

To Study the Different Infectious Etiology of Acute Febrile Encephalopathy in Children

Mahendra Kumar Pandey¹, Akshay Shukla², Swaroop Anand³, Raghuveer Siddeshwar Anantpur⁴

¹Assistant Professor, Dept. of Pediatrics, Rama Medical College and Research Center, Mandhana, Kanpur

²Assistant Professor, Dept. of Pediatrics, Rama Medical College and Research Center, Mandhana, Kanpur

³Senior Resident, ASMC, Mirzapur

⁴3rd Year Paediatric Resident, Dept. of Pediatrics, Rama Medical College and Research Center, Mandhana, Kanpur

Received: 30-05-2023 / Revised: 19-06-2023 / Accepted: 02-08-2023

Corresponding author: Dr. Raghuveer Siddeshwar Anantpur

Conflict of interest: Nil

Abstract:

Background & Method: The aim of the study is to study the different infectious etiology of acute febrile encephalopathy in children. This is prospective study of the patients of age group 2 months to 12 years with acute febrile encephalopathy during of period of one year. All patients admitted with a clinical diagnosis of AFE were included if they satisfied the inclusion criteria. A total of sixty subjects were analyzed.

Result: A male predominance was noted with ratio of 1.5:1.

Conclusion: Our study in subjects of acute febrile encephalopathy has shown that viral encephalitis as the most common presentation followed by cerebral malaria. A male predominance was noted with ratio of 1.5:1. The majority of our patients made a complete recovery and a minor number of patients were also left with neurologic sequela. The cause for maximum morbidity was seen in patients with acute viral encephalitis, followed by pyogenic meningitis.

Keywords: Infectious, Etiology, Acute Febrile Encephalopathy & Children.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

The profile of acute febrile encephalopathy varies across different geographic areas and in different seasons. In tropical countries like India, cerebral malaria (CM), viral encephalitis (VE like Japanese encephalitis-JE), and bacterial meningitis are the common causes of AFE [1]. Japanese encephalitis (JE) is, at present, the single most important cause of viral encephalitis in Asia [2]. Viral encephalitis is a severe illness in children, with an incidence of 3.5-7.4 cases per 100 000 child-years. [3]

The annual incidence of viral encephalitis is most likely underestimated, especially in developing countries, because of problems with pathogen detection. It may be sporadic like herpes simplex encephalitis (HSE), or epidemic such as Japanese B encephalitis (JE).

Agents that may be encountered in an epidemic form include Japanese encephalitis, which is a major public health problem because of large endemic areas in the country, the high case fatality rate (20-30%) and frequent residual

neuropsychiatric damage (50-70%) [4]; Enteroviruses, especially EV 71 [5], reported also from sporadic encephalitis cases; Chandipura virus; Nipah virus; and, Chikangunya virus. Another common viral agent of AES in the epidemic setting, being recognized more commonly now, is Dengue virus [6].

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 [7]. Not much information is available regarding proportion of cases due to HSE in the Indian setting. In untreated patients, mortality is high (70%), which is decreased to 30% in treated patients (risk of sequela of around 11%).

Material & Method

This was a hospital based prospective study of the patients of age group 2 months to 12 years with acute febrile encephalopathy during of period of one year. This was conducted in the Pediatric Department of Tertiary Care Centre. All patients admitted with a clinical diagnosis of AFE were included if they satisfied the inclusion criteria. A total of sixty subjects were analyzed.

Inclusion criteria:

Children of age group two month to 12 years with acute onset of fever and symptoms with a duration of <14 days and >1 of the following signs (change

in mental status including confusion, disorientation, coma, or inability to talk; new onset of seizures (excluding simple febrile seizures) were recruited into the study.

Exclusion criteria:

Patients with features of febrile seizures, developmental delay, past history of encephalopathy, chronic disorders, reys syndrome, and non-infectious encephalopathy were excluded

Results

Table 1: Age and sex distribution

Age Group	Male	Female	Total
2m-12 months	5	8	13(22%)
1-5 Y	14	7	21(35%)
> 5 Y	16	10	26(43%)
TOTAL	35(58%)	25(42%)	60

Table 2: Blood Investigations in viral encephalitis

Blood investigations	Number of cases	Percentage
Leukocytosis	6	29
Leucopenia	2	10
Thrombocytopenia	3	14
Hyponatremia	5	24

Table 3: CSF analysis of viral encephalitis

CSF Analysis	Number of Cases	Percentage
Lymphocytic pleocytosis	17	90
Proteins		
Elevated proteins	6	28
Normal proteins	14	67
PCR positive	6	30
Normal CSF study	2	10
CSF PCR Enteroviruses	4	19
CSF HSV	2	19

Table 4: Etiology of Acute Febrile Encephalopathy

Diagnosis	Number of Cases	Percentage
Viral encephalitis	21	35
Cerebral malaria	16	27
Pyogenic meningitis	15	25
Aseptic meningitis	6	10
ADEM	2	3

Discussion

Among the etiology in VE Enteroviruses was the most common etiology noted followed by HSV. In two third of the cases included in the present study, no specific etiology was found and these were labeled as viral encephalitis due to other viruses (undetermined etiology). It is possible that a more detailed diagnostic work up such as serology and antigen detection by PCR for other viruses could have picked more etiologies Different studies from India shows Post-monsoon JE as the most common etiology of VE from many parts of India. However, several recent studies have reported that novel viruses such as Enteroviruses and chandipura virus

account for VE in the regions endemic for JE Cerebral malaria was the diagnosis in 27% of cases children in this study. Studies previously by Kumar et al [8] in their study on children with acute encephalopathy found cerebral malaria in only (0.5%) cases. Increased cases of cerebral malaria in our study may be due to the endemicity of malaria in central part of India. In the endemic areas, CM remains an important differential diagnosis in patients presenting with acute fever and altered mental state.[1]

Among the subjects of viral encephalitis slight male predominance was seen with ratio of male to female ratio was 1.1:1.similar results were also

noted in studies done in India under 5 age groups consists the predominant subjects 13 (62%). Among the clinical profile of the subjects other than fever, convulsions of GTCS was the most common pattern that was seen in 90% of cases. status epilepticus was noted in 38% subjects. Previous reports of incidence of encephalitis complicated with status epilepticus in children is about 3.8–13.7%. The reason of increased incidence of status epilepticus in our study group may because of being a tertiary referral centre with more serious patients are referred from other hospitals. CSF studies shows abnormalities in 90% cases[9]. Normal study was noted in 10% cases. Among the subjects of HSV one was presented with relapse which was reported in 25% in previous studies. Neuroimaging study was done in 19 subjects. No particular diagnostic pattern was noted in any of the subjects. One subject with clinical diagnosis of AIEF (15) has MRI features of predominant frontal lobe involvement.

Conclusion

Our study in subjects of acute febrile encephalopathy has shown that viral encephalitis as the most common presentation followed by cerebral malaria. The majority of our patients made a complete recovery and a minor number of patients were also left with neurologic sequela. The cause for maximum morbidity was seen in patients with acute viral encephalitis, followed by pyogenic meningitis.

References

1. Kothari VM, Karnad DR, Bichile LS. Tropical infections in the ICU. *J Assoc Physicians India* 2006; 54:291-8.
2. World Health Organization Japanese encephalitis. 2008. http://www.who.int/biologicals/areas/vaccines/jap_encephalitis/en/index.html.
3. Koskiniemi M, Korppi M, Mustonen K, et al. Epidemiology of encephalitis in children: a prospective multicentre study. *Eur J Pediatr*. 1997;156(7):541–545
4. World Health Organization. Acute Encephalitis Syndrome. Japanese encephalitis surveillance standards. January 2006. From WHO-recommended standards for surveillance of selected vaccine-preventable diseases. WHO/V&B/03.01. DocsPDF06/843.pdf
5. Sapkal GN, Bondre VP, Fulmali PV, Patil P, Gopalkrishna V, Dadhania V, et al. Enteroviruses in patients with acute encephalitis, Uttar Pradesh, India. *Emerg Infect Dis*. 2009; 15:295-8.
6. Kumar R, Tripathi S, Tambe JJ, Arora V, Srivastava A, Nag VL. Dengue encephalopathy in children in Northern India: clinical features and comparison with non-dengue. *J Neurol Sci*. 2008; 269:41-8.
7. Steiner I. Herpes simplex virus encephalitis: new infection or reactivation? *Curr Opin Neurol*. 2011; 24:268-74.
8. Kumar R, Mathur A, Kumar A, Sethi GD, Sharma S, Chaturvedi UC. Virological investigations of acute encephalopathy in India. *Arch Dis Child* 1990; 65: 1227-1230.
9. Acute infantile encephalopathy predominantly affecting the frontal lobe (AIEF): Jequier Gy-gax M, Deonna T, Maeder P, Mayor-Dubois C, Roulet-Perez E. *Eur J Paediatr Neurol*. 2011Mar;15(2):158-62.