



## Clinical spectrum and etiological Profile Of Acute Meningitis and Encephalitis In Children Admitted To a Tertiary Care Hospital

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### Abstract

**Background:** The etiology of childhood meningitis and encephalitis has changed significantly over the past decades with the introduction of immunisation programmes against previous common causes of these infections.

**Objective:** To study the clinical, etiological profile, and outcome of meningitis and encephalitis in children admitted to a tertiary care hospital in Jammu and Kashmir.

**Study design:** Observational-descriptive study.

**Setting:** Conducted over a period of two years(September 2016-2018) in the Department of Pediatrics, Government Medical College, Srinagar.

**Participants:** 240 children aged 1 month to 18 years presenting to the hospital with signs and symptoms and CSF suggestive of meningitis and encephalitis were enrolled. **Intervention/Procedure:** Cerebrospinal fluid samples drawn from the enrolled participants were sent for biochemical and microbiological analysis using Conventional PCR for Herpes, RT-PCR for Enterovirus, and Bact/Alert Microbial detection system to determine the bacterial etiology. The clinical profile and outcome were recorded during the hospital stay.

**Outcomes:** Etiology was defined as bacterial or viral on the basis of the microbiological and biochemical evidence and the outcome was defined as discharge from the hospital or death due to the illness.

**Results:** Among 240 enrolled children, the most affected age group was 1 month to 2 years (45.41%).Fever(92.92%),vomiting (62%), neck stiffness (40.8%), headache (40.4%), seizures (36.25%) and altered sensorium (31.25%) were most common presenting symptoms. Out of 240 cases, 100 revealed pyogenic meningitis, positive for gram stain(67%) and CSF culture(59%). The most common etiological agents were S.pneumoniae (19%), E.coli(9%), Klebsiella(7%), H. influenza (6%), MRSA (6%), and Pseudomonas(1%). Out of 140 non-pyogenic cases, 105 were aseptic meningitis and 35 were acute encephalitis. PCR detected etiology in 38 (27.1%) out of 140 cases of non-pyogenic meningoencephalitis; including HSV(15%,n=21)and Enteroviruses (12.1%,n=17). Viral meningitis and encephalitis contributed more to mortality (6.42%,n=9) as compared to bacterial meningitis (3%,n=3).

**Conclusions:** Early diagnosis of CNS infections is important to prevent morbidity and mortality. Immunization has a vital role in minimizing the burden of CNS infections in the community. In our study, 79% of cases were immunised against H.Influenza which explains the low incidence as a causative agent in our study. Herpes

simplex virus and enteroviruses contribute significantly to the meningoencephalitis burden. As molecular diagnosis cannot be established in all cases of viral meningitis and encephalitis, timely initiation of empirical treatment is pivotal to prevent associated complications.

**Keywords:** NIL

## Introduction

Acute encephalitis and meningitis are central nervous system (CNS) infections with serious clinical manifestations(1). The most common etiological agents are viruses and bacteria. Bacterial meningitis is mainly caused by *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*, and enteric Gram-negative bacteria(2). It continues to be a cause for concern in low and middle-income countries either due to the low level of vaccine coverage or non-availability of these vaccines in their national immunization programs(3). Identifying the etiology of acute encephalitis is challenging. The most common viral agents involved, are human herpes viruses, enteroviruses, flaviviruses, and alphaviruses(4). Improved diagnostic tools such as Polymerase chain reaction have increased the yield of etiologies for encephalitis (5).

In this study, we evaluated the clinical profile, determined the etiology and the outcome of the children with acute meningitis and encephalitis admitted in the hospital.

## Methods

This study was conducted in the Department of Pediatrics of Government Medical College Srinagar over a period of two years. All children aged 1 month to 18 years of age with signs and symptoms suggestive of meningitis and/or encephalitis (severe headache, photophobia, nausea/vomiting, meningeal signs, rash, altered mental status, seizures, and lethargy) were enrolled. Patients with tubercular meningitis and pre-existing VP shunt in situ were excluded. Blood investigations including complete blood count, renal and liver function tests were done.

## Results

### Bacterial meningitis

CSF was collected prior to administration of antibiotics in all patients and sent for routine microscopy, biochemical analysis, and gram staining. The CSF sample for bacterial culture was inoculated into the Bact/Alert PF plus culture bottles and two automated systems namely BacT/Alert system and Vitek 2 compact were used for the early detection of organisms and their antibiotic sensitivity patterns.

CSF samples were preserved at -80 C for viral PCR. The viral PCR testing was done in samples with suspected viral etiology based on microscopy and biochemical parameters and in cases where no organism was isolated on gram staining and bacterial culture.

For HSV detection, Conventional PCR was used. Total DNA was extracted from the cerebrospinal fluid by the SDS – proteinase K - phenol-chloroform method as described by Sambrook and Russell (6). The detection was carried by PCR using primers which amplified the conserved region of the DNA polymerase gene from the herpes virus using primers P1 (5'-CGACTTTGCC AGCCTGTACC-3')

and P2(5'-

AGTCCGTGTCCCCGTAGATG-3 given by Rozenberg and Lebon(7). Human Enteroviruses were tested in the CSF samples using a real-time RT-PCR by artus Enterovirus LC RT-PCR Kit RUO.

Statistical analysis: Data was entered in a Microsoft Excel spreadsheet analysed using EpiInfo. Categorical variables were summarised as frequency and percentage. Continuous variables were summarised as mean and standard deviation, and categorical variables were compared by chi-square test.

**Table 1 gender distribution in bacterial meningitis**

Gender	No. of cases	Percentage (%)
Male	53	53
Female	47	47
Total	100	100

Among 100 cases of bacterial meningitis 53 were males and 47 were females, with a male to female ratio as 1.1:1 as shown in table 1.

**Table 2 clinical presentation**

Clinical symptom	No. of cases
Fever	95
Vomiting	75
Neck stiffness	51
Headache	50
Altered sensorium	35
Seizures	34
AF bulging	12

The most common presentation in patients with CSF suggestive of bacterial etiology was fever in 95 cases, followed by vomiting, neck stiffness and headache in 50 cases. The less common presentations were altered sensorium, seizures and bulging AF which were present in 35, 34 and 12 cases respectively as shown in table 2.

**Table 3 gram staining in bacterial meningitis**

Gram staining	No. of cases
Gram positive cocci	35
Gram negative bacilli	28
Gram negative diplococci	6

On gram staining, organism was found in 67 cases. Gram positive cocci were found in 35 cases, gram negative bacilli in 28 and gram negative diplococci were seen in 4 cases as depicted in table no. 3

**Table 4 bacterial culture**

	No. of cases	Percentage(%)
S pneumonia	19	19
E.coli	9	9
H. influenza	6	6
MRSA	6	6
Enterococcus	3	3

Klebsiella	7	7
MSSA	4	4
Neisseria species	4	4
Pseudomonas	1	1
Culture negative	41	41
Grand total	100	100

Csf culture was positive in 59 cases.among those 59 streptococcus pneumonia was seen in 19 cases ,e.coli in 9 h influenza and MRSA in 6 cases each, klebsiella in 7 cases ,MSSA in 4 cases ,Nei sseria in 4 , enterococcus in 3 cases and pseudomonas aeruginosa in 1 case as shown in table no. 4.

**Table 5 prior antibiotic use**

	No. of cases	percentage
Bacterial meningitis	100	41.67
yes	43	17.92
No	57	23.75

As shown in table 5 prior antibiotic was used in 43 cases .

**Table 6 outcome of bacterial meningitis**

	No. of cases	Percentage
Death	3	3.0
Discharged	97	97.0
Total	100	100

Among 100 cases, of bacterial meningitis 97 patients were discharged and 3 patients died in hospital as shown in table 6

**Viral meningitis**

**Table 7 viral PCR**

PCR	NO of cases	percentage
Negative	70	66.67
HSV	20	19.05
ENTEROVIRUS	15	14.29
TOTAL	105	100

Among 105 cases of viral meningitis ,CSF PCR was positive for HSV in 20 cases and enterovirus in 15 cases .and in rest 70 cases CSF PCR was negative for both organisms as shown in table no. 7

**TABLE 8 Outcomes of viral meningitis**

	No of cases	percentage
Viral meningitis	105	43.75
Discharged	104	43.33
Death	1	0.42

Out of 105 viral meningitis patients , 104 were discharged home in stable condition and there was death of one patient in hospital as shown in table 8

### Viral encephalitis

**Table 9 clinical presentation**

Presentation	No. of cases
Altered sensorium	35
Fever	30
Seizures	26
Cranial nerve palsy	22
Vomiting	15
AF bulging	15
Headache	7
Hemiplegia	4
Aphasia	2
Neck stiffnes	2
Paraplegia	1

Regarding viral encephalitis patients , out of 35 patients fever was present in 30 ,seizures in 26 patients, cranial nerve palsy in 22 cases, vomiting in 15 , AF bulging in 15 cases , headache in 7 cases , hemiplegia in 4 patients, aphasia in 2 cases, neck stiffness in 2 patients and paraplegia in 1 patient as shown in table no. 11.

**Table 10 Viral PCR**

PCR	NO. OF CASES	Percentage
Negative	32	91.42
Positive	3	8.58
Grand total	35	100

Out of 35 cases , 32 were negative for for PCR and 3 were negative.

**Table 11 Outcome of viral encephalitis**

	No of cases	Percentage
Encephalitis	35	14.58

Death	8	3.33
Discharged	27	11.25

Among 35 cases, 27 patients of encephalitis were discharged and 8 patients died in the hospital as shown in table no. 11.

## Discussion

In the current era, the introduction of newer vaccines against Hib and Pneumococcus has changed the epidemiology of meningitis and has substantially decreased morbidity and mortality(8). In India, there has been an age-standardised decline in mortality due to meningitis by at least 50% from 1990 to 2016 which is still low as compared to other vaccine-preventable illnesses(9). In recent years, acute encephalitis and aseptic meningitis have been an area of interest as etiology can be better understood with the advent of newer diagnostic modalities including Polymerase Chain Reaction. Viral agents responsible for sporadic encephalitis include Varicella zoster virus, Mumps, Human herpes virus 6 and 7, Epstein Barr virus, and most importantly, Herpes simplex virus. Herpes simplex virus encephalitis (HSE) is the most common cause of sporadic fatal viral encephalitis, with an incidence of 1-3/million in western countries (10). Not much information is available regarding the proportion of AES cases due to HSE in the Indian setting. In Western studies, mortality is high in untreated patients (70%), which decreases significantly to 30% in treated patients with a risk of sequelae of around 11%(11).

In this study, 52.2% of our study population was comprised of males. The mean age of subjects in our study was 4.3 years depicting more involvement in the under 5 years age group. In the bacterial meningitis group, the most common presentations were fever, vomiting, headache, and neck stiffness. Seizures were the presenting symptom in 34% of cases. Gram staining was positive for 67% of cases and culture was positive for 59% of cases which has a higher yield as compared to previous studies (12)(13) and can be attributed to the collection of CSF samples prior to antibiotic administration. The most common organism isolated on CSF culture was *S. pneumoniae* which was 32.2% of the total culture-positive cases. Other organisms isolated were gram-negative bacilli like *E. coli* and *Klebsiella* predominantly involving young infants. The

declining isolation of *H. Influenzae* and *Neisseria* can be attributed to the better vaccination coverage in our study population.

In the viral meningitis group, the presenting symptoms were fever, headache, vomiting, and seizures. There was a distinct lack of difference in symptoms between cases of bacterial and aseptic meningitis as seen in previous studies(14). Out of 105 cases of viral meningitis, etiology could be established in only 33% cases, 19% tested positive for HSV and 14% were positive for Enterovirus establishing more prevalence of HSV in our study population which is in contrast with the other studies in South Asian region(15).

The clinical presentation in the encephalitis group was different from bacterial and viral meningitis with fever and altered sensorium as the most common presenting symptom. Seizures (74%) and focal neurological deficits(82%) were present more in the encephalitis as compared to meningitis. The PCR was positive for HSV-1 in 2.8% and enterovirus in 5.7%, with unknown etiology in 91% of cases of encephalitis depicting the need for testing of other viruses in our study population. These observations were similar to the other studies in the western population(16)(17).

In this study, viral meningitis and encephalitis contributed more to mortality as compared to bacterial meningitis. This could be attributed to unknown etiology in the viral encephalitis group, absence of definitive therapy, and rapid progression to severe neurological involvement including poor sensorium, status epilepticus, raised ICP, and multiple cranial nerve palsies with focal deficits.

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authors approve the present version for publication and are accountable for all aspects related to the study.

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