

CLINICAL AND DEMOGRAPHIC STUDY OF JAPANESE ENCEPHALITIS PATIENTS ADMITTED IN GAUHATI MEDICAL COLLEGE AND HOSPITAL, GUWAHATI, ASSAM, INDIA DURING 2014 EPIDEMIC

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ABSTRACT

BACKGROUND

Japanese Encephalitis is one of the most common causes of Acute Encephalitic Syndrome in Asia. During the period of June to August in 2014 an epidemic occurred in Assam, a northeastern state of India.

METHODS

Patients admitted in the Medicine Department in Gauhati Medical College and Hospital (GMCH), Guwahati, Assam, India, with clinical features of Acute Encephalitic Syndrome (AES) i.e. acute onset fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset seizures (excluding simple febrile seizures) from June to August 2014 underwent ELISA for Japanese Encephalitis Immunoglobulin M in cerebrospinal fluid (CSF) at the time of admission. Clinical features, demographic profile and laboratory investigations were recorded in positive patients.

RESULTS

226 AES patients were admitted in 6 different units of Medicine ward in GMCH, out of which 76 patients were diagnosed to be JE positive with CSF IgM ESLIA, coming from 17 districts of Assam. Out of 76 patients, 69 patients were from rural area, only 7 patients were from urban area. 59 (77.63%) patients were farmers or daily labourers by occupation and 23 (30.26%) patients were illiterate. Mean age of patients was 47.7 years and male to female ratio was 1.7:1. Mean duration of fever was 6.5 days, convulsion was found in 13.15% patients, out of which most common was generalised seizure (9.2%). 55.2% patients had meningeal signs, 23.68% patients had focal neurological deficits in the form of hemiparesis and monoparesis and mean GCS score was 9.28. Extra pyramidal features present in patients were rigidity (23.68%), abnormal posturing (15.78%) and abnormal movements (23.68%). 23.68% patients had Leukocytosis and Thrombocytopenia was found in 21 (27.6%) patients. Mean CSF cell count was 34.34 cells/mm³ with mean 29.67% polymorphs, mean CSF protein and sugar was 56.15 mg/dl and 66.92 mg/dl respectively. Serum bilirubin level was normal however elevated liver enzymes were present in 63.15% of patients. CT scan brain was done in 52 JE positive patients, cerebral oedema was found in 19 (36.52%) patients and hypodensities in thalamus, midbrain and basal ganglia was found in 16 (30.65%) patients.

CONCLUSION

One of the important findings of the present study is Thrombocytopenia and elevation of liver enzymes in JE patients which were not reported in previous studies except one study in Thailand and another in India in Paediatrics patients. Though the study was small it needs further studies to prove that thrombocytopenia and elevated liver enzymes may be an important complication of Japanese Encephalitis and should not be overlooked.

KEYWORDS

Japanese Encephalitis, Thrombocytopenia, Elevated liver enzymes.

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INTRODUCTION: Japanese Encephalitis is one of the most common cause of Acute Encephalitic Syndrome in Asia. It is

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caused by Japanese Encephalitis virus which is a single stranded RNA virus and belongs to the family Flaviviridae. Japanese Encephalitis is an arthropod borne human disease, transmitted by culex Tritaeniorhynchus and Culex Vishnui. Pigs and aquatic birds are virus reservoirs. It is found throughout the Asia in Japan, China, India, Pakistan, Bangladesh, Sri-Lanka and south eastern Asia. In India the first major outbreak occurred in West Bengal in 1973.⁽¹⁾ In

Districts	No. of patients	%
Baksa	6	7.89
Barpeta	8	10.52
Bongaigaon	2	2.63
Chirang	2	2.63
Darrang	8	10.52
Dhubri	2	2.63
Goalpara	3	3.94
Jorhat	1	1.31
Kokrajhar	2	2.63
Kamrup(R)	10	13.15
Kamrup(M)	7	9.21
Lakhimpur	1	1.31
Morigaon	4	5.26
Nagaon	7	9.21
Nalbari	8	10.52
Sonitpur	2	2.63
Udalguri	3	3.94

Table 1

Table 2 shows age and sex distribution of all AES patients who were tested for CSF JE IgM ELISA. They are divided in two groups, one group AES (JE-ve) and other group AES (JE+ve). Among the JE positive group, mean age of patients was 47.7 years and male and female ratio was 1.7:1. Table 3 describes the clinical features of JE positive patients.

Age group (yrs)	AES (JE –ve)			AES (JE +ve)		
	Male	Female	Total	Male	Female	Total
13-20	13	5	18	7	3	10 (13.15)
21-30	30	11	41	16	9	25 (32.89)
31-40	20	17	37	11	7	18 (23.68)
41-50	15	12	27	6	4	10 (13.15)
51-60	9	6	15	5	3	8 (10.52)
61-70	7	5	12	3	2	5 (6.57)
Total no.(%) of patients	94 (62.67)	56 (37.33)	150	48 (63.15)	28 (36.84)	76
Mean age (yrs)±SD			45.34±21.2			47.7±19.5

Table 2: Age and sex distribution among AES(JE-ve) and AES(JE+ve) patients

Clinical Features	No. (%) of patients	Mean ± SD
Fever	76(100)	
Headache	64(84.2)	
Vomiting	26(34.2)	
Convulsion		
Generalized	7(9.2)	
Focal	3(3.94)	
Duration of symptoms (Days)		6.5±1.8
1-5	23(30.26)	
6-10	50(65.8)	
11-15	3(3.94)	
Slurred speech	46(60.5)	
Meningeal signs	42(55.2)	
Glasgow Coma Scale Score		9.28±3.06
<7	12(15.8)	
7-10	38(50)	
>10	26(34.2)	
Focal Neurological Deficit		
Monoparesis	12(15.8)	
Hemiparesis	16(21)	
Extra Pyramidal Features		
Rigidity	18(23.68)	
Abnormal Posturing	12(15.78)	
Abnormal Movements	18(23.68)	
Hepatomegaly	8(10.52)	
Splenomegaly	5(6.57)	

Table 3. Clinical features of the patients with JE IgM test Positive

Fever was present in all 76 patients and mean duration was 6.5 days, most of the patients (84.2%) had headache

but only 34.2% patients had vomiting. Convulsion was found only in 13.15% patients out of which most common was Generalised seizure (9.2%). 55.2% patients had meningeal signs, 23.68% patients had focal neurological deficits in the form of hemiparesis and monoparesis and mean GCS score was 9.28. Extra pyramidal features present in patients were rigidity (23.68%), abnormal posturing (15.78%) and abnormal movements (23.68%). Table 4 describes the investigations findings of the patients. 23.68% patients had Leukocytosis and Thrombocytopenia was found in 21 (27.6%) patients. Mean CSF cell count was 34.34 cells/mm³ with mean 29.67% polymorphs, mean CSF protein and sugar was 56.15 mg/dl and 66.92 mg/dl respectively. Serum bilirubin level was normal however elevated liver enzymes were present in 63.15% of patients. Out of 68 patients were RFT was done, mild raise in serum creatinine level was present in 16 (23.52%) patients and 3 patients had serum creatinine level more than 3mg/dl. Rapid malaria dipstick test was done in 56 JE +ve patients and all of them were negative. CT scan brain was done in 52 JE positive patients, cerebral oedema was found in 19 (36.52%) patients and hypodensities in thalamus, midbrain and basal ganglia was found in 16 (30.65%) patients.

Investigation findings	No. (%) of patients	Mean \pm SD
Haemoglobin, g per 100 mL		12.2 \pm 1.56
6 – 10	9 (11.84)	
>10	67 (88.15)	
Total leukocyte count, cell/mm		7983.89 \pm 2833.3
<4000	14 (18.4)	
4000-11000	44 (57.89)	
>11000	18 (23.68)	
Platelet count, < 150 \times 10 ³ /mm ³	21 (27.6%)	192.29 \pm 81.02
CSF analysis:		
Cell count, Cells/mm ³		34.34 \pm 40.4
<10	26 (34.21)	
10-50	33 (43.42)	
51-100	9 (11.84)	
>100	8 (10.52)	
Polymorphonuclear leukocytes in CSF %		29.67 \pm 21.93
<25	39 (51.31)	
25-50	18 (23.68)	
51-75	13 (17.1)	
>75	6 (7.89)	
Protein, mg per 100mL		56.15 \pm 24.47
20-40	11 (14.47)	
41-60	34 (44.73)	
61-80	17 (22.36)	
81-100	9 (11.84)	
>100	5 (6.57)	
Glucose, mg per 100mL		66.92 \pm 13.53
<40	3 (3.94)	
40-80	56 (73.68)	
>80	17 (22.36)	
Serum bilirubin, mg per 100mL		0.78 \pm 0.21
Serum AST level, U/L		148.30 \pm 107.13
40-100	23/71 (32.39)	
101-200	36/71 (50.70)	
201-400	7/71 (9.85)	
>400	5/71 (7.04)	
Serum ALT level, U/L		65.28 \pm 55.20
\leq 40	37/71 (52.11)	
41-100	21/71 (29.57)	
101-200	9/71 (12.67)	
>200	4/71 (5.63)	
Serum Protein level, gm per 100 mL		4.91 \pm 1.45
<4	2/71 (2.81)	
4-7	56/71 (78.87)	
>7	13/71 (18.30)	
Serum Albumin level, gm 100 mL		3.38 \pm 0.81
<3	15/71 (21.12)	
3-4	47/71 (66.19)	
>4	9/71 (12.67)	
Blood Urea level, mg per 100 mL		40.73 \pm 22.08
<40		
40-100	47/68 (69.11)	
>100	17/68 (25.0)	
Blood Creatinine level, mg per 100 mL	4/68 (5.88)	1.2 \pm 0.62
<1.2	49/68 (72.05)	
1.2-3	16/68 (23.52)	
>3	3/68 (4.41)	
Positive rapid dipstick test for PF	0/56	
CT scan brain findings		
Normal	21/52 (40.38)	
Hypodensities	16/52 (30.76)	

(Thalamus, Midbrain, Basal ganglia)		
Haemorrhage	0/52	
Cerebral Edema	19/52 (36.53)	
Hydrocephalous	0/52	
Table 4: Investigation results of patients with JE IgM positive		

DISCUSSION: Assam is situated in North Eastern part of India, it has 27 districts with 3.11 million population, 85% of which reside in rural area. In rural area the main occupation is cultivation. During the monsoon and post monsoon season which extends from June to October, rainfall is maximum and farmers cultivate paddy during this season. Temperature ranges from 35^o to 40^o C during this season and waterlogged paddy fields in village areas become perfect environment for mosquito breeding. In our study which was done in 2014, first case was reported in the month of June with maximum no. of patients in the month of July and the epidemic lasted for a short period of 3 months upto August. Maximum no. of patients were from Kamrup (Rural) district, followed closely by patients from Darrang, Nalbari and Barpeta district. This may be explained as these areas are in the vicinity of our study centre, Gauhati Medical College and Hospital, which is situated in Kamrup (Metro) district. The inclusion criteria to our study was those patients coming with AES. We attempted to test for JEV with CSF IgM ELISA in all patients of AES during these period, but out of 237 patients of AES we could perform the test in 226 patients because few patients were very sick and few died soon after arrival in hospital, and 76 patients were tested positive which were studied. The high negative result for JEV could be due to early sample collection before appearance of IgM antibody in CSF and/or ELISA kit itself, because the sensitivity of the test kit ranges from 68% in day 1 to 100% in day 7.⁽⁴⁾ Therefore, though negative result were there, we still believed that some of them were JE, because of same demographic profile and clinical presentation. Some cases of AES may have had illness due to other causes like cerebral malaria, bacterial meningitis and infections caused by other viruses. Table 3 shows maximum number of JE + cases are in the age range of 21-30 (32.89%) followed by 31-40 (23.68%). The people in these age groups are more active and work outdoor, so more likely to get infected by mosquito bites. Sex distribution shows male preponderance in all age groups implying either they are likely to get infected as they work outdoor or are more likely to be brought to hospital (females are often neglected). Like known epidemiology of JE virus our study also shows rural predominance, 90.78% patients were from rural area. Interestingly only 27.63% patients had pigs in their house and neighbourhood, suggesting involvement of other alternative hosts like wild birds.⁽⁵⁾

Clinical features show acute onset, mean duration of fever before coming to hospital was short (6.5 days). Headache was present in 84.2% of patients and vomiting was present on 34.2%, but seizure was present only in 10 patients (13.15%), among them 7 patients had GTCS. Misra UK, Kalita⁽⁶⁾ showed seizure in 46.1% in their study done on 65 patients aged from 2-57 years during 1991 to 1999, 17

had GTCS and 13 had motor with secondary generalization. This difference may be attributed to difference in study age group as their study was done on both paediatrics and adults, but our study was done only on adult population. Seizure is more common in children as shown by Rashmi Kumar and Piyush Tripathi, et al.⁽⁷⁾ Who showed seizure in 98.7% patients in paediatrics age group. Mean GCS in our study was 9.28 which indicates severity of disease. 15.8% patients had monoparesis and 21% patients had hemiparesis. Among extrapyramidal features observed in our study, common were rigidity, abnormal movements and abnormal posturing. U. K. Misra and J. Kalita, et al.⁽⁸⁾ had found dystonia, as most common extrapyramidal features in adults.

The CSF analysis in our study shows mild pleocytosis (mean cell count 34.34 cells/mm³) with Lymphocytic predominance, mild rise in protein and normal glucose level which is in accordance with other viral infections. Other significant laboratory findings were thrombocytopenia and elevation in liver enzymes. 27.6% patients had thrombocytopenia and 63.15% patients had elevated liver enzymes. In literature we have found only one report by Watt and Jongsakul⁽⁹⁾ who reported Thrombocytopenia in all 8 JE patients in their study in Thailand. Rashmi kumar and Piyush Tripathi, et al.⁽⁷⁾ also reported Thrombocytopenia in 15.6% paediatric patients in their study. Misra, et al.⁽⁶⁾ in their study conducted in Lucknow reported elevated liver enzymes level in 11 patients out of 14 laboratory confirmed JE patients. These findings may be attributed to changes in virulence of JE virus in due course of their evolution in time. In our study most common radiological findings in CT scan brain done in 52 patients were cerebral oedema (36.53%) and hypodensity in thalamus, midbrain and basal ganglia (30.76%). J. Kalita and U. K. Misra⁽¹⁰⁾ have shown thalamic hypodensity in 15 patients, midbrain and basal ganglia hypodensity in 1 patient each, cerebral oedema in 4 patients and cortical atrophy with ventricular dilatation in 2 patients out of 31 JE patients to whom CT scan was done.

One of the important findings of present study is Thrombocytopenia and elevation of liver enzymes in JE patients which were not reported in previous studies except on study in Thailand⁽⁹⁾ and another in India in Pediatrics patients.⁽⁷⁾ Though the study was small it needs further studies to prove that thrombocytopenia and elevated liver enzymes may be an important complication of Japanese Encephalitis and should not be overlooked.

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