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Community Medicine

ACUTE ENCEPHALITIS SYNDROME IN A TERTIARY CARE SETTING WITH SPECIAL REFERENCE TO JAPANESE ENCEPHALITIS: AN OBSERVATIONAL STUDY IN ASSAM, INDIA

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ABSTRACT Acute Encephalitis Syndrome (AES) is a major public health problem and Japanese Encephalitis (JE) is one of the most important causes of AES. Therefore, it is crucial to know the etiology of AES for patient management and decision making. The present study aimed to assess the morbidity and mortality profile of AES/JE patients admitted in tertiary care setting. An observational prospective cross-sectional study was conducted among 140 hospitalized AES patients admitted in Pediatric and Medicine ward of Jorhat Medical College and Hospital (JMCH), Jorhat over a period from August, 2017 to July 2018. Blood serum and cerebrospinal fluids (CSF) were tested for presence of JE specific IgM antibody by Mac ELISA during acute illness of AES. The data were compiled and analyzed using the IBM SPSS, V23.0. Of the total 140 AES cases, majority (60%) were below 15 years age (p-value 0.180). Significantly higher proportion of AES cases were from rural areas (94.3%) (p-value <0.0001). The male and female ratio was 1.3:1. The most common presenting symptoms in AES patients were fever (100%), change in mental status (100%), seizure (56.4%) and headache (42.9%). Signs of meningeal irritation were present in 69.3% of cases. Around 22.9% AES patients had GCS ≤ 8. A total 49 (35%) cases were found to be laboratory confirmed JE following detection of JE specific IgM antibody. Among the JE patients, only 4.1% were immunized with SA 14-14-2 vaccine and 14% died before discharge. The complete recoveries were observed in 78% of cases. JE is one of the major causes of AES which is highly prevalent in this part of India. The significant findings in the present study calls for policy decision to combat JE.

KEYWORDS : Acute Encephalitis Syndrome, Japanese Encephalitis, SA 14-14-2

INTRODUCTION

Acute Encephalitis Syndrome (AES) is a clinical condition caused by Japanese encephalitis virus (JEV) or other infectious and non-infectious causes[1]. According to World Health Organization (WHO) a case of AES is defined clinically as a person of any age at any time of year, with the acute onset of fever and a change in mental status such as confusion, disorientation, coma or inability to talk and/or new onset of seizures (excluding simple febrile seizure)[2]. Globally, the annual incidence of Acute Encephalitis reported to be ranging between 3.5-7.5 cases per 100,000 persons and nearly 10.5 to 13.8 per 100,000 children[3]. Among the different causes of AES, Japanese encephalitis (JE) is predominant in Southeast Asia and in Indian sub-continent[4]. JEV is a vector-borne virus that causes Japanese encephalitis, a severe zoonotic neurological disease. It is estimated that globally 30,000 to 50,000 of cases and 15,000 deaths occurs yearly due to JE[5]. The Case Fatality Rate (CFR) of JE is very high and those who stay alive may suffer from various degrees of neurological sequalae[6]. Every year, the North East states of India, mostly the upper part of the state of Assam has been facing repeated episodes of JE with different magnitudes from July to October[7]. JE infections are mostly asymptomatic and inapparent infection tends to outnumber the apparent infections. The ratios of symptomatic to asymptomatic infections vary from 1 in 300 to 1 in 1000[8,9]. Currently, there is no specific therapeutic agent available against JE. The treatment of JE is mostly symptomatic and to avoid neurological sequelae, an early stabilization and institution of intensive supportive measures are keystone of management[5]. Moreover, mortality and morbidity due to JE can be reduced by protective and preventive measures. A hospital-based quality surveillance for AES, including laboratory testing is mandatory for understanding the epidemiological and clinical determinants of AES/JE, for planning interventions and starting appropriate public health policy[1]. Keeping this in mind, it was envisaged to assess the morbidity and mortality profile of AES patients admitted to tertiary care teaching hospital with special reference to JE.

MATERIAL AND METHODS

An observational prospective cross-sectional study was conducted from August, 2017 to July, 2018 among the hospitalized AES patients admitted in Pediatric and Medicine ward of Jorhat Medical College and Hospital (JMCH), Jorhat, Assam, India. JMCH is a teaching institute with both UG and PG courses and having its own teaching hospital unit. The hospital units having 814 Numbers of In-Patient Beds and mostly cater health care services to nearby districts and bordering state Nagaland. A total of 140 AES patients above one year of age who fulfilled the WHO operational case definition of AES[2] were included in the study. We used WHO Case Investigation Form (CIF) for collection of clinico-epidemiological and outcome data. Outcome analysis of AES patients were done at the time of hospital discharge. Ethical approval was obtained from the Institutional Ethics Committee (Human) and informed written consent/assent was taken from all the participants. From each AES patient, 2 ml of blood and 1 ml of cerebrospinal fluid (CSF) without having contraindication for lumbar puncture were collected. Blood samples were collected preferably at least 5 days after the onset of illness for detection of JE specific IgM antibody. A sterile empty vial (2 ml) was used to collect the blood from the antecubital vein of each AES participant. The blood sample thus collected was centrifuged at 1000 rpm for 10 min and clear serum was separated in a labeled aliquot part. The CSF sample of 1 ml was collected following lumbar puncture after taking all aseptic and antiseptic measures. The serum thus processed was stored at − 20 °C until further use. All blood/CSF samples used in this study were collected by the attending physician. The detection of JE specific IgM antibodies in serum and CSF performed using IgM antibody capture-Enzyme-Linked Immunosorbent Assay kits obtained from National Institute of Virology (NIV), Pune, India. JE diagnosis was confirmed on detection of JE specific IgM antibody in a single sample of CSF and/or serum by Mac ELISA during acute illness of AES. The clinical and epidemiological data were compiled and analyzed using the IBM SPSS Statistics V23.0 (IBM, USA) and documented using MS Word 2019. Prevalence was expressed as a percentage and calculated by dividing the number of positive samples by the total number of AES patient tested. Chi-square analysis was used to determine the univariate association between various variables and p-value <0.05 was considered to be statistically significant.

RESULTS

Table: 1 Demographic characteristic of AES cases

Variables	AES cases (n=140) (%)	p-value
Age (yr.) at admission		
≤ 15	84(60%)	0.0180*
> 15	56(40%)	
Sex		
Male	78(55.7%)	0.1763
Female	62(44.3%)	
Religion		
Hindu	134(95.7%)	0.0001*
Non-Hindu	6(4.3%)	
Settings		
Urban	8(5.7%)	0.0001*
Rural	132(94.3%)	

*p-value <0.05 was considered to be statistically significant

A total of 140 AES patients admitted during the study period in Pediatric and Medicine ward of Jorhat Medical College & Hospital, Jorhat, Assam were enrolled as study participants. The male and female ratio was 1.3:1. Majority of the study participants, 84(60%) were below 15 years age (p-value 0.180). Significantly higher proportion of AES cases were from rural areas 132 (94.3%) (p-value <0.0001). Majority 134 (95.7%) of AES cases were belonged to Hindu religion (p-value <0.0001). Wage earner 46 (32.9%), farmer 36 (25.7%) and small-scale business 29 (20.7%) were the common occupation. (Table: 1)

Of the 140 AES patients assessed, all (100%) had history of fever and change in mental status at the time of admission. Other clinical presentations were seizure (56.4%), neck rigidity (69.3%), and headache (42.9%). About 22.1% patients were unconscious at the time of examination. We found 22.9% patients had Glasgow Coma Scale (GCS) ≤ 8 and 2.9% had paralysis. Of the total AES patients 83% were hospitalised within 7days from the onset of illness.

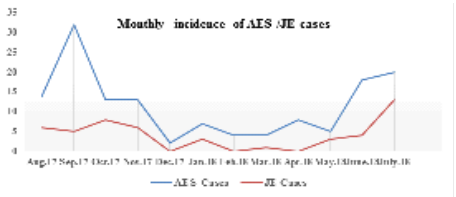
Among the enrolled 140 AES participants, we could collect 93 CSF and 113 Serum samples at the time of admission. Of whom, 49 (35%) were found to be laboratory confirmed JE following detection of JE specific IgM antibody by Mac ELISA in CSF and/or serum and 91 (65%) were AES of other etiology. We could not collect blood samples from 27 and CSF samples from 47 patients who were extremely ill and care givers were not willing to provide consent for taking biological samples or not suitable for Lumber Puncture (LP).

Table 2: District wise distribution of AES/JE cases

District name	Non-JE AES (n=91) (%)	JE (n=49) (%)	Total (n=140) (%)
Sivasagar	4 (4.4%)	3 (6.1%)	7 (5%)
Jorhat	53 (58.2%)	33 (67.4%)	86 (61.4%)
Golaghat	25 (27.5%)	5 (10.2%)	30 (21.5%)
Lakhimpur	0	1 (2%)	1 (0.7%)
Majuli	8 (8.8%)	7 (14.3%)	15 (10.7%)
Dibrugarh	1 (1.1%)	0	1 (0.7%)
Total	91 (100%)	49 (100%)	140 (100%)

With regard to the district wise distribution of AES/JE cases, it was observed that maximum number of AES cases were from Jorhat district 86 (61.4%) followed by Golaghat 30 (21.5%), Majuli 15 (10.7%), Sivasagar 7 (5%) and 1 (0.7%) each from Dibrugarh and Lakhimpur district. (Table 2)

Figure 1: Monthly incidence of AES /JE cases



During the study period, the admission load of AES/JE patients demonstrated that majority 84 (60%) of AES/JE patients were hospitalized in rainy season starting from month of June to September. (Figure 1)

It was observed that among 49 JE patients, only 2 (4.1%) were immunized with SA 14-14-2 vaccine while the status of 34 (69.4%) patients were unknown. Similarly, of the total 91 non-JE AES patients, only 6 (6.6%) had received JE vaccine and the status was unknown for 47 (51.6%) patients.

At the time of discharge of the total 140 AES cases, 110 (78%) were found to be recovered completely. 19 (14%) patients were died in hospital while 11 (8%) patients were discharged on request/Discharge against medical advice (DAMA)/Leave against medical advice (LAMA).

Discussion

The present study was undertaken among 140 AES patients admitted in Pediatric and Medicine ward of Jorhat Medical College & Hospital, Jorhat, Assam during the study period. It was observed that of the total AES cases majority (60%) were below 15 years age which was similar to the findings reported by Kakoti G et al., Kuntal M et al. and Kamble et al[5,10,11]. Contrary to this Sudhir et al. found that 70.6% belonged to the age group 1-5 years[12]. This may be explained that lower age groups are more susceptible due to low immunity to different etiological agents of AES. It was revealed that 55.7% were male. The findings were in concordance with the studies conducted by Kuntal M et al. and Sudhir et al[10,12]. Majority (95.7%) of AES cases in this study belonged to Hindu religion. Earlier studies conducted by Kakkar M et al. and Kuntal M et al. also reported that 87% and 87.50% were Hindus respectively[1,10]. In our study, it was observed that 94.3% of AES cases were from rural areas which was alike to the finding reported by Sudhir et al[12]. This may be due to certain factors such as presence of paddy fields and water-logging areas which provides favorable environment for JE vectors to breed. It has been observed that in rural areas, piggeries are in close proximity to human dwellings i.e., within 100 meters, which serves as a conducive factor for transmission of JE in the community. Moreover, there are irregular use of mosquito bed nets and repellants among the households[5]. Since, JE is the predominant cause of AES in the study area, mosquitogenic factors play a pivotal role in increasing the load of AES in rural settings. With regard to the clinical profile of the AES cases, our study noted that all (100%) had history of fever and change in mental status at the time of admission which was equivalent to the findings reported by Khinchi YR et al[13]. Other clinical presentations were seizure (56.4%), neck rigidity (69.3%), and headache (42.9%). Earlier studies conducted by Kakoti G et al. and Kuntal M et al. also reported similar findings[5,10]. In the present study, it was observed that among 49 JE patients, only 2 (4.1%) were immunized with SA 14-14-2 vaccine while the status of 34 (69.4%) patients were unknown. Similarly, of the total 91 non-JE AES patients, only 6 (6.6%) had received JE vaccine and the status was unknown for 47 (51.6%) patients. Earlier study also observed poor JE vaccine coverage among children and adults in the Assam[14,15]. This underlines the need for strengthening of the quality coverage of JE vaccination through mass and routine immunization strategy. The vaccination sessions should also be assessed for appropriate supportive measures. Currently, JE vaccine SA 14-14-2 is incorporated in national immunization schedule for the state of Assam and accordingly 2 doses should be given. For children first dost at 9-12 months and second dose at 16-24 months. For adults second dose should be given after 3 months of giving first dose. Moreover, in JE endemic districts of Assam concerted effort should be given on quality implementation of integrated vector control and personal protective measures along with JE vaccination. Timely referral of serious and complicated cases to higher center would reduce the mortality rate of AES in absence of effective antiviral drugs against JE. In our study, majority of AES/JE patients were hospitalized in rainy season starting from month of June to September. In conformity to our finding, Kuntal M et al. reported hospitalization of cases between July to October[10]. The outbreaks of JE usually coincide with monsoons and post monsoon period as the vector density goes up during this period[10]. It was found that 78% of AES cases were recovered completely, 14% patients were succumbed in the hospital while 8% patients were discharged on request or due to DAMA/LAMA. The findings correlated well with the other studies conducted by Kuntal M et al. and DuBray et al[10,16]. Differently, a study done by Khinchi et al. found that 40.6% patients were discharged and 34.3% died[13]. This necessitates that the government should have provision for making policy to reinforce the health care facilities in the endemic locality with specialized well equipped critical care unit for AES patients.

Conclusion

Acute Encephalitis Syndrome (AES) has a very complex etiology and JE virus is one of the major causes of AES in Assam state of India. High risk eco-environmental behaviors like keeping piggeries nearby houses, building human dwelling in close proximity to paddy field, poor knowledge on personal protective measures and delay in reporting to health care facilities worsens the diseases dynamics in the affected districts. Strengthening and expanding JE vaccination and improving quality integrated vector control measures as well as awareness building on personal protection against mosquito bites will help in effective prevention of JE. Since the Non-JE cases are alarmingly high, an extensive study on etiological agents is recommended for the research organization with provision of grant in this endemic locality.

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