

Acute Bacterial Meningitis In Adults: A Review Of 90 Patients

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Citation

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Abstract

Objectives: Our aim was; i) to compare *S.pneumoniae* and *N.meningitidis* meningitis for demographic, laboratory and clinical findings, and outcome, ii) to compare survivor and non-survivor meningitis cases for prognostic factors on admission, iii) to compare meningitis cases with favorable and unfavorable outcome for prognostic factors on admission.

Design: Retrospective study.

Setting, Participants, Methods: We reviewed the charts of 90 patients older than 16 years of age, in whom *S.pneumoniae* or *N.meningitidis* meningitis was diagnosed at Uludağ University Hospital, from January 1985 to October 2004.

Results: Age was found to be significantly higher in patients with meningitis due to *S.pneumoniae* ($p<0.01$). The >mortality rate was found to be 24% in pneumococcal and 8.6% in meningococcal meningitis. The cerebrospinal fluid leukocyte count, presence of bacteremia, major motor deficit and altered mental status on admission were found to be significantly different between survivor and nonsurvivor patients ($p<0.05$). Presence of cranial nerve palsy and major motor deficit on admission were significantly higher in patients with $GOS\leq 4$, when compared to patients with $GOS=5$ ($p<0.01$ and $p<0.05$, respectively). The mortality rate was found to be 60% in patients 60 years old or older and 15% in patients younger than 60 years ($p<0.05$). Mortality rate was in correlation with being ≥ 60 years old in all patients and in patients with *S.pneumoniae* meningitis ($p<0.05$). In patients with pneumococcal meningitis, presence of bacteremia, major motor deficit and mortality rate were significantly higher in patients who were 60 years of age or older ($p<0.05$).

Conclusion: In acute bacterial meningitis in adults, age ≥ 60 can be accepted as a responsible factor for higher mortality.

INTRODUCTION

Despite advances in antimicrobial therapy, bacterial meningitis continues to cause significant morbidity and mortality. Specifically, the mortality rate for adults who have *S. pneumoniae* meningitis remains 20 to 30 percent, with neurologic morbidity affecting half of the survivors (1,2). Therefore in the present study, we retrospectively reviewed acute community-acquired bacterial meningitis due to *S.pneumoniae* or *N.meningitidis*. Our aim was; i) to compare *S.pneumoniae* and *N.meningitidis* meningitis for demographic, laboratory and clinical findings and outcome, ii) to compare survivor and non-survivor meningitis cases for prognostic factors on admission, iii) to compare favorable and unfavorable meningitis cases for prognostic

factors on admission.

METHODS

We retrospectively reviewed the charts of all patients 16 years of age or older, in whom *Streptococcus pneumoniae* or *N.meningitidis* meningitis was diagnosed at Uludağ University Medical School Hospital (a tertiary medical centre with a capacity of 1000 beds) from January 1985 to October 2004. From the patient's charts, we extracted information on demographic data, presenting symptoms, physical signs, laboratory findings and clinical outcome.

The diagnosis of *S.pneumoniae* or *N.meningitidis* meningitis was based on the presence of clinical symptoms and signs of acute meningitis and identification of *S.pneumoniae* or

N.meningitidis in the cerebrospinal fluid by culture or Gram stain or in the blood by culture.

The duration of disease was accepted as the time frame from the first day of meningitis related symptoms until admission to our hospital. If the patient had somnolence, stupor or coma on admission, it was accepted as "altered mental status". Patients were considered to have neurologic sequelae if at least one of the following conditions were present on discharge: motor deficit, cranial nerve palsy, clinically detected hearing impairment, behavioral, memory or speaking disturbances, or hydrocephalus. For patients with recurrent meningitis, only the first episode was included.

Mortality was considered as meningitis-related if death was due to meningitis or its complications within the first 14 days of admission (3).

All patients were treated with antibiotics (chloramphenicol plus penicillin before 1995, ceftriaxon after 1995). Antibiotic susceptibility test was performed by disk diffusion method according to NCCLS criteria, and only six isolates of S.pneumoniae susceptibility tests underwent the E-test.

During the study period, performance of a cranial CT scan or administration of adjunctive therapy such as corticosteroids or mannitol were not based on the protocol but depended on the physician's decision.

Patient outcome was assessed on discharge with the Glasgow Outcome Scale (GOS) (1=death, 2=persistent vegetative state, 3=severe neurologic deficit, 4=moderate neurologic deficit, 5=good recovery) (4). Outcomes were combined into two categories: good recovery (GOS=5) and unfavorable (GOS≤4).

Mann-Whitney and Chi-square tests were used to compare differences between the groups. The correlation between mortality or unfavorable outcome according to GOS and the factors identified as prognostic factors on admission (altered mental status, major motor deficit, cranial nerve palsy, positive cerebrospinal fluid Gram stain, positive CSF culture, presence of bacteremia, age ≥60 years old, sex, type of meningitis) by other investigators were examined by logistic regression analysis(5).

RESULTS

Ninety patients were included in the study. Patient characteristics, clinical features and clinical outcome are

shown in Table 1. The age was significantly higher in pneumococcal meningitis ($p<0.01$). There were no significant differences for other parameters between the two groups.

Figure 1

Table 1: Patient characteristics, clinical features and clinical outcome in S.pneumoniae and N.meningitidis meningitis cases.

	S.pneumoniae	N.meningitidis	p
Age(mean±SD, range)	40±18, 16-87	29±15, 16-62	<0.01
Sex			
Female	25	12	NS
Male	42	11	NS
Duration of symptoms(days) (mean±SD)	2.6±2	2.1±1.7	NS
<u>Clinical features</u>			
Headache	53/67	19/23	NS
Altered mental status	46/67	14/23	NS
Vomiting	50/67	19/23	NS
Seizures	8/67	3/23	NS
Nuchal rigidity	65/67	23/23	NS
Major motor deficit	6/67	3/23	NS
Cranial nerve palsy	9/67	4/23	NS
<u>Clinical outcome</u>			
Survived(without neurologic sequelae)	43/67	14/23	NS
Survived(with neurologic sequelae)	8/67	7/23	NS
Mortality	16/67(24%)	2/23(8.6%)	NS

NS:Not Significant

S.pneumoniae was isolated from blood cultures in three, from CSF cultures in 30, and from both blood and CSF cultures in 13 patients. S.pneumoniae meningitis was diagnosed by Gram stain in 21 patients with negative cultures. N.meningitidis was isolated from blood cultures in three, from CSF in nine, and from both blood and CSF cultures in three patients. N.meningitidis meningitis was diagnosed by Gram stain in eight patients with negative cultures. Resistance to penicillin, ceftriaxon and chloramphenicol was not detected in S.pneumoniae and N.meningitidis strains. There were no significant differences between the two groups according to cerebrospinal fluid findings.

Of the 11 patients, 16% had recurrent meningitis in the S.pneumoniae group. Predisposing factors such as terminal complement deficiency or splenectomy were not found in patients with meningitis due to N.meningitidis.

When the survivor and nonsurvivor patients were compared; the cerebrospinal fluid leukocyte count, presence of bacteremia, major motor deficit on admission and altered mental status on admission were found to be statistically different between the two groups ($p<0.05$) (Table 2). In

addition, this comparison was performed for patients with meningitis due to *S.pneumoniae*. The presence of bacteremia, major motor deficit on admission and altered mental status on admission were found to be statistically significant between the two groups with pneumococcal meningitis ($p<0.05$) (Table 3).

Figure 2

Table 2: Comparison of survivor and nonsurvivor patients

Age(mean±SD, range)	35±16,16-68	46±24,16-87	NS
CSF leukocyte(cells/mm ³)	8802±9735	5881±10195	<0.05
CSF blood glucose ratio(mg/dl)	0.20±0.18	0.16±0.20	NS
CSF protein(mg/dl)	298±255	294±266	NS
The duration until admission(day)	2.5±1.9	2.4±1.8	NS
Sex			
Female	30	7	NS
Male	42	11	NS
Positive CSF Gram stain	61/70	16/17	NS
Positive CSF culture	11/17	45/71	NS
Bacteremia	14/72	8/17	<0.05
Presence of major motor deficit	4/72	5/18	<0.05
Cranial nerve palsy	9/72	4/18	NS
Altered mental status	42/72	18/18	<0.05

NS:Not Significant

Figure 3

Table 3: Comparison of survivor and nonsurvivor patients in pneumococcal meningitis.

	Survivor patients	Nonsurvivor patients	p
Age(mean±SD, range)	37±15,16-68	49±24,17-87	NS
CSF leukocyte(cells/mm ³)	7792±9061	6245±10415	NS
CSF blood glucose ratio(mg/dl)	0.21±0.19	0.16±0.2	NS
CSF protein(mg/dl)	276±222	294±266	NS
The duration until admission(day)	2.7±2.0	2.3±1.8	NS
Sex			
Female	18	7	NS
Male	33	9	NS
Positive CSF Gram stain	45/51	15/16	NS
Positive CSF culture	33/51	10/16	NS
Bacteremia	9/51	7/16	$p<0.05$
Presence of major motor deficit	2/51	4/16	$p<0.05$
Cranial nerve palsy	5/51	4/16	NS
Altered mental status	30/51	16/16	$p<0.05$

NS:Not Significant

Comparison was also made for patients with favorable (GOS=5) and unfavorable (GOS≤4) outcomes. Presence of cranial nerve palsy and major motor deficit on admission were significantly higher in patients with GOS≤4 when compared with patients GOS=5 ($p<0.01$ and $p<0.05$ respectively) (Table 4). Cranial nerve palsy was found to be significantly higher in patients with GOS≤4 and pneumococcal meningitis, when compared to patients with GOS=5 and pneumococcal meningitis (6/22 vs. 3/45, $p<0.05$). Duration of symptoms was significantly longer in patients with GOS≤4 and meningococcal meningitis when

compared to patients with GOS=5 and meningococcal meningitis (4.5±2.6 days vs.1.6±1 days, $p<0.01$).

Figure 4

Table 4: Comparison of patients with GOS≤4 and patients with GOS=5

	GOS≤4	GOS=5	p
Age(mean±SD, range)	43±22,16-87	35±16,16-68	NS
CSF leukocyte(cells/mm ³)	6531±8825	8917±10202	NS
CSF blood glucose ratio(mg/dl)	0.15±0.18	0.21±0.19	NS
CSF protein(mg/dl)	303±282	296±249	NS
The duration until admission(day)	2.8±2.1	2.3±1.8	NS
Sex			
Female	12	25	NS
Male	14	39	NS
Positive CSF Gram stain	23/25	52/64	NS
Positive CSF culture	16/25	40/63	NS
Bacteremia	9/25	13/64	NS
Presence of major motor deficit	6/26	3/64	<0.05
Cranial nerve palsy	8/26	5/64	<0.01
Altered mental status	21/26	39/64	NS

NS:Not Significant

The mortality rate was found to be 60% in ten patients who were 60 years old or older and 15% in eighty patients younger than 60 years old($p<0.05$). There was no significant difference for other parameters. In patients with pneumococcal meningitis, presence of bacteremia, major motor deficit and mortality rate were significantly higher in patients 60 years old or older ($p<0.05$).

There was no significant difference for mortality rates and outcome according to GOS scale between 24 patients who received only chloramphenicol plus penicillin combination and 25 patients who received only seftriaxon as antibiotic treatment.

The correlation between mortality and altered mental status, major motor deficit, cranial nerve palsy, positive cerebrospinal fluid Gram stain, positive CSF culture, presence of bacteremia, age ≥60 years old, sex and type of meningitis was examined in all patients and in patients with meningitis due to *S.pneumoniae*. The correlation between mortality and age ≥60 years old was found to be significant in both groups, respectively ($p<0.05$, OR 31, %95 CI 2.2-423.4 for all patients and $p<0.05$, OR 31, %95 CI 2.2-423.3 for pneumococcal meningitis). In addition, the correlation between unfavorable outcome (GOS≤4) and altered mental status, major motor deficit, cranial nerve palsy, positive cerebrospinal fluid Gram stain, positive CSF culture, presence of bacteremia, age ≥60 years old, sex and type of meningitis was also examined in all patients, and in patients with meningitis due to *S.pneumoniae*. The

correlation between unfavorable outcome and the presence of cranial nerve palsy on admission was found to be significant ($p=0.21$, OR 54, %95 CI 1.8-1605.6).

DISCUSSION

Despite advances in antibiotic therapy, bacterial meningitis continues to cause significant morbidity and mortality. Mortality rate is 19-41% for pneumococcal meningitis and 4.8-13% for meningococcal meningitis in the literature (^{2,3,5,6,7}). In addition, van de Beek et al. reported that the mortality rate was significantly higher in adult pneumococcal meningitis (⁸).

The mortality rate was found to be 24% in pneumococcal meningitis and 8.6% in meningococcal meningitis in our study. There was no significant difference in our mortality rates between pneumococcal and meningococcal meningitis despite this difference, and this might be due to low number of cases in our study.

We found that the mortality rate was higher in patients who were 60 years old or older. The mortality rate, bacteremia and major motor deficit were found to be significantly higher in 60 years old or older patients with pneumococcal meningitis when compared to younger pneumococcal meningitis cases (Table 2 and 3). In addition, the only independent prognostic factor for mortality in our study cases was found to be advanced age. Advanced age could be considered as a risk factor for higher mortality in pneumococcal meningitis. Age of ≥ 60 is a known risk factor for mortality both from acute bacterial meningitis and pneumococcal meningitis (⁶).

We also know that meningitis-associated systemic complications were found to be more frequent causes of death in older patients than in younger patients (⁹).

Aronin et al. reported that hypotension, altered mental status and seizures on admission were independently associated with adverse clinical outcome in community-acquired bacterial meningitis (⁵).

Kastenbauer et al. found that chronic debilitating diseases, low Glasgow Coma scale Score and focal neurologic deficits on admission, low CSF leukocyte counts, pneumonia, bacteremia are factors associated with a bad outcome ($GOS \leq 4$) in adult pneumococcal meningitis (⁹). Therefore, we think that higher bacteremia rates in older pneumococcal meningitis cases might be another cause of higher mortality rates.

We could not find a significant association between low CSF leukocyte count and higher mortality or bad clinical outcome in patients with pneumococcal meningitis in our study, like other previous studies, except for the study by Kastenbauer et al. They reported that lower CSF leukocyte counts were associated with an adverse outcome in pneumococcal meningitis (^{3,9}). In addition, McMillan et al. reported a significant association of low CSF leukocyte count with adverse outcome in adult bacterial meningitis (¹⁰). However, we found lower CSF leukocyte counts in all non-survivor meningitis cases when compared to survivors ($p < 0.05$, table 2).

A significant association of low CSF leukocyte count with adverse outcome could be explained by the presence of high bacterial titres in CSF. An association of low CSF leukocyte counts with high bacterial titres has been shown in animal pneumococcal meningitis (^{11,12}). In addition, other factors such as serotypes of *S.pneumoniae* and apoptosis in neurons and microglial cells induced by *S.pneumoniae* could contribute for this significant association in pneumococcal meningitis (^{13,14,15,16}).

In our study, we found no significant differences between two antibiotic regimens according to mortality and GOS. This might be due to the low number of cases in our study. However, a recent meta-analysis showed similar results between the two antibiotic regimens (¹⁷).

In conclusion, we found higher mortality and higher bacteremia in patients ≥ 60 years old with pneumococcal meningitis. Age of ≥ 60 and bacteremia could be accepted as responsible factors for higher mortality in pneumococcal meningitis.

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