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Original Article

Demographic Profile, Respiratory Presentation and Outcome Analysis of Acute Encephalitis Syndrome in a Tertiary Hospital in Bangladesh

BK Tarafder[1], MAI Khan[2], TA Dola[3], M Shabnam[4], MM Uddin[5], MA Amin[6], R Saha[7], AR Hawlader[8], MT Miah[9]

Abstract:

Acute encephalitis syndrome has been a major health problem worldwide due to its high morbidity and mortality. The aim of this study was to find out the demographic profile of acute encephalitis syndrome and to determine the association of the outcome of the disease with the demographic factors and respiratory symptoms at presentation. This observational analytic cross-sectional study was conducted in the departments of Medicine, Paediatrics, and Neurology in Bangabandhu Sheikh Mujib Medical College Hospital in Bangladesh from September 2013 to August 2014. People of all ages who fulfilled the inclusion criteria of acute encephalitis syndrome were included in the study. In this study, 270 cases were diagnosed with acute encephalitis syndrome. Most cases were clustered around the age groups of 0-5 year (24.1%), 6-17 year (24.8%), and 18 -45 year (28.5%). Death was higher among the 18-45 age groups (33.3%) as well as in males (59.3%). Apart from neurological symptoms, respiratory symptoms on presentation were present in 66.9% cases with 89.6% death and this association was found statistically significant (p value < 0.001, AOR 6.96, COR 5.3 with 95% CI). Influence of socio-demographic factors and delay in seeking hospital admission on adverse outcome was not statistically significant. Most cases occurred in January-February (12.6% and 11.1%) and in July (14.4%). Overall mortality was 17.8%. Encephalitis presenting with respiratory symptoms in association carries higher mortality.

Key words: Acute encephalitis syndrome (AES), Respiratory features in encephalitis.

Introduction:

Acute encephalitis syndrome (AES) is defined as a condition in which a person of any age at any time of year develops 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 (except febrile seizure)[1]. The incidence varies in different studies, but the average incidence is 3.5 to 7.4 per 100,000 patients annually[2]. Incidence is higher in children[2]. The etiology of AES can be broadly grouped under the infective and non-infective categories, which widely varies depending on the geography, host factors and seasonal variation[3]. Though in most of the cases, the

1. Dr. Binoy Krishna Tarafder, MBBS, FCPS (Medicine) Associate Professor, Department of Medicine, Dhaka Medical College, Dhaka.
2. Dr. Mohammad Ashik Imran Khan, MBBS, FCPS (Medicine), MD (Chest Disease) Medical Officer, National Institute of Disease of Chest and Hospital, Dhaka.
3. Dr. Taslima Ahmed Dola, MBBS, Lecturer, Department of Community Medicine, East West Medical College, Dhaka.
4. Dr. Mahbuba Shabnam, MBBS, FCPS (Medicine) Assistant Professor, Department of Medicine, Green Life Medical College, Dhaka.
5. Dr. Md. Mohi Uddin, MBBS, FCPS (Medicine) Indoor Medical Officer, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
6. Dr. Mohammad Ashraful Amin, MBBS, Department of Public Health, North South University, Dhaka.
7. Dr. Radheshyam Saha, MBBS, FCPS (Medicine), MD (Neurology), Professor, Department of Neurology, Diabetic Association Medical College, Faridpur.
8. Dr. Anisur Rahman Hawlader, MBBS, FCPS (Medicine), Associate Professor, Department of Medicine, Bangabandhu Sheikh Mujib Medical College, Faridpur.
9. Prof. Dr. Md. Titu Miah, MBBS, FCPS (Medicine), Professor of Medicine & Director General, DGME, Mohakhali, Dhaka.

Address of correspondence:

Dr. Binoy Krishna Tarafder, MBBS, FCPS (Medicine) Associate Professor, Department of Medicine, Dhaka Medical College. Phone : +88 01815 005 452, E-mail: binoymmch@yahoo.com

etiologic agent is not identified; in cases with identified etiology, viruses are responsible in majority of cases[3]. Children and young adults are common victims of encephalitis. Recovery is the usual rule in most of the viral encephalitis (VE) cases, but some are associated with considerable morbidity and mortality. Unfortunately, virological diagnosis is complex, expensive and time consuming. In the Western world, Herpes Simplex virus is the most important cause[4]. Annual incidence of VE is presumed to be under-reported in developing countries due to lack of facilities for pathogen detection[4]. In Asia, Japanese encephalitis (JE) is reported as the major cause of encephalitis[4]. But the scenario is always changing, and many viral strains may cause epidemics. Very few studies of VE have emanated from Bangladesh. Though JE is considered as childhood disease in most JE endemic countries, it also causes encephalitis in Bangladeshi adults[5]. Furthermore, outbreaks of Nipah encephalitis has been continuing to occur since 2001 in different districts causing high mortality[6,7]. Prominent respiratory involvement and human to human transmission were reported as unique characteristics of these outbreaks[8,9]. Therefore, the scenario of encephalitis in Bangladesh seems to be diverse. In this study, we observed some demographic features and immediate outcome of patients with AES admitted in a tertiary care hospital in a district of Bangladesh where multiple outbreaks of Nipah encephalitis were also reported previously. Association of the outcome of AES in the presence of respiratory features in encephalitis was analyzed as well.

Materials and methods:

This was a hospital based cross-sectional study conducted in Bangabandhu Sheikh Mujib Medical College Hospital in Bangladesh from September 2013 to August 2014. All the patients with diagnosis of AES were included in the study. The clinical case definition of AES included new onset of fever (temperature ≥ 38°C) or history of fever during the present illness along with altered mental status, (e.g., confusion, disorientation, coma) and/or a neurological deficit (i.e., focal or diffuse neurological dysfunction or new onset of seizures) with onset of the neurological symptoms within five days prior to hospitalization. Following ethical clearance from the ERC of the institute, AES cases of any age were included from the departments of Medicine, Paediatrics, and Neurology in the hospital. Diagnosis was done based on the clinical features fulfilling the criteria of AES supported by the investigations including CSF analysis for cell count, analysis of protein and sugar, and brain imaging in relevant cases. Investigation to identify virological etiology could not be done as facilities were not available. In some patients, CSF analysis could not be done due to time constrain or contraindication. All the patients received standardized treatment for acute encephalitis. Informed written consent was taken from the patients or guardians of the paediatric patients. Data were recorded using a preformed questionnaire where demography, predominant symptoms and outcome were recorded. Data were analyzed in SPSS version 20 using the appropriate statistical formula accordingly.

Result:

A total of 270 cases with diagnosis of AES were included in this study. Among them, most cases were clustered in three age groups of 0-5 year (24.1%), 6-17 year (24.8%) and 18-45 year (28.5%). Death was highest among the 18-45 age group (33.3%) followed by 0-5 age group (29.2%). Sex distribution showed that, incidence was higher among the males than females (59.3% vs 40.7%). But mortality was higher in female (21.8%) than in male (15%). Overall mortality was 17.8% (Table I).

Regarding occupation, most cases were unemployed (74.8%) including housewives, students, children, infants and people without any job. Most of the patients were presented within 1-5 days of symptoms onset (60%). Death was also high in this group (64.6%). Among 263 patients, 66.9% had respiratory involvement (cough or respiratory distress) in association and 33.1% did not have any respiratory symptom. In 7 patients, data regarding respiratory symptoms was not obtained. Those having respiratory complaints during presentation were associated with higher death outcome (89.6%) in comparison with those having no respiratory symptom at presentation (10.4%), which was found statistically significant (p value < 0.001). It means, most of the patients having respiratory symptoms on presentation did not survive (Table I).

Table I: Bivariate analysis for association studies among the factors

Exposure factors	Encephalitis n=270 (%)	Death outcome n=48 (%)	P value
Age (year)			
0-5	65 (24.1)	14 (29.2)	0.559
6-17	67 (24.8)	8 (16.7)	
18-45	77 (28.5)	16 (33.3)	
46-60	26 (9.60	5 (10.4)	
>60	35 (13)	5 (10.4)	
Sex			
Male	160 (59.3)	24 (50)	0.15
Female	110 (40.7)	24 (50)	

Occupation			
Service	18 (6.7)	1 (2.1)	0.562
Unemployed	202 (74.8)	37 (77.1)	
Labour	45 (16.7)	9 (18.8)	
Others	5 (1.9)	1 (2.1)	
Delay (days)			
0	18 (6.7)	4 (8.3)	0.769
1-5	162 (60)	31 (64.6)	
6-10	63 (23.3)	9 (18.8)	
>10	27 (10)	4 (8.3)	
Respiratory symptoms at presentation			
Yes	176 (66.9)	43 (89.6)	<0.001
No	87 (33.1)	5 (10.4)	

Pearson's chi-square test was used to find out the association between the variables.

In Table II, a multiple logistic regression model was used to predict the death outcome with the associated risk factors (e.g., age, sex, occupation, delayed hospital admission and presence of respiratory symptom). The Odds Ratio (OR) with 95% Confidence Interval (CI) was calculated to measure the effects of the covariates or associated risk factors of the death outcome. To test the significance of the exposure factors OR likelihood ratio test was used. It revealed that age, sex, occupation, delay in seeking hospital admission had no significant influence on adverse outcome of encephalitis. But respiratory symptoms at presentation had a significant impact on death outcome in an adverse way (AOR 6.96, COR 5.3 with 95% CI).

Table II: Multiple logistic analysis for risk factors studies

Exposure factors	**Death outcome**	
	COR (95% CI)	**AOR (95% CI)**
Age (years)		
0-5	1.00	1.00
6-17	0.48 (0.19, 1.24)	0.49 (0.18, 1.34)
18-45	0.91 (0.41, 2.06)	1.34 (0.48, 3.76)
46-60	0.82 (0.26, 2.56)	1.46 (0.36, 5.87)
>60	0.59 (0.19, 1.81)	0.75 (0.21, 2.69)
Sex		
Female	1.00	1.00
Male	0.64 (0.34, 1.2)	0.54 (0.23, 1. 26)
Occupation		
Unemployed	1.00	1.00
Service	0.25 (0.03, 1.95)	0.26 (0.03, 2.55)
Labour	1.07 (0.47, 2.41)	1.14 (0.34, 3.79)
Others	1.07 (0.12, 9.83)	0.21 (0.01, 4)
Delay (days)		
0	1.00	1.00
1-5	0.54 (0.16, 1.86)	0.29 (0.06, 1.43)
6-10	0.38 (0.1, 1.51)	0.19 (0.03, 1.07)
>10	0.39 (0.08, 1.91)	0.24 (0.03, 1.65)
Respiratory symptoms on presentation		
No	1.00	1.00
Yes	5.3* (2.02, 13.93)	6.96* (2.49, 19.42)

*COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio; *Significant at 5% level.*

Geographical distribution shows (Figure 1), cases were from surrounding 11 districts and most of the cases were from Faridpur, Rajbari and Madaripur.

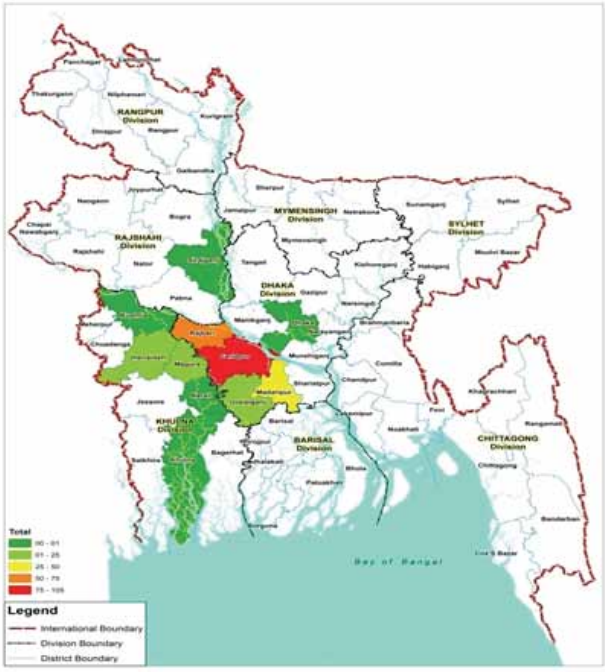

Figure 1: Geographical presentation of the cases

Figure 2 shows that AES occurred throughout the year with a peak in January and February (12.6% and 11.1% respectively) and another peak in July (14.4%).

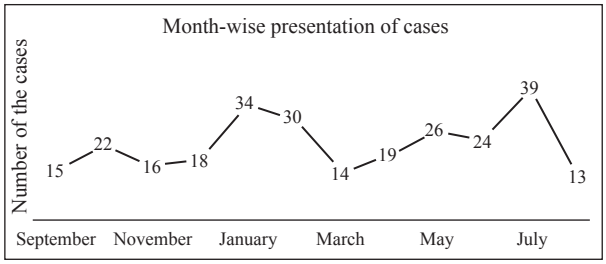

Figure 2: Month-wise distribution of the cases

Discussion:

Encephalitis is a grave disease which carries significant mortality and morbidity. Though the etiological spectrum of AES seems to be very wide, viral etiology is mostly responsible. In India, after 2000, rise of non-JE outbreaks were detected which caused dramatic change in AES scenario there. After 2012, it again shifted towards JE[10]. In 2014, the total number of AES cases and number of deaths reported from India were 10,853 and 1,717, respectively[3]. In Bangladesh, etiological pattern is not sufficiently studied. A study to assess the etiology of encephalitis in Bangladesh was conducted in four tertiary care hospitals from 2003 to 2005 and provided evidence that JE was the most common identifiable cause of viral encephalitis[11]. Paul et al. found the highest JE in northwest Bangladesh (Rajshahi) among 4 different districts in different corners of Bangladesh. People of all age groups were affected with a median age of 15 years. Peak incidence was noted in October each year[5]. Unfortunately, Faridpur district was not included in any of these studies. Due to lack of availability of facilities, etiological diagnosis is not possible in most of the centers in Bangladesh. Commonly, characteristic pattern of neurological manifestation and other systemic symptoms like respiratory symptoms may point to a particular virus or any newer strain; some of which are associated with significant morbidity and mortality[9]. Nipah was first detected in Malaysia in 1998 when there was a change in the clinical pattern of encephalitis with presence of cough or respiratory distress in addition to neurological features; and, higher mortality than previous cases was noticed in affected patients as well.[9] In Bangladesh, the 2004 outbreak of Nipah encephalitis shared a similar presentation of respiratory component like cough or respiratory distress in addition to the neurological features in majority of patients. Mortality was also remarkably high. In this study, we found a large number of patients of AES in a year (270 cases). Among them, incidence was slightly higher among the males than that of females (59.3% vs 40.7%). Similar results were observed in previous studies in India (Male 57.19%, female 42.81%) and Nepal (Male 72.34% and Female 27.65%)[12,13]. The male predilection may be explained by more outdoor activities, wearing fewer clothes, sleeping outside home, and these factors often lead to increased exposure to Culex mosquito and other vectors[14,15]. The mortality of the cases in our study was 17.8 %. Recent studies in India showed an overall death rate of 24.96% due to AES[13-16]. Bivariate analysis revealed no significant association of death outcome with the demographic factors ($p>0.05$) as well as delay in seeking hospital admission ($p>0.05$). But it revealed that, respiratory symptoms at presentation of AES had significant association with adverse outcome ($p\leq0.001$). A significant percentage (89.6%) of the patients having associated respiratory complaints during presentation did not survive. Multiple logistic analysis for risk factors could not find any significant influence of demographic profile on the outcome of encephalitis (AOR at 95% CI around 1 in almost all age groups, AOR 1.00 in male, 1.06 in female). Delayed admission into hospital did not impact the death outcome in this study. But those who had respiratory symptoms at presentation had a grave outcome (AOR 6.96). As these significant findings cannot be readily explained, it demands further interest as it may provide any clue regarding etiology. A study in UK reported respiratory involvements were more common in patients with ADEM[17]. Associated respiratory complaints were usually found in Nipah virus infection occurred in Bangladesh and India. In this study, respiratory symptoms were present in 66.9% of the cases, which may indicate possible Nipah encephalitis. But the number of such cases in our study does not corelate with the reported Nipah virus infected cases in Bangladesh during or around the study period. Data from 2001-2015 in Bangladesh shows that, most reported Nipah encephalitis cases were in 2004 (67 with 75% mortality). In 2013 and 2014, number of the reported such cases were 26 and 38 respectively in the whole country[18]. Therefore, undiagnosed, or unreported Nipah encephalitis cases could be a possibility or any other etiology of encephalitis responsible for associated respiratory symptoms at presentation with high mortality rate may remain there. Our study found an extremely high cluster of AES cases in greater Faridpur region in geographical distribution and those cases were distributed throughout the year though two peaks were observed, one in January-February and another in July. Outbreaks of Nipah virus infection usually occur between December-May and peak of JE is seen during warm season between May-October[18-20]. Thus, the peaks we found in our study corelate with that of both Nipah encephalitis and Japanese encephalitis (JE).

Conclusion:

Acute encephalitis syndrome (AES) is a serious condition which can be due to infectious and non-infectious causes. But infective etiology is more common and may lead to significant morbidity and mortality. In Bangladesh, Nipah virus encephalitis and Japanese B encephalitis cases were reported previously during epidemics. However, the changing spectrum of AES in recent years should be considered as a matter of concern. Therefore, this study was intended to find out the association of the outcome of encephalitis with the

demographic profile and associated respiratory symptoms at presentation. The present study revealed that, considerable number of cases of AES presented with associated respiratory symptoms and they carried higher mortality as well. But the findings did not follow any reported common trend of AES in our country. It was a single-centered study & facilities to identify virological etiology were not available. Hence, further research needs to be undertaken for better understanding of the etiological pattern.

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