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Original Research Article

Thrombocytopenia in children with acute encephalitis syndrome: a prospective observational study

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ABSTRACT

Background: The objective of this study is to find out the proportion of children with thrombocytopenia in acute encephalitis syndrome (AES); second, to compare the aetiology of AES in thrombocytopenic cases with non-thrombocytopenic cases; and finally, to find out clinical and laboratory predictors of thrombocytopenia in AES, as well as to study platelet aggregation and compare it in both scrub positive and scrub negative AES cases.
Methods: This prospective observational study was conducted on 176 children with presumed viral aetiology were investigated to find out the cause of AES.
Results: The majority of patients presented with thrombocytopenia. The most common aetiologies are Japanese encephalitis (JE). No significant difference was observed in the aetiology of AES between the thrombocytopenic and non-thrombocytopenic groups. Rash, bleeding, swelling, hepatomegaly, and splenomegaly were significantly more common in thrombocytopenic AES cases. Among the laboratory parameters, haemoglobin, PCV, and serum protein were found to be significantly low in the thrombocytopenic group. Liver enzymes, serum AST, and serum ALT were significantly high in the thrombocytopenic group. Platelet aggregation percentage was found to be significantly high in AES children who were positive for scrub typhus in comparison to other AES cases. Eighty-seven patients were discharged from the hospital. The mortality rate was 18%. There was no significant difference in the outcome of AES cases in relation to thrombocytopenia.
Conclusions: This approach may help clinicians in the diagnosis of AES due to the scrub along with other tests available. There was no significant difference in the short-term outcome of AES cases in relation to thrombocytopenia.

Keywords: Thrombocytopenia, AES, Children, Mortality, Scrub positive

INTRODUCTION

Acute encephalitis syndrome (AES) is a leading cause of hospitalisation and mortality among children in India. AES is defined as an illness in a person of any age and at any time of year characterised by the acute onset of fever with a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or the new onset of seizures (excluding simple febrile seizures). Other early clinical findings may include an increase in irritability, somnolence, or abnormal

behaviour greater than that seen with a usual febrile illness.[1]

This illness has a very wide variety of causes, both infectious and non-infectious. Non-infectious causes include toxins, chemicals, etc. Infections leading to AES include viruses, bacteria, protozoa, Rickettsia, fungi, and parasites, as these can invade the brain, causing AES.[2] An AES patient may have both infectious and non-infectious encephalitis; for example, a patient with viral encephalitis may have accompanying metabolic problems such as hyponatremia, liver dysfunction, or renal dysfunction.

The agents causing AES can vary from region to region and from time to time. Three phases of AES have been documented based on various surveillance reports in India: Prior to 1975, when a few instances of JE were detected, between 1975 and 1999, more JEV cases were reported with frequent outbreaks, resulting in the development of JE-endemic regions near the Gangetic plains and in parts of Deccan and Tamil Nadu. Between 2000 and 2010, a dramatic change was observed in the AES with a rise in non-JE outbreaks such as Nipah virus, Chandipura virus, and other enteroviruses.[3]

From January 2008 to August 2014, 44097 cases and 5728 fatalities were recorded in India as a result of AES. There is a significant increase in the number of reported cases, although there is a decrease in the fatality rate of around 13%. An average of 8139 cases per year have been reported from 2011 to 2013, and an increase of 22% has been noted over the period of 2003 to 2007.[4]

AES is a major public health problem in many states of India, including Uttar Pradesh, the country's most populous state. Cases of JE have declined in the Gorakhpur region (possibly because of vaccine campaigns) since 2006, but surprisingly, there has been no reduction in AES cases. Hospitals also continuously receive a large number of AES cases annually, some of which have proven aetiology, but for most of the patients, their etiological diagnosis could not be made. Rickettsial infections are one of the most important causes of AES in Uttar Pradesh. In the monsoon and post-monsoon months of every year, this illness occurs as outbreaks and epidemics. Treatment is mainly supportive; injection ceftriaxone intravenous is usually used, and empirical acyclovir is used occasionally.

Rashes and thrombocytopenia are significantly documented in AES cases at the time of presentation. More than 50% of AES cases presented with thrombocytopenia. In a similar study done at SGPGI, thrombocytopenia was found in about 50% of cases of AES admitted to the PICU, and in another study done at KGMU, Lucknow, thrombocytopenia was found in 16% of JE-positive AES cases.[5,6]

Thrombocytopenia is more common in AES cases in which causative organisms are known (like JE, dengue, scrub typhus, etc.). Of them, scrub typhus (the most common occurring rickettsial infection caused by Orientia tsutsugamushi) is most commonly associated with thrombocytopenia, which is due to platelet aggregation occurring in scrub typhus infection, known as pseudo-thrombocytopenia. Recent studies support pseudothrombocytopenia due to platelet aggregation in scrub typhus infection.[7]

In this study, we aimed to find out the proportion of children with thrombocytopenia in AES. Secondly, we attempted to compare the aetiology of AES in thrombocytopenic cases with non-thrombocytopenic cases and to correlate thrombocytopenia with the severity of AES. We also attempted to find out clinical and laboratory predictors of thrombocytopenia in AES, study platelet aggregation, and compare it in scrub-positive and scrub-negative AES cases.

METHODS

This prospective observational study was conducted at the department of paediatrics, King George medical university, Lucknow, Uttar Pradesh, a tertiary care teaching hospital, after receiving ethical approval from the institutional ethics committee (Ref. Code: 93rd ECM II B-Thesis/P9)**.** The duration of the study was one year (September 2018-August 2019).

Enrolment of cases

Consecutive children hospitalized with complaints of fever and either altered sensorium or/and new onset of seizures were studied. Those with possible or confirmed AES, according to the international encephalitis consortium 2013 (Table 1), were enrolled in the study.[8]

Children between the ages of 6 months and 14 years old with a fever for less than 7 days prior to the onset of neurological symptoms and an altered sensorium for more than 24 hours who were previously neurologically normal and whose parents consented to the study were the key inclusion criteria.

Children with known non-infectious causes of acute CNS presentation, including trauma, toxic exposure, cerebrovascular accident, malignancy, epilepsy, or suspected metabolic disorder, were excluded.

Sample size

Sample size was computed as for a prevalence study with dichotomous outcome using the formula:

$N=4\ z\alpha^2\ P(1-P)/W^2$

Where p is the expected proportion, zα is the standard, normal deviate and W is the total width of confidence interval. With p taken as 10% and Was 0.1, zα as 1.96, sample size came to 100 approximately.[9]

Data collection

Details about the patient's history and examination were recorded on a pre-designed data collecting form. The investigations include complete blood counts including platelet count, liver function tests, blood urea and creatinine, serum electrolytes, blood glucose level, peripheral smear and rapid test for malaria, CSF microscopy for cell count, protein, sugar and culture sensitivity, CSF IgM for J.E, CSF real time PCR for HSV-1, serum IgM for chikungunya, dengue, scrub typhus. Neuroimaging (if advised by the treating physician). Platelet aggregation test was done in children with a platelet count of more than 1 lac/ cu mm. Those diagnosed as pyogenic meningitis or tuberculous meningitis on the basis of clinical features and CSF analysis were not investigated for other etiologies like JE, dengue, herpes and scrub typhus.

Laboratory tests

Serum IgM ELISA for Orientia Tsutsugamushi was done using a commercial kit (InBios international, Inc., USA) as per the manufacturer's instructions. Serum IgM ELISA for dengue virus was done using commercial kit marketed by the ICMR-NIV, Pune, India, as per manufacturer's instructions. IgM ELISA for dengue virus and chickengunya virus was done using a commercial kit by the ICMR-NIV Pune, India, as per manufacturer's instructions. CSF IgM ELISA for JE virus was done using a commercial kit marketed by ICMR-NIV, Pune, India, as per manufacturer's instructions. CSF real-time PCR for HSV-1 was done using commercial kit (Agpath). Real-time PCR was performed on CSF samples using HSV-1 detect (Applied biosystems by the Thermofisher scientific) as per the manufacturer's instructions.

An optical density (OD) of 0.5 was considered positive.[10] Platelet aggregation test: (done by the CHRONO-LOG machine). It was done in those AES cases with a platelet count of more than one lakh/cu mm (Figure 1).

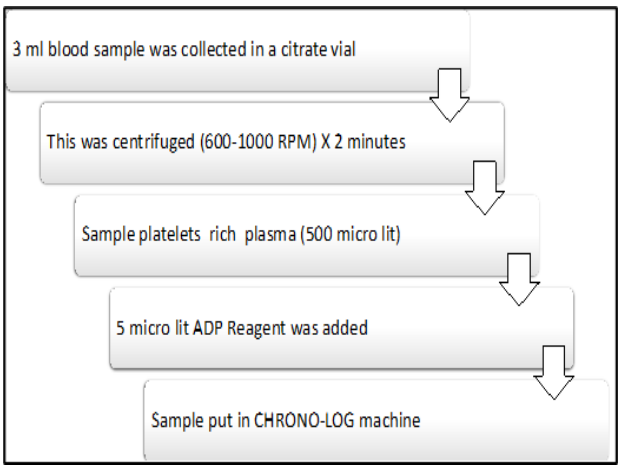

Figure 1: Platelet aggregation test.

Follow up of cases

All supportive treatment for AES was given. In addition, for a total of 7 days, injection ceftriaxone 100 mg/kg/day was given in 2 divided doses, and oral doxycycline (5 mg/kg/day) was administered twice daily. The patients were followed on a daily basis until discharge or other outcome. All the treatment received was carefully charted, including drug dose and duration. Vitals, temperature, feeding, GCS and condition upon discharge were all noted.

Statistical analysis

Statistical analysis was performed using SPSS version 23. ANOVA or 2 sample t-tests were used for continuous variables, while the Chi square test was used for categorical variables in univariate analysis. A p=0.05 or less was considered significant.

RESULTS

Patient flow

Over the course of the study, 176 children were screened for enrolment. Out of these, 6 patients were excluded because their parents were unwilling to participate in the study, while 4 patients died soon after arriving at the hospital and could not be enrolled. There were 29 cases of pyogenic meningitis and 9 cases of tuberculous meningitis. One hundred twenty-eight children with presumed viral aetiology were further investigated to find out the cause of AES (Figure 2).

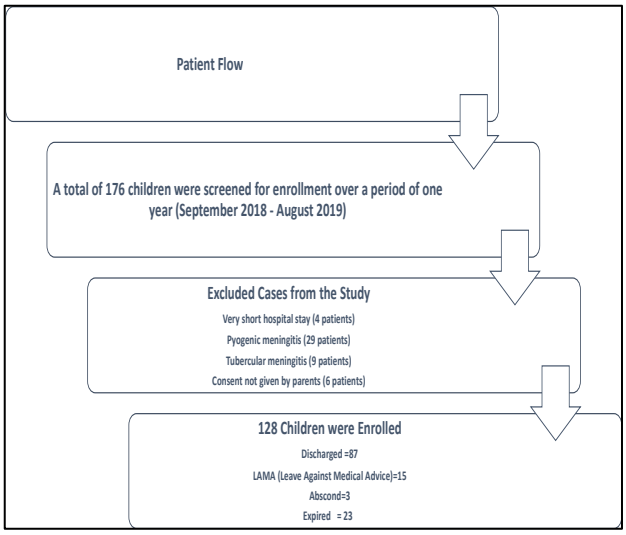

Figure 2: Patient flow.

Demographic profile

The maximum number of patients was between the ages of 1 and 10 years old. AES was found to be less common in children under the age of 1 year. The mean age of patients was 72.8±38.59 months. Males outnumbered

females, with a male-to-female ratio of 1.6:1. Majority of patients belonged to the lower socioeconomic group 121. (94.5%). Only 19 (14.8%) of the 128 patients resided in urban areas, while remaining 109 (85.2%) lived in rural areas. Out of 128 patients, 67 (52.3%) presented with thrombocytopenia (platelet counts <1.5 lakhs) (Table 2).

Table 1: Criteria for the diagnosis of acute encephalitis syndrome.[8]

Criteria	Diagnosis
Major criterion (required)	Patients presenting to medical attention with altered mental status (defined as decreased or altered level of consciousness, lethargy/personality change) lasting ≥24 h with no alternative cause identified.
Minor criteria (2 required for possible encephalitis; ≥3 required for probable or confirmed encephalitis)	Documented fever ≥38°C (100.4°F) within the 72 h before or after presentation
	Generalized or partial seizures not fully attributable to a preexisting seizure disorder
	New onset of focal neurologic findings
	CSF WBC count ≥5/cubic mm
	Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset
	Abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause.

Table 2: Thrombocytopenia and platelet count in enrolled patients of AES.

Thrombocytopenia	N	Percentage (%)	Platelet count (per cu mm)	N	Percentage (%)	
Present	67	52.3	<50,000	24	18.7	67 (52.3)
			50,000 to 99,999	29	22.7	
			1,00,000 to 1,49,999	14	10.9	
Absent	61	47.7	≥1.5 lac	61	47.7	
Total	128	100.0				

Table 3: Etiological profile of enrolled cases (n=128).

Etiology	N	Percentage (%)
JE	21	16.4
Dengue	14	10.9
Chikungunya	11	8.6
Scrub typhus	17	13.3
HSV-1	2	1.6
Leptospira	3	2.3
Typhoid	3	2.3
Malarial parasite	4	3.2
Unknown	53	41.4
Total	128	100

Table 4: Comparison of clinical features in thrombocytopenic AES cases with non-thrombocytopenic AES cases.

Clinical features	Thrombocytopenia, N (%)		P value
	Present	Absent	
Fever	67 (100)	61 (100)	NA
Headache	4 (6.0)	7 (11.5)	0.267
Vomiting	15 (22.4)	22 (36.0)	0.088
Diarrhoea	3 (4.5)	3 (4.9)	1.000#
Seizures	61 (91.0)	53 (86.9)	0.451
Altered consciousness	67 (100)	61 (100)	1.000#
Focal deficit	14 (20.8)	13 (21.3)	0.167
Mean Glasgow coma score	8.24 (2.8)	7.89 (2.7)	0.468
Rash	24 (35.8)	9 (14.8)	0.007
Breathing pattern (Hyperventilation)	29 (43.3)	18 (29.5)	0.106
Bleeding	20 (29.9)	9 (14.8)	0.042
Swelling	25 (37.3)	11 (18.0)	0.015

Continued.

Clinical features	Thrombocytopenia, N (%)		P value
	Present	Absent	
Signs of meningeal irritation	14 (20.9)	14 (23.0)	0.779
Fundus examination (Papilloedema)	5 (7.5)	4 (6.6)	1.000
Cranial nerve palsy	0 (0)	4 (6.6)	0.049
Abnormal movements	10 (14.9)	5 (8.2)	0.237
Signs of ↑ intracranial tension	44 (65.7)	48 (78.7)	0.102
Enlarged liver	45 (67.2)	27 (44.3)	0.009
Enlarged spleen	16 (23.9)	5 (8.2)	0.017

#Statistically significant

The most common aetiologies are JE, scrub typhus, and dengue infection, accounting for 16.4 percent, 13.2%, and 10.9% of all cases, respectively. There was no aetiology established in 53 (41.4%) of cases (Table 3).

Among the laboratory parameters, haemoglobin, PCV and serum protein were found to be significantly low in thrombocytopenic group. Liver enzymes, serum AST and serum ALT were significantly high in thrombocytopenic group (Table 4).

Platelet aggregation percentage was found significantly high in AES children who were positive for scrub typhus in comparison to other AES cases (Table 5).

Eighty-seven (68%) patients were discharged from the hospital. Mortality rate was 18%, 14.1% cases left hospital against medical advice or absconded from the hospital. There was no significant difference found in outcome of AES cases in relation to thrombocytopenia. Good outcome includes discharged cases and LAMA/ abscond cases in good general condition. Bad outcome includes expired cases and LAMA/ abscond cases in low general condition (Table 6). In the current study, even severe thrombocytopenia is not associated with a poor outcome when compared to those who do not have severe thrombocytopenia (Table 7).

Table 5: Comparison of laboratory findings between thrombocytopenic group and non-thrombocytopenic group.

Investigation	Thrombocytopenia	N	Mean	SD	P value
Hemoglobin (gm/dl)	Present	67	9.2	1.63	<0.001
	Absent	61	10.5	1.84	
Total leucocytic count (/cu mm)	Present	67	17012	8621	0.925
	Absent	61	16840	11890	
% polymorphs	Present	67	64.96	12.84	0.17
	Absent	61	68.48	15.99	
% PCV	Present	67	27.71	5.09	0.001
	Absent	61	31.24	6.24	
% platelets aggregation	Present	14	53.14	17.14	0.387
	Absent	61	56.59	12.4	
CSF cell count (/cu mm)	Present	67	19.3	35.51	0.453
	Absent	61	24.75	46.27	
CSF% polymorphs	Present	67	24.85	18.87	0.389
	Absent	61	22.13	16.49	
CSF protein (mg/dl)	Present	67	142.47	79.97	0.188
	Absent	61	123.80	79.32	
CSF sugar (mg/dl)	Present	67	72.21	43.02	0.43
	Absent	61	67.02	28.93	
S. Urea (mg/dl)	Present	67	53.88	60.19	0.232
	Absent	61	43.26	35.66	
S. Creatinine (mg/dl)	Present	67	0.87	0.96	0.308
	Absent	61	0.74	0.24	
S. Na+(mmol/l)	Present	67	138.70	6.88	0.46
	Absent	61	137.01	17.17	
S. K+(mmol/l)	Present	67	4.40	0.65	0.748
	Absent	61	4.44	0.84	
S. Bil (mg/dl)	Present	67	0.75	0.89	0.521
	Absent	61	0.65	0.91	

Continued.

Investigation	Thrombocytopenia	N	Mean	SD	P value
S. AST (IU/L)	Present	67	136.02	172.42	0.001
	Absent	61	57.64	34.71	
S. ALT (IU/L)	Present	67	78.74	58.94	0.001
	Absent	61	47.84	46.58	
S. Total protein (g/dl)	Present	67	5.75	0.86	0.014
	Absent	61	6.70	3.02	

Table 6: Comparison of platelet aggregation in scrub positive and scrub negative AES cases.

	Scrub typhus	N	Mean	SD	P value
Platelets aggregation (%)	No	63	52.47	11.39	0.001
	Yes	12	74.16	5.95	

Table 7: Comparison of outcome in thrombocytopenic and non-thrombocytopenic cases.

Variables	Thrombocytopenia present	Thrombocytopenia absent	P value
Good outcome	60	37	0.185
Bad outcome	15	16	
Platelets count<0.5 lac/ cumm			
Good outcome	17	80	0.530
Bad outcome	7	24	

DISCUSSION

AES is a significant public health issue in India, particularly in Uttar Pradesh. Every year, hundreds of youngsters in the eastern UP are afflicted with this disease, and many of them die. This illness occurs due to both infectious and noninfectious causes. Causative agents of AES can vary by region and time. AES cases caused by dengue virus, rickettsial infection, enterovirus, and leptospirosis are on the rise recently. Many of these causes of AES are associated with thrombocytopenia. Thrombocytopenia has been identified as a prevalent laboratory finding in AES children coming to our department throughout the years. There are limited studies that have documented thrombocytopenia in AES.[11-13] In the present study, we further studied its prevalence in AES in children. We also attempted to determine whether patients with AES with thrombocytopenia have some differences in clinical features in comparison to those who do not have thrombocytopenia.

A few recent studies on scrub typhus have shown that these cases can be associated with pseudo-thrombocytopenia due to platelet aggregation, which helped in the diagnosis of scrub typhus.[14-16] In the present study, we did a platelet aggregation test to find out if platelet aggregation has increased in AES cases due to scrub typhus, which is a common aetiology of AES nowadays. This test was not done in any of the previous studies, which primarily focused on thrombocytopenia in scrub typhus cases.

One hundred twenty-eight children with presumed viral aetiology were studied further to find out the cause of AES. Male patients outnumbered female patients in the current research, with a M:F ratio of 1.6:1. Other authors have similarly documented a male prevalence in AES cases.[17,18] This male predominance might be attributed to boys' greater participation in outdoor activities or to the fact that male children are taken to the hospital more frequently than female children when they are ill. The majority of cases were above one year of age, indicating that AES is less probable in children below one year of age. The majority (94.5%) of enrolled cases were of low socioeconomic status and resided in rural areas (85.2%). Mostly from Lucknow's bordering areas. These districts are usually associated with specific habitats such as abandoned plantations, rice fields, river banks, grassy fields, etc. These ecological patches may attract natural hosts. Similar ecological patches were also observed in other parts of India where AES has been commonly reported. Unhygienic conditions in rural areas also contribute to various infectious diseases, including the AES.

Thrombocytopenia is common in children with AES in this region. It was documented in 24 cases, and 18.7% had a platelet count below 50,000/cu mm. In comparison to the previous study, in which thrombocytopenia was found in 15.6% of cases, we found a higher prevalence of thrombocytopenia.[13] This can be due to a change in the aetiology of AES in this region over a time period, as now we see relatively more cases of AES due to dengue virus and rickettsial infections, which are commonly associated with thrombocytopenia. In this study, 10.9% of cases were positive for dengue infection, and 13.3% were positive for scrub typhus. Other recent studies have also documented that AES due to dengue infection and scrub typhus is common today in comparison to older

studies. In another study, a similar higher prevalence of thrombocytopenia was found.[5] They have documented thrombocytopenia in 50% of AES cases.

We did not find any difference in the aetiology of AES in thrombocytopenic patients compared to cases without thrombocytopenia. This indicates that not all cases of AES caused by dengue virus, scrub typhus, leptospirosis, or chickungunya will have thrombocytopenia. Multiple factors may be responsible for this difference, like host factors, previous infections, differences in serotypes, etc.

On comparison of clinical features of AES cases, we found no significant difference in fever, headache, vomiting, diarrhoea, seizures, altered sensorium, focal deficit, mean GCS, breathing pattern (hyperventilation), signs of meningeal irritation, abnormal movements, or increased intracranial tension in thrombocytopenic cases from non-thrombocytopenic cases. But rashes, bleeding, swelling, hepatomegaly, and splenomegaly were significantly higher among thrombocytopenic patients. Few studies have reported that AES cases may present in two ways: one group presents with pure neurological involvement, and the other group presents with multisystem involvement. Pure neurological presentation occurs in herpes encephalitis and JE. Multisystem involvement with neurological involvement occurs in dengue, rickettsia infection, malaria, and leptospirosis. So, thrombocytopenia can be a part of this multisystem involvement in AES. This is the probable reason why oedema, rash, hepatomegaly, and splenomegaly were seen more in AES cases with thrombocytopenia.

Among laboratory parameters, mean haemoglobin, PCV, and serum protein were significantly low in thrombocytopenic patients. On the other hand, liver enzymes were significantly high in thrombocytopenic cases. Again, this indicates that thrombocytopenia is more common in AES cases with multisystem involvement. Mittal et al have also reported splenomegaly and raised liver enzymes.[19]

In the present study, we did a platelet aggregation test with the aim of finding out whether children with AES due to scrub typhus have increased platelet aggregation in comparison to others, which may contribute to thrombocytopenia in these children. But, unfortunately, this test could not be done in children with a platelet count of less than one lac/cu mm due to technical problems. Also, we received reports of platelet aggregation percentages in AES cases. The AES cases due to scrub typhus have significantly high platelet aggregation in comparison to other AES cases. Other studies also found pseudothrombocytopenia due to platelet aggregation in scrub typhus.[14-16]

Outcomes of the study

In this study, 24.2% of enrolled cases had a bad outcome, and 18% died in the hospital. Previous studies have reported a mortality rate of 14.7%, 27%, and 21% among AES cases, respectively. We found no significant difference in outcome between thrombocytopenic AES cases and non-thrombocytopenic AES cases.[18-20] Thrombocytopenia did not affect the outcome, even when the platelet count was less than 50,000 cu mm. Also, the mean GCS did not differ between the two groups. Patients in the current research were only followed up on until they were discharged; therefore, long-term outcomes could not be evaluated. As it was found to be associated with other systemic manifestations like rash, hepatitis, and hepatosplenomegaly, the long-term neurological outcome of thrombocytopenic cases may be different from that of AES cases with predominant neurological involvement only. In conclusion, thrombocytopenia did not affect the short-term outcome of AES in children.

Strength and limitations

The fact that we followed strict inclusion and exclusion criteria was one of our study's strengths. Enrollment was unbiased because we included all patients with AES on three pre-decided weekdays to avoid selection bias. Except for a few cases with a very short hospital stay, the majority of cases were completely investigated to find out the common etiologic agents of AES in our region. All virological and AES tests to determine the etiology were performed at a state-level referral laboratory. Because all of the patients were hospitalized, they could be carefully monitored until discharge or other outcomes.

There are certain limitations to our study. First, because research was conducted in a tertiary care referral hospital, the current data do not reflect the entire community. There are many etiological agents that cause AES, and it is almost impossible to look at them all. We investigated all of the usual causes of AES reported here, including JE, dengue encephalitis, HSV1, Chikungunya, cerebral malaria, and scrub typhus.

CONCLUSION

Thrombocytopenia is a common finding in AES children. Dengue virus, JE, and scrub typhus were found to be common aetiologies of AES. The etiological agent could not be identified in a large number of cases. No difference in aetiology was found between AES cases with thrombocytopenia and those without thrombocytopenia. Rash, bleeding, swelling, hepatomegaly, and splenomegaly were significantly more common in thrombocytopenic cases in comparison to non-thrombocytopenic cases. Haemoglobin, PCV, and serum proteins were found to be significantly lower in the thrombocytopenic group. Liver enzymes serum AST and serum ALT were significantly high in the thrombocytopenic group. The platelet aggregation percentage was significantly higher in scrub typhus-positive patients in comparison to scrub-negative patients. This method, in conjunction with other existing

testing, may aid clinicians in the diagnosis of AES due to scrub. There was no significant difference in the short-term outcome of AES cases in relation to thrombocytopenia. Because this study was conducted at a tertiary care referral center, the current data do not reflect the whole population.

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REFERENCES

1. Reddy MN, Belavadi G, Priyanka VH. Study on acute encephalitis syndrome in children and their correlation with clinical parameters and etiological factors. Int J Contemp Pediatr. 2019;6(6):2628-33.
2. Jmor F, Emsley HC, Fischer M, Solomon T, Lewthwaite P. The incidence of acute encephalitis syndrome in Western industrialised and tropical countries. Virol J. 2008;5(1):1-3.
3. Panwar RS, Kumar N. Cassia occidentalis toxicity causes recurrent outbreaks of brain disease in children in Saharanpur. Indian J Med Res. 2008;127(4):413-5.
4. Operational Guide for Japanese Encephalitis Vaccination in India, MoHFW, Immunization Division, Department of Family Welfare, Ministry of Health and Family Welfare, Government of India. 2010. Available at: http://www.nipccdearchive.wcd.nic.in/sites/default/files/PDFMOHFW.pdf. Accessed on 5 March 2024.
5. Misra UK, Mani VE, Kalita J. A cost-effective approach to the diagnosis and management of acute infectious encephalitis. Eur Neurol. 2017;77(1-2):66-74.
6. Kumar R, Tripathi P, Singh S, Bannerji G. Clinical features in children hospitalized during the 2005 epidemic of Japanese encephalitis in Uttar Pradesh, India. Clin Infect Dis. 2006;43(2):123-31.
7. Lamech TM, Chellaraj M, Penchalaiah R, Dhanasekaran D. Pseudothrombocytopenia in patients with scrub typhus infection. Indian J Hematol Blood Transf. 2020;36(1):171-3.
8. Venkatesan A, Tunkel AR, Bloch KC, Lauring AS, Sejvar J, Bitnun A, et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. Clin Infect Dis. 2013;57(8):1114-28.
9. Daniel WW, Cross CL. Biostatistics: a foundation for analysis in the health sciences. Wiley. 2018.
10. Blacksell SD, Tanganuchitcharnchai A, Nawtaisong P, Kantipong P, Laongnualpanich A, Day NP, et al. Diagnostic accuracy of the InBios scrub typhus detect enzyme-linked immunoassay for the detection of IgM antibodies in Northern Thailand. Clin Vaccine Immunol. 2016;23(2):148-54.
11. Mittal M, Kushwaha KP. AES: Clinical presentation and dilemmas in critical care management. J Communicable Dis. 2014;46(1):50-65.
12. Tripathy SK, Mishra P, Dwibedi B, Priyadarshini L, Das RR. Clinico-epidemiological study of viral acute encephalitis syndrome cases and comparison to nonviral cases in children from Eastern India. J Global Infect Dis. 2019;11(1):7.
13. Kumar R, Tripathi P, Singh S, Bannerji G. Clinical features in children hospitalized during the 2005 epidemic of Japanese encephalitis in Uttar Pradesh, India. Clin Infect Dis. 2006;43(2):123-31.
14. Mohan BP, Sheeja S, Prabhalekshmy KK. EDTA dependent pseudothrombocytopenia in a patient with scrub typhus-a case report. BMH Med J. 2016;3(1):15-8.
15. Rajajee S, Subbiah E, Krishnamurthy N, Paranjothi S, Lohiya N. Pseudothrombocytopenia and usefulness of platelet aggregates in peripheral smear in the diagnosis of scrub typhus. Indian J Pediatr. 2019;86(1):93-4.
16. Lamech TM, Chellaraj M, Penchalaiah R, Dhanasekaran D. Pseudothrombocytopenia in patients with scrub typhus infection. Indian J Hematol Blood Transf. 2020;36(1):171-3.
17. Karmarkar SA, Aneja S, Khare S, Saini A, Seth A, Chauhan BK. A study of acute febrile encephalopathy with special reference to viral etiology. Indian J Pediatr. 2008;75(8):801-5.
18. Kumar S, Pandey AK, Gutch M, Razi SM, Gupta A, Jain N, Shakya S, Gupta KK. Acute viral encephalitis clinical features and outcome: Experience from a tertiary center of North India. Ann Trop Med Publ Heal. 2015;8(6):1.
19. Mittal M, Kushwaha KP. AES: Clinical presentation and dilemmas in critical care management. J Communicable Dis. 2014;46(1):50-65.

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