Outcome of Patients with Meningitis and Encephalitis at Tertiary Care Hospital in Eastern Nepal

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ABSTRACT

Background

There are several etiologies of meningitis and encephalitis which must be considered in any patient presenting with fever, headache, neck stiffness and vomiting. Bacterial meningitis and viral encephalitis are medical emergencies and need urgent attention and treatment. Any delay in diagnosis and treatment has been shown to increase morbidity and mortality. Some of the survivors also have neurological sequel with a need for long term physical and occupational rehabilitation.

Objective

To find out common causes of meningitis, encephalitis, predictors of outcome, early and late complications of meningitis and encephalitis at Tertiary Care Hospital in Eastern Nepal.

Method

It is a prospective study which was conducted at Nobel Medical College Teaching Hospital from April 2015 to March 2016.

Result

A total of 52 patients participated in the study. Bacterial meningitis was the most common type of neuroinfection (40.4%) followed by tubercular meningitis (27%), viral encephalitis (17.3%) and viral meningitis (15.4%). Pneumococcus was the most common identified cause of meningitis accounting for 28.9% of bacterial meningitis. Japanese encephalitis was the most common identifiable cause of encephalitis accounting for 33% of cases. Low Glasgow Coma Scale at admission was significantly associated with worse neurological outcome (P<0.001).Similarly, high white blood cell count in blood was associated with worse neurological outcome (P=0.001).

Conclusion

Meningitis and encephalitis are neurological emergency. Prompt diagnosis and treatment is needed to improve survival. Neurological sequel is common after those infections which require long term rehabilitation.

KEY WORDS

Bacterial meningitis, tubercular meningitis, viral encephalitis

INTRODUCTION

Meningitis is a common disease worldwide. In 2002, meningitis caused an estimated 173 000 deaths worldwe.[1] In developing countries overall case fatality rate of patients with bacterial meningitis have been reported to be 33-44%. Steptococcus pneumoniae accounts for the highest mortality worldwide.[2-5] Tubercular meningitis typically presents in a subacute manner with mean duration of symptoms typically more than 5 days.[6,7] In adults, 80-85% of viral meningitis cases are due to non-polio enteroviruses such as Coxsackie A and B viruses and echovirus, with the remaining cases due to other viruses.[8,9]

Herpes simplex virus type 1, Varicella-Zoster virus, Epstein–Barr virus, mumps, measles, and enteroviruses are responsible for most cases of viral encephalitis in immune-competent individuals.[10] Japanese encephalitis is the leading cause of viral encephalitis in Asia, with 30,000-50,000 cases reported annually. The mortality rate from Japanese Encephalitis in Nepal is 13.2%.[11] Out of the survivors, up to 30% may develop some type of permanent neurological disability and about 10% recover to pre infective status.[12]

Diagnosis

Meningitis and encephalitis is diagnosed based on the clinical features and laboratory tests, lumbar puncture and cerebrospinal fluid analysis.[13]

Cerebrospinal fluid Findings in Normal Patients and Those with Various Types of Meningitis[14,15,16]

	Normal	Bacterial	Viral	Neoplastic	Fungal	Tuberculous
Opening pressure (mmH_2O)	<170	>300	<300	200	300	>250
WBC count (per mm^3)	< 5	>1000	<1000	<500	< 500	50-1000
Neutro-phils	0%	>80%	<20%	1-50%	1-50%	<80-90% in adults
Glucose (mg/dL)	> 40	<40	>40	<40	< 40	<40
Protein (mg/dL)	< 50	>200	<200	>200	>200	50-250
Gram stain	negative	positive	negative	negative	negative	negative

This study was undertaken to identify the causes of meningitis and encephalitis in Eastern part of Nepal, to identify the outcome of those patients and note common neurological sequel resulting from such infection.

METHODS

It is a prospective study which was conducted at Nobel medical college from April 2015 to March 2016. All the patients who came to Nobel medical college with complaint of fever, headache, vomiting and seizure were enrolled in the study. Patients were followed up during entire hospital stay. They were also followed up one month after hospital discharge either during the patient's hospital visit or via telephone.

Ethical clearance was obtained from the institutional review board before the start of the study. Informed consent was obtained from all the participants.

The following case definitions were used in this study: (1) a diagnosis of meningitis was based upon clinical assessment, with features including fever, headache, vomiting, neck stiffness and altered consciousness; (2) bacterial meningitis was confirmed by cerebrospinal fluid analysis which included elevated white blood cell count with predominant neutrophil, raised protein, decreased cerebrospinal fluid Glucose, positive Gram stain of cerebrospinal fluid, by cultural isolation of a relevant microorganism from cerebrospinal fluid and/or blood, or by detection of bacterial antigens in cerebrospinal fluid; (3) viral meningitis was diagnosed presumptively on clinical ground and findings of cerebrospinal fluid analysis (4)Viral encephalitis was diagnosed on clinical ground, cerebrospinal fluid analysis ,serology, Polymerase chain reaction and brain imaging.

Inclusion Criteria

1. All the patients admitted to medical ward and Intensive care unit with diagnosis of meningitis and encephalitis.

2. Those patients who gave informed consent for the study.

Exclusion Criteria

1. Those patients who did not give informed consent for the study.

Data were entered and analyzed by using the SPSS Statistical Software (Version 16; SPSS; Chicago, IL) and were analyzed on the same software. Wherever applicable, the data were presented using either tabular form or descriptive statistics. The strength of association was estimated by linear regression analysis and t- test which was used as appropriate. P value of less than 0.05 was considered statistically significant.

RESULTS

In patients who presented to our hospital with complaint of headache, fever, vomiting and altered sensorium bacterial meningitis was the most common. Gram stain and CSF culture identified the causative organism in 47.6% of patients with bacterial meningitis. *Streptococcus pneumonae* was the most common identified organism accounting for 28.9% of bacterial meningitis while N. meningitidis and H. influenza each accounted for 9.5%.In 52.4% of patients with bacterial meningitis the pathogen could not be isolated.

In patients diagnosed as viral encephalitis Japanese encephalitis was the most common identified organism (33%). Herpes simplex virus type 1 was the next common

organism responsible for 22.2% of patients with viral encephalitis. The cause could not be identified in four patients.

Table 1. The demographic profile of the patients and their clinical characteristics (n=52)

Variables	Number (%)
Men	31(59.6%)
Women	21(40.4%)
Age of Patient	37±16
Bacterial meningitis	21(40.4%)
Viral meningitis	8(15.4%)
Tubercular meningitis	14(27%)
Viral encephalitis	9(17.3%)
Outcome	
Improved	46(88.5%)
Dead	6(11.5%)
Duration of hospital stay (In days)	11.4±6.24
Pneumococcus as a cause of bacterial meningitis	15(28.9%)
Japanese Encephalitis as a cause of encephalitis	17(33%)
White Blood cell count	
Normal	21(40.4%)
Raised	31(59.6%)
Glasgow Coma Scale at admission	
Normal	15(29%)
Decreased	37(71%)

Table 2. Age Distribution of patients

Age in years	Number(%)
<20	9(17.3%)
20-39	21(40.4%)
40-59	14(27%)
≥60	8(15.4%)

Table 3. Clinical presentation of patients

	Number(%)
Fever	49(94.2%)
Headache	47(90%)
Vomiting	42(80.8%)
Seizure	13(25%)
Hemiparesis	4(7.7%)
Cranial Nerve deficit	4(3.8%)
Neck Rigidity	40(77%)
Altered Sensorium	21(40.4%)

Fever, headache, vomiting and neck rigidity were the most common symptoms and signs in our patients. Few patients presented with seizure, hemi paresis and cranial nerve deficit.

Table 4. Etiology, Complications, and Mortality in 52 Patients

Etiology	Number of Cases	Complete Recovery	Sequel	Death
Bacterial meningitis	21	15(71.4%)	5(23.8%)	1(4.8%)
Viral Meningitis	8	8(100%)	-	-
Tubercular meningitis	14	8(57%)	5(35.7%)	1(7%)
Viral encephalitis	9	2(22.2%)	3(33.3%)	49(44.4%)

Complete recovery occurred in all of our patients with viral meningitis while 71.4 % of patients with bacterial meningitis and only 22.2% of patients with viral encephalitis had complete recovery. Patients with viral encephalitis had the highest case fatality rate of 44.4%.

All the patients who died had Glasgow coma scale score of less than eight at hospital admission.

Table 5. Glasgow Coma scale at admission

Glasgow coma scale	Number of patients
15 (Normal Glasgow Coma Scale)	15(28.8%)
9-14	20 (38.5%)
4-8	13(25%)
3	4 (7.7%)

Fifteen patients had normal Glasgow coma scale score. Twenty patients were either drowsy or stupor. Patients who had Glasgow coma scale score of eight or less underwent intubation to protect their airway. Four patients were deeply comatose at hospital admission.

Table 6. Complications during hospital stay

Complications	Number(%)
Pneumonia	8(15.4%)
UTI	8(15.4%)
DVT	2 (3.8%)
PE	1(1.9%)
Hydrocephalus	5 (9.6%)
Stroke	4 (7.7%)
Seizure	5 (9.6%)
Bedsore	15 (28.8%)

DISCUSSION

In our study we identified *Streptococcus pneumonae*, Neisseria meningitides and H influenza as the common organisms of bacterial meningitis while Japanese encephalitis was found to be the most common cause of viral encephalitis in Eastern part of Nepal. Etiological agent of meningitis and encephalitis could be established in only 28.8% of 52 patients as some patients had received

Table 7. Cerebrospinal fluid profile of patients

CSF Profile	Bacterial Meningitis (n=21)	Viral Meningitis (n=8)	Tubercular Meningitis (n=14)	Viral Encephalitis (n=9)
Cell count				
Increased	21(100%)	8(100%)	14(100%)	9(100%)
Normal	-	-	-	-
Protein				
Increased	19(90.5%)	8(100%)	14(100%)	8(88.9%)
Normal	2(9.5%)	-	-	1(11.1%)
Glucose				
Decreased	16(76.2%)	-	7(50%)	-
Normal	5(23.8%)	8(100%)	7(50%)	9(100%)
Gram Stain				
Positive	10(47.6%)	-	-	-
Negative	11(52.4%)	8(100%)	14(100%)	9(100%)
AFB Stain				
Positive	-	-	1(7.1%)	-
Negative	21(100%)	8(100%)	13(92.9%)	9(100%)
CSF Culture				
Positive	11(52.4%)	-	8(57.1%)	-
Negative	10(47.6%)	8(100%)	6(42.9%)	9(100%)
ADA				
Increased	2(9.5%)	-	13(92.9%)	1(11.1%)
Normal	19(90.5%)	8(100%)	1(7.1%)	8(88.9%)

antibiotic treatment prior to presentation to our hospital. Indeed 20(38.5%) patients had received at least one dose of antibiotic before admission. This finding agrees with that of other authors.[17]

Bacterial meningitis is a medical, neurological, and sometimes neurosurgical emergency that requires a multidisciplinary approach. Bacterial meningitis has an annual incidence of 4 to 6 cases per 100,000 adults (defined as patients older than 16 years of age), and Streptococcus pneumoniae and Neisseria meningitidis are responsible for 80 percent of all cases.[18,19] Meningitis and encephalitis was most common in the young population between 20 and 40 years of age.

The outcome of the study was assessed in terms of survival, mortality and any complications developed by the patients during hospital stay and follow up visit. The most frequent causes of neuroinfection were also noted. The overall mortality rate in our study was 11.5%. Complete recovery occurred in all of our patients with viral meningitis while 71.4 % of patients with bacterial meningitis and only 22.2% of patients with viral encephalitis had complete recovery. Patients with viral encephalitis had the highest case fatality rate of 44.4%.

Predictors of death in our study were low Glasgow Coma Scale at admission (P<0.001), high white blood cell count (P=0.001) and an infection with Japanese encephalitis. In patients suspected of having encephalitis empirical Acyclovir was started in the emergency room .This probably accounted for lower mortality rate with Herpes simplex virus in our study which otherwise also has a high case fatality rate. One patient with bacterial meningitis who died had streptococcal pneumonae infection. Similarly one patent with tubercular meningitis died because of progressive hydrocephalus. He had Modified Medical research council stage three disease with Glasgow coma scale of 6 at presentation.

Pneumonia, Urinary tract infection and pressure ulcer were common early (in-hospital) complications while seizure, hearing impairment and cranial nerve palsies were the most frequent late complications of meningitis and encephalitis in our study. Patients with pneumococcal meningitis, tubercular meningitis and viral encephalitis were more prone to such complications. Recently Dodge et al, in a prospective study, showed that deafness, which is a frequent complication of bacterial meningitis, is more likely to follow pneumococcal meningitis.[20] The dependence on clinical signs and symptoms for diagnosis makes it critical to institute prompt empirical antibiotic treatment. The empirical regimen must cover Streptococcus pneumoniae and Neisseria meningitidis, the most prevalent species, whenever clinical findings and macroscopic examination of the cerebrospinal fluid are suggestive of bacterial meningitis.

Our study also stresses the usefulness of cerebrospinal fluid Adenosine deaminase with a cut of value of more than 10 U/L taken as positive in the diagnosis of tubercular meningitis. It was 93% sensitive. However Adenosine deaminase was raised in two patients with bacterial meningitis and one patient with viral encephalitis who recovered completely without anti-tubercular medications. Similar finding was noted in study conducted by Gupta et al. who showed Cerebrospinal fluid Adenosine deaminase to be 94.73% sensitive and 90.47% specific in differentiating tubercular from non-tubercular meningitis with 90% positive predictive and 95% negative predictive value.[21]

The diagnosis of majority of our patients was based mainly on the clinical features and the laboratory tests available at our hospital. Serological test which were specific for diagnosis but too costly could not be carried out in some patients due to financial constraints.

CONCLUSION

Bacterial meningitis and viral encephalitis are medical emergency and need expeditious diagnosis and treatment whereas viral meningitis is most often self-limited. Delays in diagnosis and treatment have been shown to increase morbidity and mortality. There are several etiologies of meningitis and encephalitis, which must be considered in any patient presenting with fever, headache, or neck stiffness.

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