▪ Stiff neck	15/23 (65.2%)	44/64 (68.8%)	0.85(0.31 - 2.33)	0.76
▪ Altered mental status	14/23 (60.9%)	25/64 (39.1%)	2.42(0.91 - 6.44)	0.08
Predisposing conditions				
▪ DM	3/20 (15%)	4/43 (9.3%)	1.72(0.35 - 8.54)	0.51
▪ HIV	0/17 (0%)	2/41 (4.9%)	0.45(0.02 - 9.9)	0.61
▪ Immunosuppressive therapy	0/17 (0%)	3/42 (7.1%)	0.32(0.02 - 6.58)	0.46
Specific abnormalities on CT brain	9/14 (64.3%)	37/44 (84.1%)	0.34(0.9 - 1.33)	0.12

Table 9 (continued.)

Characteristic	Neurological complications (N = 23)	No complications (N = 64)	Odds ratio (95%CI)	P Value
CSF inflammatory index				
▪ Open pressure >20-40 vs.≤20	8/14 (57.1%)	26/44 (59.1%)	0.92 (0.27 - 3.12)	0.90
▪ Open pressure >40 vs. ≤20	0/6 (0%)	4/22 (18.2%)	0.32 (0.01 - 6.71)	0.46
▪ WBC count >100-1000 vs. ≤100	9/15 (60%)	31/53 (58.5%)	1.06 (0.33 - 3.43)	0.92
▪ WBC count >1000-5000 vs. ≤100	3/9 (33.3%)	8/30 (26.7%)	1.38 (0.28 - 6.84)	0.70
▪ WBC count >5000 vs. ≤100	3/6 (50%)	3/6 (50%)	7.33 (0.99 - 54.41)	0.051
▪ %Neutrophil >20-80 vs. ≤20	4/6 (66.7%)	25/44 (56.8%)	1.52 (0.25 - 9.19)	0.65
▪ %Neutrophil >80 vs. ≤20	14/16 (87.5%)	20/39 (51.3%)	6.65 (1.33 - 33.24)	0.02
▪ CSF protein >45-200 vs. ≤45	5/6 (83.3%)	33/39 (84.6%)	0.91 (0.09 - 9.22)	0.94
▪ CSF protein >200 vs. ≤45	15/16 (93.8%)	25/31 (80.6%)	3.6 (0.39 - 32.87)	0.26
▪ Low CSF glucose (≤40)	8/21 (38.1%)	32/63 (50.8%)	0.6 (0.22 - 1.643)	0.32
▪ CSF/serum glucose ratio ≤0.5	13/20 (65%)	45/57 (78.9%)	0.5 (0.16 - 1.51)	0.22
Positive CSF gram stain	0/21 (0%)	3/59 (5.1%)	0.38 (0.02 - 7.58)	0.52
Positive CSF culture	0/20 (0%)	5/58 (8.6%)	0.24 (0.01 - 4.48)	0.34
CIE	0/2 (0%)	2/9 (22.2%)	0.6 (0.02 - 17.22)	0.77
Pneumonia on chest radiograph	1/11 (9.1%)	0/28 (0%)	8.14(0.31- 215.95)	0.21
Positive hemoculture	1/21 (4.8%)	12/58 (20.7%)	0.19 (0.02 - 1.58)	0.12
Prior antibiotics	11/23 (47.8%)	28/64 (43.8%)	1.18 (0.45 - 3.06)	0.74

Discussion :

Acute bacterial meningitis had more incidence in men more than women in our study. Mean age of patients is 50.98 ± 18.62 years old which is similar to study in Netherlands by Van de Beek, et al.[3] Therefore it is higher than other studies in Thailand.[8,9] The ratio of men to women with acute bacterial meningitis is 2.08, which is higher than other studies.[3,5,6,8,9]

Although typical features of acute bacterial meningitis include headache, fever, stiff neck and alteration of mental status, not all patients present with all of classical symptoms. Our study has found that only 15 patients (12.2%) present with all four classical symptoms. Thus, majority of our patients present with at least two of four classical symptoms 106 patients (86.2%).

Typically, CT brain findings include meningeal enhancement, hydrocephalus, cerebral infarction, subdural effusion, abscess, lesions consistent with septic

emboli, cavernous-sinus thrombosis and lesion consistent with a disruption of blood brain barrier.[3,4] There are less availability for emergency contrast CT brain scan in our hospital, therefore, most CT brain performed in our study is non-contrast CT scan which result in less sensitivity for detect abnormalities in CT scan. In our study, 78.9 % of patients had performed CT scan but only 13 patients (10.6 %) has abnormalites specific with meningitis which is much lower than others study.[3,4]

CSF findings in acute bacterial meningitis include increase opening pressure on lumbar puncture which was found only 42.9% of patients.[4] Increase CSF WBC count, increase neutrophil percentage >80%, increase CSF protein, low CSF glucose, low CSF/serum glucose ratio are found 68.9%, 40.3%, 92.4%, 48.7% and 67.2% of our patients respectively. This finding is much different from other studies.[4,10-14] There are 2 patients (1.6%) whose initial CSF profile were not consistent with bacterial meningitis but later revealed positive bacterial culture, CIE on repeated CSF examination. The incidence of atypical CSF findings is found 0.5-12%[10-13,15] therefore the incidence is low in our study. The causes of initial normal CSF and positive microbio-

logical studies may be due to immunocompromised host e.g.HIV, immunosuppressive therapy, incorrect diagnosis[10-13], contamination of CSF specimen, and improper CSF specimen processing.[14]

In our study, CSF and hemoculture were positive only 9 patients (7.6%) and 19 patients (15.4 %) respectively which were much lower than other studies such as study by Van de beek et al.[3] Most of positive hemoculture were Streptococcus group B which were different to other studies in which most positive culture were Streptococcus pneumoniae.[1-9] Almost half of patients (44.7%) had received antibiotics from rural hospital before arrived our hospital.

However, prior antibiotic administration was not significant for good or poor prognostic factor. Poor outcome, determined by no improvement at discharge and death, in this study is 17.9% (22 patients). Almost all of our patients had improvement and recovery from the disease (82.1%). Only 10 patients were death in hospital (8.1%). Residual neurological deficit was found in 23 patients (18.7%). Case motality rate in our study is lower than other studies such as study conducted by Van de Beek which had mortality rate 21%.[3] This was due to relatives of some patients with not-improve

outcome had decided to refused treatment in hospital and brought patient to their home which may result in death at home. Factors predicted poor outcome are elderly age, altered mental status as presenting symptom OR 4.5 (95% CI 1.44 to 14.66) and neutrophil more than 80% in CSF white blood cell OR 6.65 (95% CI 1.33 to 33.24) p=0.02 which were similar to other studies.[3,7,15,16]

Limitations of our study are retrospective study design, missing data, low sample size number. There is no information of adjuvant dexamethasone use, timing of antibiotics after diagnosis of meningitis.

Conclusion :

Acute bacterial meningitis has more incidence in men than women. The major presenting symptoms include headache, fever, stiff neck and altered of mental status. Common CSF findings include high CSF opening pressure, CSF pleocytosis with neutrophil predominate, high CSF protein and low CSF glucose. Poor prognostic factors include elderly, altered mental status as presenting symptoms and more than 80 percent of neutrophil in CSF. Prior antibiotics administration does not correlate with good or poor outcome. Therefore, early antibiotics treatment should be administered as soon as possible.

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