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Study of clinical and etiological profile of acute viral encephalitis in children

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Abstract

Introduction: Acute encephalitis is the clinical diagnosis of children with signs of inflammatory lesions in the brain. Very few studies of viral encephalitis with etiological diagnosis have emanated in India. We present the clinical and etiological study of acute viral encephalitis in children admitted in a tertiary care centre.

Methods: A descriptive, observational study was conducted at a paediatric tertiary care centre in association with department of Pathology and Defence Research and Development Establishment, Gwalior. Blood, cerebrospinal fluid and serum samples were collected from Pediatrics patients aged 1 month to 15 years suffering from acute encephalitis admitted from 1st July 2017 to 31st June 2018. Viruses were identified by carrying out molecular tests (Polymerase Chain Reaction) of both serum and CSF.

Results: Seventy eight patients were enrolled in our study. Viral etiology was confirmed in 16(20.5%) cases using Polymerase chain reaction. Most common virus identified in our study was Herpes Simplex virus-1 which was found in 7 (43.75%) cases, followed by Enterovirus-71 in 5 (31.25%), Epstein Barr Virus in 2 (12.5%) and Measles and Dengue virus in 1 case each (6.5%). Most common clinical feature was fever (91%) followed by altered sensorium, headache and seizures. Most of the cases showed increased cell count (80.76%), decreased sugar (55%) and increased protein (58.97%) in cerebrospinal fluid.

Conclusions: New molecular techniques facilitate early diagnosis of viral encephalitis and can prove a big asset to the health care. Herpes simplex virus was major cause of viral encephalitis in our study. More such studies are required to assess the role of emerging viruses causing viral encephalitis in different regions.

Keywords: Children, CSF, enterovirus, herpes simplex virus, viral encephalitis

1. Introduction

Acute encephalitis is the clinical diagnosis of children with signs of inflammatory lesions in the brain. The clinical picture usually consists of a prodromal phase (one to three days) with fever, malaise, headache and altered level of consciousness, seizures, abnormal movements or paralysis. It can lead to considerable morbidity and mortality. If infection is not fatal, individuals often have severe physical, cognitive, emotional, behavioural, and social difficulties [1]. Although bacteria, viruses and protozoan parasites may cause encephalitis, among these the viruses are the most common cause of encephalitis. Epidemiologic studies estimate the incidence of viral encephalitis (VE) at 2.5–8.8 per 100 000 persons per year [2, 3]. However the annual incidence of VE is most likely underestimated, especially in developing countries where there are problems with pathogen detection. Very few studies of VE have emanated from India, although it can be considered the epicentre of many emerging viral diseases.

Cases of viral encephalitis have been reported from many states of India, but aetiological agent has been identified in only 20-30 % cases [4]. Every day new viruses are being associated with encephalitis of varying severity. Effective interventions exist for some causes of encephalitis. Vaccination against mumps, measles, and rubella has substantially reduced the number of encephalitis cases associated with these diseases [5]. Herpes simplex virus (HSV) and varicella zoster virus (VZV) have well established antiviral treatments.

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Timely and appropriate treatment is crucial for improving acute encephalitis outcome; hence, rapid identification of the cause is key.

We present the clinical, laboratory and etiological results of an observational study of children with viral encephalitis in a tertiary care centre in Madhya Pradesh.

2. Methods

This study was a hospital-based descriptive, observational study conducted at a paediatric hospital in collaboration with Department of Pathology, GRMC, Gwalior and Defence Research and Development Establishment (D.R.D.E) Gwalior over a period of 1 year, i.e. from 1st July 2017 to 31st June 2018. Patient age varied from 1 month to 15 years. Acute encephalitis was defined by fever < 1 week duration, with or without altered sensorium, seizures, headache, vomiting, abdominal pain &/or neurological deficit. Patients with seizure disorder, febrile convulsions, bacterial meningitis, head injury, tuberculosis, brain tumour, cerebral malaria, metabolic disorder were excluded from the study. Detailed clinical history was elicited from the attendants after explaining the purpose of the study and obtaining verbal informed consent. Results of routine blood investigations along with CSF examination were noted. Viral agents were identified by carrying out polymerase chain reaction/reverse transcriptase polymerase chain

reaction (PCR/RT-PCR) examination of both serum and CSF.

3. Results

The study group comprised a total of 78 children in age group 1 month to 15 years with maximum number under 5 years (59%) of age (Table 1). Male to female ratio was 1.3:1. 67 children (85.89%) belonged to the lower socio economic class as per the Kuppuswamy scale [6].

Table 1: Age and sex wise distribution of patients (n=78)

Age group	Male	Female	Total
0-5 years	23	23	46(59%)
6-15 years	21	11	32(41%)
Total	44	34	78(100%)

Virus identification was possible in a total of 16 (20.5%) cases. No statistically significant difference was found in positivity in male and female. Most common virus identified in our study was HSV-1 which was found in 7 (43.75%) cases, followed by Enterovirus-71(EV 71) in 5 (31.25%), Epstein Barr Virus (EBV) in 2 (12.5%), and Measles virus (MV) and Dengue virus (DV) in 1 case each (6.5%). In all these cases viruses were identified by PCR/ RT-PCR (Table 2). No Japanese B encephalitis was identified in our study.

Table 2: Diagnosis of viral etiology

Virus causing encephalitis	Total Positive	Positive in CSF	Positive in serum
Herpes Simplex Virus	7	7	5
Enterovirus	5	5	1
Epstein Barr Virus	2	2	2
Dengue virus	1	1	1
Measles virus	1	1	1

Majority of patients with encephalitis had fever (91%) during the presenting illness (Table 3). Most of them also had altered sensorium (79.48%), headache (51.28%) and seizures (51.28%). Vomiting (47.43%), neurological signs (19.23%), rashes (6.4%) and upper respiratory tract

infection (URTI) (5.1%) were also recorded (Table 3). Seizures appeared to be significantly associated with HSV and EV-71. Skin rash was present in 5 patients, 4 with HSV and 1 with MV. Total 5 patients (6.4%) died, 2 were diagnosed with HSV and 1 with EBV.

Table 3: Comparison of clinical features of patients with viral etiology.

Clinical features	Total cases	HSV	EV	EBV	DV	MV
Fever	71(91%)	6	3	2	1	1
Altered sensorium	62(79.48%)	5	4	1	1	1
Seizures	40(51.28%)	5	3	1	0	1
Headache	40(51.28%)	2	3	2	0	1
Vomiting	37(47.43%)	5	3	1	1	0
Neurological signs	15(19.23%)	3	2	0	0	1
Rashes	5(6.4%)	4	0	0	0	1
URTI	4(5.1%)	0	1	1	0	1
Mortality	5(6.4%)	2	0	1	0	0

CSF cell count was increased in 63 cases (80.76%). Out of the 78 cases, 23(29.48%) showed normal (> 50mg/dl or 75% of serum glucose) while 43 cases (55%) showed

reduced CSF sugar. CSF protein was found to be normal (20-45mg/dl) in 19 cases (24.35%) and increased in 46 (58.97%) (Table 4).

Table 4: Biochemical findings of CSF examination

CSF (normal values)	Normal	Increased	Decreased
Cell count(<5/cmm, >= 75% lymphocytes)	15 (19.23%)	63 (80.76%)	-
Sugar(>50 mg/dl or 75% of serum glucose)	23 (29.48%)	12 (15.38%)	43(55%)
Protein(20-45 mg/dl)	19 (24.35%)	46 (80.76%)	13(16.68%)

4. Discussion

Various aetiological agents cause CNS infections even in the same geographical location [7]. For better management of patients, it is important to understand the profile of viruses causing encephalitis in the given area so that necessary immediate treatment can be started before laboratory results are available.

About one-fifth of patients presenting with viral encephalitis had a proven infectious cause in this study. Similar results were obtained in studies conducted by Beig *et al.* [8] and Rathore *et al.* [9]. On the contrary, studies done at New Delhi, Karnataka and Uttar Pradesh showed more than 50% positivity of viral etiology [7, 10, 12].

Majority of positive cases in our study were below 5 years of age. Similar trend of small children being affected more is shown in earlier studies [7, 8, 12-14]. The number of boys with acute encephalitis enrolled in our study was higher but viral positivity in both sexes was similar. Studies done by Kabilan L *et al* and Sharma J *et al* had similar findings [15, 16]. The most common etiological agent of VE in our study was HSV-1, which occurred in 43.75% of positive cases, followed by EV-71 in 31.25% cases. Herpes group remains the most common causative agent in acute sporadic encephalitis cases in the developed world [17] and in India too [8, 9-11]. EV-71 is emerging as an important encephalitogenic virus. Owing to poor sanitation services, overcrowding, and lack of awareness of good hygiene habits in developing countries, it forms an important causative agent causing viral encephalitis in children as shown in previous Indian studies [7, 8].

In our study only 1 case was positive for Measles virus. This girl was not vaccinated for measles. Before the start of nationwide MMR vaccination programs, mumps and measles were most common causative agents detected in encephalitis suspected children. From developed countries, these organisms have almost disappeared; however, they continue to be most common causative agents of AES in developing countries like India, probably because of suboptimal immunisation rates [11].

One case was found to be positive for Dengue encephalitis in our study. In contrast, in a Thai study, dengue virus was identified in a maximum number of cases, followed by Japanese encephalitis virus (JEV), HSV, human herpes virus 6, EV, VZV, and rabies [19]. JEV, although a major health problem in India causing frequent outbreaks and high mortality [15, 20, 21], no case was reported in our study. Thus, a wide variation exists in the viral etiological agents across the country. Several factors such as age, geographic location, season, climate, and host immune competence affect the epidemiology of VE.

Fever, convulsions along with altered sensorium were the significant 'trio of clinical features' in our study in patients with VE. Similar findings were reported earlier by Beig *et al.* [8]. In other studies, focal neurological signs with alteration of consciousness have been the major findings [3, 19]. Of the 78 encephalitis cases in our study, 6.4% died. Previous studies report higher mortality (32.1%, 17%) [8, 19]. We could not establish any association of mortality and clinical signs/symptoms and CSF or blood investigations. In contrast, Avabratha *et al* revealed association between mortality and meningeal signs in encephalitis patients [22]. A point worth mentioning here is that ours is an ongoing study with small number of patients. More number of patients

might help in establishing any association of mortality with other factors.

Out of 78 cases in our study, CSF pleocytosis (CSF cell counts > 5 cells /cmm) was seen in most of the cases (80.7%), similar to study done by Jain *et al* (2015) with pleocytosis in more than 90% cases. We found viral etiology in CSF of all 16 positive cases, while serum showed positivity in 10 cases (62.5%). Beig *et al* study demonstrates contradictory result with more cases (21.7%) positive in serum as compared to CSF (12.6%) [8].

5. Conclusions

Microbiological diagnosis of VE is difficult. New molecular techniques like RTPCR facilitate early diagnosis of viral encephalitis and can prove a big asset to the health care. HSV is an important cause of VE in children in our centre. Specific antiviral therapy is available (acyclovir) for it and early diagnosis can alert the clinician for timely initiation of specific therapy and prevent the high mortality and morbidity which can occur in absence or delay in treatment. There is a need for further studies to delineate the etiologies of viral encephalitis.

6. Declarations

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Conflict of interest: None declared

Ethical approval: Not required

7. References

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