Spectrum of Complications and Mortality of Bacterial Meningitis: an Experience from a Developing Country

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Objective: The aim of this study was to obtain data on predisposing factors, causative organisms and their associated mortality and complications related to acute bacterial meningitis.

Methods: The chart review of all patients in whom acute bacterial meningitis was diagnosed at The Aga Khan University Hospital from January 1995 through December 2001.

Results: One hundred ninety-four patients were included in study. There were 146 males and 48 females. The mean age of our study population was 41±12.3 years. One hundred and ninety (97.9%) patients had community-acquired meningitis; only 4 (2.0%) patients developed meningitis nosocomially. The two most common predisposing factors were diabetes mellitus (13.9°/x) and otitis media (7.7%) among all 194 patients. A significant proportion of patients with complications had diabetes mellitus (24.6°/x, p<0.001). CSF and blood cultures were positive in 53 (27.3%) and 42 (21.6%) patients respectively; there was no statistical difference found. The most common organisms isolated were Streptococcus pneumoniae in 35 (36.8%) patients followed by Neisseria meningitides in 30 (31.5%) patients. Approximately 68% of positive cultures yielded S. pneumoniae and N. meningitides (p<0.0001). The overall mortality rate was 22.1 %. The mortality rate for Streptococcus pneumoniae was 17.1 %. The highest mortality was observed in patients with Pseudomonal meningitis where all four patients expired followed by mortality rate of 85.7% in Escherichia coli afflicted patients (p<0.001). Complications occurred in 73 (37.6%) patients with persistent complications in 31 (42.4%) patients. Complications resolved in 34 (46.5%) patients. The most common complications were seizures (12.8%) and cranial nerve palsies (11.3%). Seizures were more likely to occur in older patients (p<0.05) whereas hydrocephalus was more common in younger patients (p<0.05).

Conclusion: Bacterial Meningitis remains a serious disease associated with substantial morbidity and mortality. Most cases are community acquired with S. Pneumoniae being the most common pathogen. Old age, diabetes mellitus, a positive culture, seizures as a complication and late stage in the disease are the important predictors of a poor outcome (JPMA 53:580;2003).

Introduction

Before the advent of antibiotics, bacterial meningitis was almost exclusively a fatal disease, with a case fatality rate of 95% to 100% for patients with pneumococcal meningitis, 90% for those with Haetnophilus influenzae meningitis and 70-90% for those with rneningococcal meningitis1. The use of antibiotics has drastically reduced mortality. However, despite further progress in antimicrobial therapy, the fatality rate and sequelae of meningitis due to pneumococcus, which is the organism most often responsible for bacterial meningitis in adults, has remained unchanged (20% to 40%) during the last decades. [1-3]

A major cause for mortality and sequelae of bacterial meningitis are intracranial complications arising during the acute phase of the disease causing secondary brain damage.-1,7 Most of the clinical reports on such complications during bacterial meningitis stem from cases involving infants and children where H. influenzae is the most frequent etiological agent, however only a few studies have focused on the clinical and pathological features of the illness in adults.[b,7-10]

Knowledge of the entire clinical spectrum of complications and their prompt detection are a prerequisite for the improved management of the disease. Therefore, the aim of this study was to obtain data on predisposing factors, causative organisms and their associated mortality and complications.

Methods

We reviewed the charts of all patients in whom acute bacterial meningitis was diagnosed at The Aga Khan University Hospital from January 1995 through December 2001. Patients who were initially treated at other hospitals but were transferred to this hospital for further therapy, those with acute illness (less than seven days of symptoms) and a definite or probable bacterial cause were also included. A nosocomial infection was defined accordim, to

the 1988 guidelines of the Centers for Disease Control.,, Although these guidelines do not specify a length of hospitalization before the onset of meningitis, in our study nosocomial infection was defined as development of meningitis after 48 hours of hospitalization or within one week of discharge.

The diagnosis of meningitis caused by a specific bacterial pathogen was based on a compatible clinical picture and one of the following: a positive cerebrospinal fluid culture; or a negative cerebrospinal fluid culture with a finding of neutrophilic pleocytosis and one of the following: a positive blood culture, identification of gram-negative diplococci on Gram's staining of cerebrospinal fluid, or sputum or throat cultures positive for Neisseria meningitides in patients with a petechial or purpuric rash and a fulminant course. In addition, episodes of "culture-negative" bacterial meningitis were included in our analysis. These episodes were diagnosed on the basis of a compatible clinical picture and pleocytosis of at least 100 neutrophils per cubic millimeter (0.1 x 109 per liter) despite negative blood and cerebrospinal fluid cultures and results of cerebrospinal fluid Gram's staining that were negative, with any one of the following: a cerebrospinal fluid pressure of greater than 180 mm of Hg, a cerebrospinal fluid protein concentration greater than 45 mg /dl, or a cerebrospinal fluid glucose concentration less than 40 mg/dl or less than 40% of random blood glucose measured concomitantly, provided that random blood glucose is greater than 250 mg/dl.

Partially treated meningitis was defined as cases of meningitis, which were diagnosed at some other hospital and received initial antibiotics there, were later shifted to AKUH. Stage I of bacterial meningitis was defined as patients with classical triad of Bacterial Meningitis (fever, stiff neck, altered mentation). Stage 11 comprised of stage I together with complications secondary to bacterial meningitis. Stage III represented patients with coma.

Mortality was classified as meningitis-related if death was due to meningitis or its complications, but not if it was due to a preexisting serious illness after bacteriologic cure and clinical recovery from meningitis.

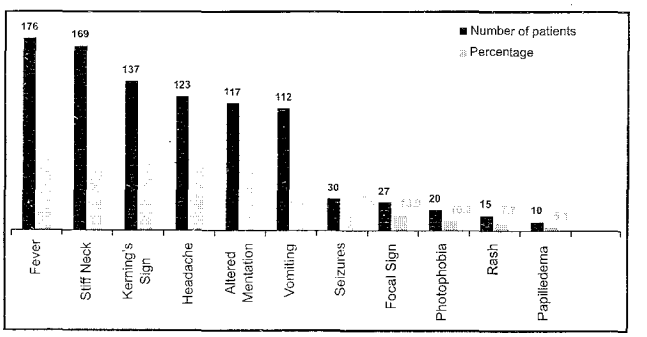
The data was analyzed using SPSS version 10.0 software. The chi-square and Fisher's exact tests were used for statistical analysis.

Results

We analyzed the medical charts of 194 patients between the study period of January 1995 to July 2002. There were 146 males and 48 females. The mean age of our study population was 41±12.3 years. One hundred and ninety (97.9%) patients had community-acquired meningitis; only 4 (2.0%) patients developed meningitis nosocomially. The underlying predisposing factors are summarized in Table 1. The two most common predisposing factors were diabetes mellitus (13.9 0%) and otitis media (7.7%) among all 194 patients. A significant proportion of patients with complications had diabetes mellitus (24.6%, p<0.001).

Table 1. The underlying predisposing factors in 194 patients with acute bacterial meningitis.

Predisposing Factor	No. ofpatients	Percentage
Nil	77,	39.6
Diabetes	27	13.9
Otitis Media	15	7.7
Tuberculous meningitis	11	5.6
CSF Leakage	9	4.6
Upper Respiratory Tract Infection	8	4.1
Pneumonia	7	3.6
Upper respiratory tract infection	5	2.5
Neurosurgery	4	2.0
Pulmonary T13	4	2.o
Sinusitis	3	1.5
Contact with patients	2	1.0
Mastoiditis	2	I.0
Conjunctivitis	1	0.;>



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The most common presenting" symptoms were 1cver (90.7%) and headache (83.5`.'-0). The most common sign \vas neck stiffness (87.1%). An overview ol'symptoms and signs are shown in Figure.

CSF and blood cu1turCS wccc positive in 53 (27.')(0 and 42 (21.6`%) patients respectively;_ there was no statistical difference found. Tlie most common ort anis+ns isolated were Streptococcus pneumoniae in 35 (36.8"-) patients followed by Neisscria mcnjnl-iit9des ill 3() 139 patients. Approximately 68% of positive cultures y'ieided s. pneumoniae and N. meningitides (1r==0.0001).

Table 2. Culture isolated pathogens vs mortality.

Pathogens	No. of patients	%	No. expired	
Fatality				
Strep. Pncumoniae	35	36.8	6	17.1
N. Meningitides	30	31.5	3	10.0
Staph. Aureus	8	8.4	3	37.5
E. Coli -	7	7.3	6	85.7
Pseudomonas	4	4.2	4	100
Acinetobactor	4	4.2	3	75
Klcbsiella	4	4.2	3	75
Cryptococcal	2	2.1	0	0
Multiple	1	1.0	0	0

Table 3. Various. complications in 194 patients.

Complication	No. of patients	Percentage
Seizures	25	12.8
Cranial Nerve Palsies	22	11.3
8th Nerve Palsy	11	50.0
7th Nerve Palsy	7	31.8
6111 Nerve Palsy	2	9.0
3rd Nerve Palsy	2	9.0
SIADII	14	7.2
1-lemiplegia	14	7.2
Hydrocephalus	12	6.1
Deafness	11	5.6
DIC	9	4.6
Monoplegia	8	4.1
Aphasia	6	3.0
Septic Arthritis"	4	2.0
Paraplegia	2	1.0
I-lopes labial is	2	1.0
Acute renal failure	1	0.5
Tinnifus / VCrll(-)o	1	0.5

The overall mortality rate was 22.1%. The mortality rate for Streptococcus pneumoniae was 17.1%. The highest mortality was observed in patients with Pseudomonal meningitis where all four patients expired followed by mortality rate of 85.7% in Escherichia coli afflicted patients (p<0.00I). Table 2 shows all the organisms and respective tuortaliiv, rates.

Complications occurred in 73 (37.6%) patients with persistent complications in 31 (42.4%) patients. Complication resolved it. 34 (46.5%) patients: eight patients were lost to follow-up. Table 3 summarizes all the complications observed in 194 patients. The most common complications were seizures (12.8%) and cranial nerve palsies (11.3%). Seizures were more likely to occur in older patients (p< 0.05) whereas hydrocephalus was more common in younger patients (p<0.05). The difference in proportion of cranial nerve palsies between pediatric and adult population was, however, not significant. Table 4 shows complications and mortality rates in various stages of bacterial meningitis. A statistically significant difference was observed among different stages of bacterial meningitis with respect to complications and mortality (p<0.05).

Table 4. Predictors of mortality of bacterial meningitis in 194 patients.

Variable	Fatal cases	Fatal Cases (%)	P value
Age (years)			
< 60	26/146	17.8	< 0.05
>60	17/48	35.4	
Gender			
Male	30/146	20.5	=0.21
Female	13/48	27.0	
Diabetes mellitus			
Yes	18/27	66.6	< 0.0001
No	25/167	14.9	
Culture			
Positive	32/95	33.7	< 0.00•
Negative	11/99	11.1	
Seizures			
Yes	13/25	52.0	< 0.005
No	30/169	17.7	

Discussion

Acute bacterial meningitis causes many deaths and substantial long-term morbidity throughout the world.! In countries with few resources, the incidence of this disease is about 10 times greater than that in well-resourced Countries. In developing countries, 12-15% of individuals with this disease die, compared with 5% in developed countries."

Bacterial meningitis is more common in the very young and the elderly. In the present series. more elderly patients were affected by acute bacterial menitt-itis. In bacterial meningitis there is a slight male predominance. Men outnumbered women by a ratio of 6:5 in a German study of bacterial meningitis in adults. 13 However, one Taiwanese study of Gram-negative bacillary meningitis ill adults found a ration of 6:1. 14 A male predominance of 3:1 was also found in our study.

The majority if episodes of acute bacterial meningitis in our study were community-acquired (97.9%). In contrast, Durand et all y reported a nosocomial infection rate of 40%, this significant discrepancy is likely attributable to the inclusion of neurosurgical patients in this Massachusetts review.

More than 70% of our patients had at least one underlying disease or condition. Predisposing factors for acute bacterial meningitis include otitis media, sinusitis, pneumonia, endocarditis, head injury, neurosurgical procedures, immunodeficiency, diabetes mellitus, alcoholism and CSF leak. [5] Diabetes mellitus came out to be the most important underlying condition in this study.

The vast majority of patients presented with fever and nuchal rigidity, yet only 63% completed the classic triad by reporting headache. The incidence of seizures in our study was 15.4%. This is comparable with earlier studies, which reported rates of 5-23%. [13,15,16] Seizure activity was significantly associated with mortality ($p<0.05$). The frequency of hydrocephalus in our study (6.1%) is comparable with observations of other authors in childhood meningitis. [7-19]

Hearing impairment is a well-known sequela of acute bacterial meningitis in children. [20,21] In a prospective study, the incidence of hearing loss as determined by electric response audiometry and conventional tests was 31% with S. Pneumoniae. [-°] Although out clinical experience leads us to believe that hearing abnormalities are more frequent in children, we have no scientific evidence to substantiate the observation since long-term follow-up investigations were not performed.

Streptococcus Pneumoniae species have been the major cause of bacterial meningitis in many countries. [16,22] As a whole it was the most common causative microorganism demonstrated in our patients followed by Neisseria Meningitides.

Despite advances in anti-microbial therapy, an overall mortality of 22.1% (43 patients) was observed, similar to rates seen in other studies. 15,16,21 Previous studies, as well as our own, have shown that certain prognostic factors correlate with a poor outcome in patients with bacterial meningitis. [15,16] In this study, a higher mortality was observed in the elderly, in patients with diabetes mellitus, in those with seizures when occurring as a complication, positive cultures, and stage III of bacterial meningitis.

Conclusion

Bacterial Meningitis remains a serious disease associated with substantial morbidity and mortality in spite of developments in microbial diagnostic techniques and advances in antibiotics. Most cases are community acquired with S. Pneumoniae being the most common pathogen. Old age, diabetes mellitus, a positive culture, seizures as a complication and late stage in the disease are the important predictors of a poor outcome.

Better management of the complications might be an important factor in decreasing the mortality rate in bacterial meningitis. The disease must be suspected on clinical grounds, and pursued with the prompt lumbar puncture and blood cultures. Given the inherent urgency of bacterial meningitis, appropriate antibiotic therapy should be instituted promptly and should not be delayed until brain imaging is completed. Since S. Pneumoniae is the major pathogen, the importance of prevention of infection cannot be overemphasized.

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