

# Association of Clinical Features of Acute Viral Encephalitis with Mortality and Neurodevelopmental Outcomes

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## Abstract

**Background :** Acute viral encephalitis is a world-wide health problem with severe morbidity, significant mortality and a high incidence of residual sequelae in survivors.

**Objective :** To identify the association of clinical features of acute viral encephalitis with mortality and neurodevelopment outcomes.

**Methodology :** It is a hospital based comparative observational prospective study done in Dhaka Shishu Hospital during the period of October 2005 to March 2006. Children with 1 month to 12 years of both sex presenting with specific clinical features and laboratory evidences suggestive of acute viral encephalitis (seizures, altered consciousness, features of raised intracranial pressure, cerebrospinal fluid evidences of viral encephalitis) were included. 44 children were enrolled according to inclusion criteria. Data were collected on clinical and socio demographic status. SPSS 16 version program was used for data analysis.

**Result :** Among the 44 cases, the mean age below 2 years was 14 months and above 2 years was 66 months. The incidence of acute viral encephalitis was highest within first 3 years of age. Most of the mortality 8(72.73%) occurred in low income group (P=0.003). 29(66 %) patients had Glasgow Coma Score < 8 on admission, low Glasgow Coma Score at presentation had significant association with outcome, 11(100%) patients who died had Glasgow Coma Score < 8(P=0.003). 28(68 %) patients stayed in hospital for > 7 days, indicating more time taking for improvement from acute illness. There was significant association of duration of hospital stay and outcome (P=0.008). In Neurodevelopmental assessment domains were Gross motor, Fine motor, Vision, Hearing and Cognition and impairments were different in different patients. Impairments persisting in different domain at follow up comparing with admission showed satisfactory improvement. Improvement was significant in case of Gross motor (P=.005), Fine motor (P=.08) and Cognition (P=.09).

**Conclusion :** It was observed from this study that children with acute viral encephalitis are at high risk of mortality and morbidity. Lower age at presentation, low socio-economic status, low Glasgow Coma Score on admission and short duration of hospital stay were associated with high mortality and were at high risk of future neurodevelopmental impairments.

**Key words :** Clinical features, encephalitis, neurodevelopmental, mortality.

## Introduction

Acute viral encephalitis is uncommon complication of common systemic viral infection remarkably little is known about the factors that determine why a few patients are affected but most are not<sup>1</sup>, there is variable degree of involvement of brain tissue and

meninges. In most instances, the infections are self-limiting, however in some cases substantial morbidity and mortality occur<sup>2</sup>. It continues to be a worldwide health problem with severe morbidity, significant mortality and a high incidence of residual sequelae in survivors<sup>3</sup>. Acute viral encephalitis occurs most commonly in the first decade of life with a peak incidence of 1-2 cases per 1000 in first 6 months of life. In children mortality rate ranges from 3.8 to 28%<sup>4</sup>. Study done in American pediatric population showed that 40% of children who recovered from acute viral encephalitis had persistent non progressive neurological abnormality<sup>5</sup>. Commonest causative agents are Enterovirus which is responsible for more than 80% of all causes. Other frequent causes of infection include Arbovirus, Respiratory virus, Rubella, Mumps, Varicella zoster, Cytomegalo virus<sup>3</sup>.

Clinical features resulting from infection with same pathogen varies widely. Some children may appear to be mildly affected initially, only to lapse into coma and die suddenly. In others, the illness may be ushered in by high fever, violent convulsion interspersed with bizarre movements and hallucinations alternating with brief periods of clarity, followed by complete recovery<sup>2</sup>. In Finnish studies, the most characteristic neurologic symptoms of viral encephalitis during the acute phase were lowered consciousness manifested by disorientation, confusion, somnolence or coma. These symptoms were recorded in 58% of patients. Ataxia was seen in 58%, an altered mental status, notable aggressiveness, and apathy were seen in 40%, seizures, either generalized (32%), focal (5%), or both, were encountered less commonly, neurologic finding were generally nonspecific and meningeal symptoms and signs were not always present. Focal sign on neurologic examination and abnormal neuroimaging studies were the only two factors present on admission that predicted a poor short-term outcome<sup>6</sup>.

## Methods

Total forty four children were selected for this study according to inclusion criteria.

## Inclusion criteria

All children with specific clinical features and laboratory evidences suggestive of acute viral encephalitis<sup>2,6,7,8</sup>

(a) Seizures (b) Altered consciousness (c) Features of

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raised intracranial pressure (d) CSF evidences of acute viral encephalitis (e) Age group: 1 month to 12 years.

**Exclusion criteria**

(a) Neonatal age group (b) Those with evidences of bacterial meningitis in CSF (c) Congenital malformation, neurodevelopmental delay including perinatal asphyxia or impairment prior to the development of this illness.

Neurodevelopmental impairment in Gross motor, Fine motor and Cognition were graded according to guidelines provided by World Health Organization 2001 (International Classification Of Functioning, Disability and Health) as mild, moderate or severe if functions were >50%, 25% to 50%, or <25% of the gold standard<sup>9</sup> (functional activities for chronological age).

In our study for the purpose of easy understanding we rearrange the grading as

1. No problem (0-4% impairment): Normal
2. Mild (5-24% impairment) and moderate (25-49% impairment) impairment: Some impairment
3. Severe impairment (> 50% impairment): Severe impairment.

Vision Graded as

1. Normal: If he / she had age appropriate vision
2. Some impairment: In between 1 and 3
3. Severe impairment: Only have light perception<sup>10</sup>.

Hearing graded as

1. Normal: If he / she had age appropriate hearing/ no or very slight hearing problems, able to hear whisper<sup>11</sup>
2. Some impairment: In between 1 and 3
3. Severe: No useful hearing<sup>10</sup>.

Final outcome of individual patient categorized as :

1. Normal : If achieved normal activities as before the illness and lowest score of normal among the 5 parameters regarded as normal
2. Cured with some impairment: In between 1 & 3
3. Cured with severe impairment: If patient had one domain with severe impairment.

Gross motor, fine motor, vision, hearing and cognition were assessed within 72 hours of hospital admission and in follow up after 3 month of hospital admission to assess the neurodevelopmental outcome.

Data were collected on clinical and sociodemographic status. Clinical data recorded using a structured performa which included details about the case history, clinical finding, laboratory investigations and management. Data were subjected to statistical analysis according to standard procedure. EPI info version 6.04 programs and SPSS 16 version program were used for data analysis.

**Result**

Follow up done after 3 months of hospital admission, among 44 patients of initial enrolment 17 patients returned back for follow up and 11 patients died. Rest 16 patients did not come.

Among the 44 patients the incidence of acute viral encephalitis was highest within first three years of age that is 29(63.6%). The mean age bellow 2 years was 14 months and above 2 years was 66 months. There was association of mean age with outcome (P=0.42). 8 (72.73%) death occurred in low income group (P=0.003). (Table 1)

**Table-1 : Sociodemographic characteristics of study population by mortality outcome (n=44)**

	Description	Follow-up completed group (%)	Death group (%)	Dropout group (%)	P value	Df
Age group	1 year	04 (23)	03 (27)	04 (25)	0.476	20
	1-2 year	04 (23)	04 (36)	04 (25)		
	2-3 year	01 (06)	02 (18)	02 (12)		
	3-4 year	0 (00)	01 (09)	02 (12)		
	4-5 year	02 (12)	0 (00)	0 (00)		
	5-6 year	03 (18)	0 (00)	02 (12)		
	6-7 year	0 (00)	0 (00)	02 (12)		
	7-12 year	03 (18)	1 (06)	0(00)		
Socio economic Status	Low income	01 (06)	08 (73)	07 (44)	0.009	6
	Lower middle income	08 (47)	02 (18)	05 (31)		
	Upper middle income	04 (23)	0 (00)	04 (25)		
	Higher income	04 (23)	01 (09)	0(00)		

29 (66%) patients had Glasgow Coma Score < 8 on admission, low Glasgow Coma score at presentation had significant association with outcome, that is all the 11(100%) patients who died had Glasgow Coma Score <8 (P=0.036) on admission.

28(68%) patients stayed in hospital for >7 days indicating more time taking for improvement from acute illness. There was significant association of duration of hospital stay and outcome (P=0.008).

27(61.4%) patients had history of duration of fever for 4-7 days on admission, there was no significant association between during of fever and outcome.

26 (60%) patients got antiviral treatment, rest 18 (40%) patients did not get antiviral treatment may be due to higher cost of drugs, problem isolation of organism and unavailability of specific anti viral drugs. (Table II.)

**Table-II : Clinical characteristics of study population by mortality outcome (n=44)**

Clinical characteristics	age distribution	Follow up completed group	Death group(%)	Drop out group(%)	P value	Df
<b>Glasgow coma score</b>	Up to 3 days	09 (53)	06 (54)	05 (31)	0.393	3
	4-7 days	07 (41)	05 (45)	08 (50)		
	>7 days	01 (06)	0 (00)	03 (19)		
<b>Hospital Stay</b>	1-3 days	01(06)	04(34)	01(06)	0.008	3
	4-7 days	02(12)	05(45)	03(18)		
	>7 days	14(82)	02(18)	12(36)		
<b>Duration of fever</b>	Up to 3 days	09(53)	06 (54)	05 (31)	0.393	3
	4-7 days	07(41)	05(45)	05(50)		
	>7 days	01 (06)	0(00)	03 (19)		
<b>Antiviral treatment</b>	Yes	12 (76)	07(64)	07 (44)	0.275	2
	No	05(29)	04(36)	09 (56)		

Among the 17 patients who completed the follow-up, there was much improvement in every domain after 3 months of hospital admission.

There were total (17x5=85) 85 domains; improvement was present in 68 domains on admission and 29 domains on follow-up. So one patient had on average, impairments in 4 domains on admission and < 2 domains on follow up (Table-III).

Impairment persisting in different domain at follow up, comparing with admission showed satisfactory improvement. Improvement was significant in case of Gross motor (P=.005), Fine motor (P=.08) and cognition (P=.09). (Table III)

**Table-III : Status of neurodevelopmental parameters on admission & follow up completed**

Domain	Grading	Admission	Follow up	p value
Gross motor	Normal	05 (29)	06 (36)	0.005
	Some impairment	02 (11)	10 (59)	
	Severe impairment	10 (59)	01 (06)	
Fine motor	Normal	05 (29)	09(53)	0.08
	Some impairment	01(06)	05(29)	
	Severe impairment	11(65)	03(18)	
Vision	Normal	09 (53)	13 (76)	0.113
	Some impairment	01 (06)	01 (06)	
	Severe impairment	07 (41)	03 (18)	
Hearing	Normal	10 (59)	15 (88)	0.669
	Some impairment	0 (00)	00 (00)	
	Severe impairment	07 (41)	02 (12)	
Cognition	Normal	08 (47)	13 (76)	0.09
	Some impairment	0 (00)	02 (12)	
	Severe impairment	09 (53)	02 (12)	

## Discussion

This study revealed that 52.3% acute viral encephalitis cases were below 2 years of age with mean age 14 months, our observation were same as with the study done in Pakistan, a developing country like Bangladesh, Kennedy CR et al<sup>4,7</sup>. The high incidence of acute viral encephalitis in this age group may be due to immunodeficiency, malnutrition and vulnerability of infection which is more prevalent in the developing country. Low socioeconomic status increases the incidence of central nervous system infection<sup>1,2</sup>.

16(36%) and 15(34%) admitted patients came from low and lower middle income group respectively and most of mortality, 8(73%) death occurred in low income group(p=.009) may be due to that low income group were generally malnourished, uneducated and lived in overcrowded places which decreases body immunity and increases the mortality. Michael J et al showed similar findings in there study that there was significant association between mortality and low income group (P < 0.01).<sup>13</sup>

29(66%) patients had Glasgow Coma Score < 8 on admission reflecting impaired consciousness at the time of presentation, which had significant association(P=0.02) with outcome, 9(53%) patients of follow up completed group had Glasgow Coma Score < 8 on admission and all the 11(100%) patients (Table-1) who died had Glasgow Coma Scale <

8 on admission. In this study there was no association between duration of fever with outcome. 28(68%) patients stayed in hospital >7 days indicating more time taking for improvement from acute illness, there was significant association (p=.003) between duration of hospital stay and outcome. Gitali Kakoti et al did similar study in India and there result was consistent with our study result<sup>14</sup>. Impairment persisting in different domain at follow up, comparing with admission showed satisfactory improvement. Improvement was significant in case of Gross motor (P=.005), Fine motor (P=.08) and cognition (P=.09). (Table III) This result was nearer to the study of Kennedy CR et al<sup>7</sup>. Their finding was 17% death and 42% moderate to severe handicap, which was almost similar to our study (25% death, 46% some impairment and 18% severe impairment).

## Conclusion

This study showed lower aged at presentation, low socio- economic status, low Glasgow Coma Score on admission and short duration in hospital are associated with high mortality and are at risk of future neurodevelopmental impairments.

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