IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 2 Ver. 1 February. (2018), PP 14-19
www.iosrjournals.org

An Epidemiological Study On Clinical Profile And Short Term Outcome In Children Of Acute Encephalitis Syndrome In A Tertiary Care Centre Of West Bengal With Special Reference To The Various Prognostic Markers

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Abstract :
Introduction : *Incidence of acute encephalitis is high in children and associated with high mortality and sequalae. It is critical to evaluate the child immediately to reduce mortality and sequalae and to identify the cause of Acute Encephalitis Syndrome (AES). Aim of the study was to document the clinical profile, short term outcome, find out possible etiologies of AES and effect of different prognostic markers in outcome of AES at the end of hospital stay.*
Methods : *This prospective observational study was conducted in the pediatric department of NRS medical College & Hospital, Kolkata for period of one year (1st April 2015 to 31st March 2016) on a sample size of 140 patients presenting with fever and altered sensorium (between ages one month to 12 years) and etiology of AES was determined on the basis of history, clinical examination, relevant investigations. Outcome of patients was graded with functional outcome score (Glasgow outcome scale)*
Results : *The most common cause of AES was acute viral encephalitis (JE and non JE). Second most common cause was pyogenic meningitis followed by tubercular meningitis, ADEM and cerebral malaria. 19.01% cases died and 23.23% patients were discharged with sequalae. 57.74% patients were discharged with complete recovery. Maximum mortality and maximum sequalae was found in viral encephalitis (age group 1-5 years, male). Most common type of sequalae was extrapyramidal abnormality. 11 cases of JE IgM positive cases were found out of which 5 died and 6were discharged with sequalae. Out of 14 significant variables, only 10 were found to be significant ($p<0.05$) lke seizure, shock, GCS <8 and ↑ICT.*
Conclusion : *AES is a disorder of multiple and varying etiology with significant mortality and morbidity. Early diagnosis, appropriate investigation, prompt management and prevention by vaccination go a long way in reducing mortality and sequalae in AES.*
Keywords : *Japanese encephalitis, AES, Coma, neurological manifestations*

I. Introduction

Acute encephalitis syndrome is a major illness affecting children of West Bengal and other part of country with significant mortality and morbidity. AES is one of the most common causes of PICU admission all throughout the state of West Bengal and also in our hospital. Acute Encephalitis Syndrome (AES) is a disorder of varied etiology and is now one of the leading causes of morbidity and mortality in children in India. AES is a disease of major public health importance due to its high epidemic potential, high case fatality rate (CFR), and sequalae among survivors.[1-3]

Encephalitis is defined as an inflammatory process of central nervous system with dysfunction of brain. According to WHO, clinically a case of acute encephalitis syndrome (AES) is defined as a person of any age, at any time of year, with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures). Other early clinical findings can include an increase in irritability, somnolence or abnormal behaviour greater than that seen with usual febrile illness. [4-7]

The present prospective study was done for one year (April 2015 – March 2016) at a tertiary care teaching hospital in Kolkata, West Bengal and had objectives to study various clinical features, find out possible etiologies and to determine outcome and effect of different prognostic markers in outcome of acute encephalitis syndrome (AES) at the end of hospital stay

II. Materials And Method

This prospective observational study was conducted at Pediatrics department, NRS Medical college & Hospital, Kolkata, a tertiary care teaching institute in the state of West Bengal for a period of one year (April 2015 – March 2016). Due permission was taken from ethical committee of the institute.

All cases of fever with altered sensorium from > 4 hours but < 2 weeks, aged 1month to 12 years admitted in Pediatric Medicine ward of NRS Medical College & Hospital were enrolled for the study. The target sample size was 140. Patients with metabolic encephalopathy, head injury, mental retardation, space occupying lesion, granuloma, endocrinal encephalopathy and febrile seizure were excluded from the study.

Each patient was studied in a methodical manner in predesigned structural proforma after obtaining written consent from parents or guardians regarding their willingness to participate in the study.

After admission, detailed history was taken and management of fever, raised ICT and seizure were carried out simultaneously. Clinical examinations were done. Urgent supportive management, and blood samples were sent for different baseline biochemical tests. Blood and urine samples were sent for culture and sensitivity in all cases by maintaining proper aseptic technique. Neuroimaging and CSF analysis were performed in all cases of fever with altered sensorium.

The clinical variables recorded were heart rate, respiratory rate and patterns, blood pressure(average of three recordings, using mercury sphygmomanometer, by auscultatory method), temperature, sensorium (using modified Glasgow Coma Scale), pupillary size and response to light, extra ocular movement, posture, motor pattern (recorded subjectively by assessing the passive tone), seizure if any, type of seizure, involuntary movement and fundus picture. The etiology of AES was determined on the basis of history, clinical examination and relevant laboratory investigations. The investigations such as blood culture, MPDA, CSF and blood for serology by IgM ELISA, MRI of brain, depending on the clinical presentation and as determined by the consultant in-charge were done Etiology was classified into viral encephalitis (JE and non JE), bacterial meningitis, tubercular meningitis, cerebral malaria and ADEM (acute disseminated encephalomyelitis),

Outcome was recorded as survived and died .We also found out effect of different prognostic markers. The outcome of patients was graded with a functional outcome score (Glasgow Outcome Scale, GOS), as follows: Grade I –death, Grade II-Severe sequalae greatly impairing function and incompatible with independent living, Grade III -Moderate sequalae mildly affecting function (including seizures), but compatible with independent living, Grade IV-Minor sequalae including altered personality or clinical signs not affecting functions, Grade V- full recovery and normal neurologic examination findings.

Fischer's exact test, Chi-square test and logistic regression analysis were used to determine predictors of outcome and analysis of result. Wherever applicable statistical significance has been evaluated by 'p' value <0.05. The categorical variables like age of diagnosis vs. outcome or etiology of disease vs. outcome etc. have been presented as N (%) and compared. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. The Statistical software namely SPSS, Graph Pad instat 3, and MedCalc were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc

III. Results

In our hospital total 142 cases of AES (3.38% of total admission) were admitted in 1 year (1st April 2015-31st march 2016). In our study out of 142 children from age group 1month to 12 years. 82 (57.74%) cases were boys and 60(42.26%) cases were girls. Maximum patients62 (43.66%) were from age group of 1year to 5 years. Majority of the parents of the patients were from the low socioeconomic group, that is 83 (58.45%) were illiterate, 113(79.58%) were from low income group and 89 (62.67%) cases were from those persons residing in mud house. Out of 142, most of the cases 123 (86.61%) were from rural areas where as 19(13.39%) cases from urban areas. It may be because of most of the cases admitted in our hospital were referred from Murshidabad and Nadia district Most of the cases were seen in the post monsoon period, that is out of 142 cases 60(42.25%) cases were seen in the month of September to November, because mosquito density increased in this season. Fever with altered sensorium was the most commom presenting feature, ubiquitously present in almost all cases (100%). Other clinical features we found were seizure 110(77.46%), vomiting 69(48.59%), loose stool 23(16.19%), breathlessness 27(19.01%) and limb weakness in 11 (7.74%). On examination we found that at the time of admission GCS was below 8 in 47(33.09%). Other important findings that were present were signs of meningeal irritation 49(34.50%), cranial nerve involvement 46(32.39%), abnormal pupil 91(64.08%), planter extension 94(66.19%), papilledema 13 (9.13%), neurological deficit 23(16.19%), features of raised ICT 63(44.36%) and extrapyramidal signs in 19 (13.38%).

Out of 142 subjects, 76(45.78%) were diagnosed as viral encephalitis. Amongst them 11(7.75%), 26(18.30%) as pyogenic meningitis, 16(11.26%) were tubercular meningitis, 9(6.34%) were ADEM, and 8 (5.64%) cases were cerebral malaria. There were 7(4.93%) cases which remained undiagnosed. It was inferred that infective pathology was the most common cause of AES in India.

We found mortality in 27(19.01%) and 115(80.99%) cases survived. Amongst them 33(23.23%) had sequalae and 82(57.74%) patients were discharged with complete recovery. In our study higher 11(40.74%) mortality and maximum 19(57.57%) sequalae was seen in age group of 1 year to 5 years while least mortality 7(25.92%) was seen in age group of 5-12 years. Sex wise maximum 18(66.66%) mortality and sequalae 19(57.57%) both were seen in male than female. Out 0f 33 cases with sequalae, 11(33.33%) cases developed severe (GOS- II) sequalae, while 9(27.27%) moderated (GOS-III) and 13(39.39%) mild (GOS-IV) sequalae. Out of 11 severe sequalae, etiology wise 5 (45.45%) were of Japanese encephalitis cases. Age wise 6 (54.54%) were from age group 1-5 years and sex wise 7(63.63%) were seen in males. In our study out of 142 cases, 11(7.75%) cases were diagnosed as Japanese Encephalitis, among them 9 positive cases were diagnosed by serum and CSF testing positive for anti- JEV IgM antibodies and in 2 cases only in serum. Among the JE positive cases 6 cases were male and 5 cases female. The predominant age group affected was 2-12 years. Out of 11 cases of JE, 5 cases died and amongst rest six, five developed severe sequalae and one developed moderate sequalae. We found maximum mortality 12(44.44%) in viral encephalitis and least in cerebral malaria and ADEM 1(3.37%). Maximum sequalae 15(55.55%) was also due to viral encephalitis while least 1(3.03%) was due to cerebral malaria.

Out of 33 cases of sequalae most common type of sequalae in 21(63.63%) was extrapyramidal abnormality, followed by speech disturbance in 17(51.51%) and behavioural abnormality in 7(21.21%) cases. The most common CT scan/ MRI brain finding was diffuse cerebral oedema in 72(50.70%) cases. Other findings were Hyperintensity lesion on T2WI in thalami, brain stem, cerebellum and cortex in 13(9.15%), Diffuse basal enhancement with basal exudates in 17(11.97%).,and multiple hyper intensities in T2 image in white matter were found in 11(7.74%) cases. In 29(20.42%) of cases neuroimaging were normal or not done.

In our study, out of fourteen independently significant variables ,only 10 variables that is seizure, shock (Requiring inotropic support), GCS <8,severe anaemia, raised ICT, respiratory failure, meningeal sign, use of mechanical ventilator, JE IgM + and severity of sensorium were found to be significant($p<0.05$). Other variables like age, sex, papilledema and tone were not found to be significant. GCS<8 had higher risk of death and was found to be statistically significant ($p=0.001$). Presence of refractory seizures was significantaly associated with mortality ($p=0.040$). Subjects who were in shock and required inotropic support at the time of admission had more risk of death than those subjects without shock and was found to be statistically significant($p=0.0128$).

We found that presence of severe anaemia was significantly ($p= 0.0182$) associated with mortality. Presence of JE IgM positivity was significantly ($p= 0.035$) associated with mortality. Presence of variables like respiratory failures ($p=0.0033$),meningeal sign ($p=0.0012$), severity of coma grade($p=0.001$), features of raised ICT($p=0.0045$) and use of mechanical ventilator ($p=0.001$) had higher risk of death and were statistically significantly.

IV. Figures and Tables

Table 1: Total Percentage of AES cases admitted

Total admission	Total no of AES cases	Percentage of AES
4190	142	3.38%

Table 2: Age and Sex distribution of AES cases. (n=142)

Age (year)	Male	Female	Total	Percentage
1month-< 1Yr	15	12	27	19.01%
1Yr<5Yr	37	25	62	43.66%
5-12Yr	30	23	53	37.33%
Total	82(57.74%)	60(42.26%)	142	100%

Table 3: Area wise distribution of AES cases (n=142)

Area	No. of AES cases	Percentage
Rural	123	86.61%
Urban	19	13.39%

Table 4: Clinical symptoms on admission in AES cases (n=142)

Symptoms	No. of cases(n=142)	Percentage
Fever	142	100%
Altered sensorium	142	100%
Seizure	110	77.46%
Vomiting	69	48.59%
Loose stool	23	16.19%
Rash	4	2.81%
Bleeding manifestation	3	2.11%
Breathlessness	27	19.01%
Swelling of body	7	4.92%
Paralysis/limb weakness	11	7.74%

Table 5: CNS Examination findings of AES cases: (n=142)

CNS examination findings of AES cases		No. of AES cases (142)	Percentage
GCS	<8	47	33.09%
	>8	95	66.91%
Signs of meningeal irritation		49	34.50%
Cranial nerve involvement		46	32.39%
Pupil			
Normal		51	35.91%
Abnormal (91)	Non-Reactive	37	26.05%
	Reactive	54	38.02%
Fundus (Papilledema)		13	9.13%
Hypertonia		39	27.46%
Hypotonia		13	9.15%
Neurological deficit		23	16.19%
DTR	Brisk DTR	21	14.78%
	Diminished DTR	7	4.92%
Planter extensor		94	66.19%
Cerebellar sign		7	4.92%
Extra pyramidal signs		19	13.38%
Features of raised ICT		63	44.36%
Coma/ sensorium severity	Grade I	47	24.64%
	Grade II	69	42.25%
	Grade III	26	15.49%

Table 6: Outcome of the AES cases (n=142)

Outcome	No. of AES cases(n=142)	Percentage
Death	27	19.01%
Discharge with sequalae	33	23.23%
Discharge without sequalae	82	57.74%
Total	142	

Table 7: Distribution of total cases of AES according to etiology (n=142)

Etiology		No. of AES cases(n=142)	Percentage
Viral	JE	11	(7.75%)
	Non JE	65	(45.78%)
Pyogenic		26	(18.30%)
Tubercular		16	(11.26%)
Cerebral malaria		8	(5.64)
ADEM		9	(6.34%)
Undiagnosed		7	(4.93%)
Total		142	

Table 8 : Different type sequalae in AES cases(n=33)

Sequalae	Total No.	Percentage
Hearing loss	3	9.09%
Speech loss	17	51.51%
Extrapyramidal abnormality	21	63.63%
Behavioural abnormality	7	21.21%
Cranial nerve deficit	2	6.06%

Table 9: Outcome of AES and predictor variables at admission

Variables	**Present/Absent**	**No (%)**	**Death (%)**	**Survival (%)**	**P-value**
Age	1month-<1 yr	27(19.01%	9(33.33%)	18(66.67%)	0.889
	1-5 yrs	62(43.66%)	11(17.74%)	51(82.26%)	
	5-12 yrs	53(37.33%)	7(13.20%)	46(86.80%)	
Sex	Male	82(57.74%)	18(21.95%)	64(78.04%)	0.387
	Female	60(42.26%)	9(15.00%)	51(85.00%)	
Seizure	Present	110(77.46%)	25(22.72%)	85(77.28%)	**0.040**
	Absent	32(22.54%)	2(6.25%)	30(93.75%)	
Shock	Present	9(6.33%)	5(55.55%)	4(44.45%)	**0.0128**
	Absent	133(93.67%)	22(16.54%)	111(83.46%)	
GCS	<8	47(33.09%)	21(44.68%)	26(55.32%)	**0.001**
	>8	95(66.91%)	6(6.31%)	89(93.69%)	
Papilledema	Present	13(9.15%)	3(23.07%)	10(76.93%)	0.713
	Absent	129(90.85%)	24(18.60%)	105(81.40%)	

Raised ICT	Present	63(44.36%)	19(30.15%)	44(69.85%)	**0.0045**
	Absent	79(55.64%)	8(10.12%)	71(89.88%)	
Respiratory failure	Present	39(27.46%)	14(35.89%)	25(64.11%)	**0.0033**
	Absent	103(72.54%)	13(12.62%)	90(87.38%)	
Severe anaemia	Present	13(9.15%)	6(46.15%)	7(53.85%)	**0.0182**
	Absent	129(90.85%)	21(16.27%)	108(83.73%)	
Meningeal sign	Present	49(34.50%)	17(34.69%)	32(65.31%)	**0.0012**
	Absent	93(65.50%)	10(10.75%)	83(89.25%)	
Use of ventilator	Present	29(20.42%)	18(62.06%)	11(37.94%)	**0.001**
	Absent	113(79.58%)	9(7.96%)	104(92.04%)	
JE IgM +	Present	11(7.74%)	5(45.45%)	6(54.55%)	**0.035**
	Absent	131(92.26%)	22(16.79%)	109(83.21%)	
Tone	Hypertonia	39(27.46%)	7(17.94%)	32(82.06%)	0.9063
	Hypotonia	13(9.15%)	2(15.38%)	11(84.62%)	
	Normal tone	90(63.38%)	18(20.00%)	72(80.00%)	
Sensorium grade	Grade I	47(33.09%)	5(10.63%)	42(89.37%)	**0.001**
	Grade II	69(48.60%)	9(13.04%)	60(86.96%)	
	Grade III	26(18.30%	14(53.84%)	12(46.16%)	

V. Discussion

Acute Encephalitis Syndrome (AES) is a disorder of varied etiology and is now one of the leading cause of morbidity and mortality in children in India. AES is a disease of major public health importance due to its high epidemic potential, high case fatality rate (CFR), and sequalae among survivors.The present study had objectives to study various clinical features, find out possible etiologies and to determine outcome and effect of different prognostic markers in outcome of acute encephalitis syndrome (AES) at the time of end of hospital stay.A better understanding of presenting features, causes and outcome is essential to help to improve the approach and to plan rational management of AES.

The present study demonstrates that most of the cases of AES were from rural area and from low socio economic group and maximum patients were admitted in the post monsoon season that is in the months of September to November. The most common age group affected were 1-5 yrs, males. Most of the patients presented with fever with altered sensorium, seizures, vomiting, loose stools and breathlessness. These findings were consistent with studies by Bokade et al, Dongol et al, Bandyopadhyay et al, Saumyen De et al. [5-10]

Common physical examination findings like raised temperature was found in all cases. Other findings commonly found were tachycardia, bradycardia, pallor, hepatomegaly and shock .On CNS examinations at the time of admission GCS was below 8 in most of the patients. Other important findings presents were signs of meningeal irritation, cranial nerve involvement, abnormal pupil, planter extension, papilledema, neurological deficit, features of raised ICT and extrapyramidal signs. Similar finding were also found by Khinchi Y R et al, Bandyopadhyay Bhaswati et al, Avabratha et al and Dongol S et al and others.[4,6,7,9,11]

Findings we found from the investigations was that in most of the cases serum sodium were <135 mg/dl. Serology for JE IgM was positive in 11 cases and in 8 cases MPDA was positive. CSF analysis showed polymorphic predominance and pleocytosis in most of the cases and CSF sample for JE IgM was positive in 9 cases. The most common CT scan/ MRI brain finding was diffuse cerebral oedema. [3,5,6,7,12]

In this study the most common cause of AES was acute viral encephalitis (JE AND Non JE).Second most common cause was pyogenic meningitis followed by tubercular meningitis, ADEM and cerebral malaria. 19.01% cases died and 23.23% patient were discharged with sequalae and 57.74% discharged with complete recovery. In our study maximum mortality and maximum sequalae was found in viral encephalitis cases between age group 1- 5years, male. Most common type of sequalae observed in our study was extrapyramidal abnormality followed by loss of speech and behavioural abnormality. [2,3,5,6]

In our study 11 cases of JE IgM positive were found, in which 5 cases were died and rest 6 cases were discharged with sequalae.[2,6,7,9,13]

Out of fourteen independently significant variables ,only 10 variables that is seizure, shock (requiring inotropic support), GCS <8,severe anaemia, raised ICT, respiratory failure, meningeal sign ,use of mechanical ventilator, JE IgM + and sensorial grade were found to be significant ($p<0.05$) and these were independent predictors for mortality in children of AES . Other variables like age, sex, papilledema and tone were not found to be significant. These findings were similar to studies of Bokade et al, Idro et al. Nayana Prabha et al and others.[4,5,14,15,16]

VI. Conclusion

In conclusion, AES is a major illness affecting children of West Bengal as well as other parts of country with significant morbidity and mortality. Its control is very important from public health aspect as it has significant impact on resources of state, nation and public exchequer. Most importantly, the chance of lifelong sequalae leaves scarring on the face of survivor, their family and society.

Since AES is a disorder of multiple and varied etiology, better understanding of features, causes and outcome will definitely help the patients and most importantly the health infrastructure of state and country.

On the whole it can be said that prevention by vaccination, early diagnosis, appropriate investigations, strict monitoring and prompt management go a long way in reducing mortality and sequalae in AES.

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Rajarshi Basu "An Epidemiological Study On Clinical Profile And Short Term Outcome In Children Of Acute Encephalitis Syndrome In A Tertiary Care Centre Of West Bengal With Special Reference To The Various Prognostic Markers." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 2, 2018, pp. 14-19.