Encephalitis in children A three years experience in a teaching hospital
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Abstract

Background: Encephalitis is a very dreadful disease in children with high mortality rate. It is endemic throughout the year with occasional epidemics in various localities in our country. But there is no available data of this in the northern districts. Objectives: To know the present situation of the social, clinical and aetiological characteristics of acute endemic encephalitis in children admitted in a tertiary care hospital from the northern Districts of Bangladesh. Methodology: This study was conducted for period of three years from January 2006 to December 2008. This was a descriptive type of study. The children were selected purposively (nonrandom sampling). At first, the children admitted with the complaints of fever, convulsion, impaired consciousness or coma were provisionally diagnosed as encephalitis and selected for investigations. Cerebrospinal fluid (CSF) analysis was performed in all these cases along with Computed Tomographic (CT) scanning of brain and selected viral markers. The children having above clinical features with (a) diffuse or focal oedema of the brain or (b) lymphocytic pleocytosis with normal brain scan or (c) both were regarded as encephalitis and selected for analysis. Results: A total of 705 children were admitted during the study period and after exclusion by defined criteria 285 were finalized for analysis. The mean age was 4± 2.4 years and male:female ratio was 63:37. Death rate was 44.56%. Coma (85%), convulsion (75%), respiratory prodromal features (75%) and fever (65%) were the presenting complaints. About 98% children came from rural areas and low socio-economic families and 88% of them were malnourished. Only 15% of the families were using mosquito nets during sleep time and 68% children had free movement surrounding the household environment. CSF analysis showed lymphocytic pleocytosis in 35% of cases. CT scanning findings showed generalized or focal oedema of brain in 78% of cases and IgM antibody against Herpes Simplex Virus (HSV), cytomegalovirus (CMV) and Toxoplasma gondii were positive in 4% of cases each. Conclusion: Acute endemic encephalitis is a serious infectious disease in children with high mortality. Clinical diagnosis remains the mainstay and etiological diagnosis remains uncertain in maximum cases.

Key words
Acute endemic encephalitis, children, northern districts, Bangladesh.

Introduction
Encephalitis means inflammation of the brain material. Two forms of encephalitis are found-Primary encephalitis (acute) is due to direct invasion of the brain cells. Secondary (post-infectious) encephalitis follows a systemic infection and is due to allergic or immunologic reaction of the causative organisms. The causative organisms are usually viruses and the clinical features are usually impaired consciousness or coma, fever and respiratory symptoms. It is a serious infection in children with usually no specific treatment. The mortality rate is also high. The admission rate is gradually increasing as other infectious diseases are decreasing due to various control measures in our country. It is endemic throughout the year with occasional epidemics in various localities in our country. There were
four epidemics in our country during the period of 2001-2004. Epidemiological and laboratory study conducted in these with the collaboration of some international organizations has shown evidence of infection by Nipah viruses. In the Department of Paediatric of Rangpur Medical College Hospital (RMCH) a total of 14726 children were admitted in the years of 2004 and 2005, and among them 225 children were suffering from encephalitis with a mortality rate 53.8% (121 in number). All these were endemic but the aetiology was unknown. Thus this was a great concern to the department and it was felt to conduct a study on encephalitis.

RMCH has a catchment area of five districts with a population of about 5.5 million. From the trend of previous 2 years it was predicted that same number or more children would be admitted in the coming 3 years. In this catchments area almost all children with encephalitis are admitted in RMCH as there is no other tertiary care hospital in this region and private hospitals usually reject these cases to admit there but there is no organized data of these patients in the department. Considering all these the study was conducted as a part of an overall study to get a baseline data by analyzing the social, clinical and aetiological characteristics of acute endemic encephalitis in children admitted in this hospital.

Materials and methods
A descriptive type of study was conducted by the Child Neurology Center attached to the Department of Paediatrics of RMCH. The sampling method was purposive (nonrandom). At first, children admitted with convulsion, impaired consciousness or coma and fever were provisionally diagnosed as encephalitis and selected for investigation. CSF study, CT scanning of brain and viral markers were done in all cases. The children having the above clinical features with (I) diffuse or focal edema of the brain or (II) lymphocytic pleocytosis with normal brain scan or (III) both were regarded as encephalitis and selected for analysis. The study was conducted for a period of 3 years from January 2006 to December 2008.

A research instrument was developed containing familial, socio-economic and health related indicators. This was revised several times before finalization. Immediately after admission of the child, resuscitation measures were applied if necessary. Glasgow Coma Scale (GCS) was assessed in all children. A blood sample was collected for determination of blood sugar, serum calcium, blood urea and complete blood count during resuscitation. Within 24 hours of admission lumbar puncture (LP) was done and CSF analysis was performed from the Department of Microbiology of the attached Medical College. CT scanning of brain was done within 48 hours. Serum and a second sample of CSF of the patients was also examined for detection of IgM antibody against Herpes Simplex Virus (HSV), Cytomegalovirus (CMV), Toxoplasma gondii and Dengue virus and a four fold rise by Immunochromatographic test (ICT) and Enzyme Linked Immunosorbert Assay (ELISA) was considered as diagnostic. These were done within 4th-7th day of admission from the private laboratory of the second author. Other antiviral markers were not done because of lack of facilities in the setting and also in the nearby private laboratories.

Treatment was started with an antibiotic and antiviral drug from the beginning. The children having the diagnosis of primary encephalitis were only included and those having meningitis, other CNS disorders, para-infectious encephalopathies, toxic encephalopathies, co-morbid systemic illness and recovering from coma within 24 hours were excluded from analysis. The children whose parents were the residents of the Districts of greater Rangpur (Rangpur, Gaibandha, Kurigram, Nilphamari and Lalmonirhat) were included in the study. The age range was from birth to 15 years. All the children were followed up to discharge or death. Verbal permission was taken from mother or care taker before data collection.
Data were being entered into a computer from the beginning of the study and after data collection is over analysis was done by SPSS+PC method. Descriptive statistical procedures were applied and data were presented as simple tables.

Results
A total of 705 children were admitted during the study period and after exclusion by defined criteria 285 were selected for analysis. The mean age was 4±2.4 years and male: female ratio was 63:37 (Table 1).

Death rate was 44.56% (127) and all death occurred in children having CGS <6. The trend of admission was same all over the year. Coma or impaired consciousness (85%), convulsion (75%), respiratory prodromal features (75%) and fever (65%) were the presenting complaints (Table 2). About 98% children came from rural areas and low socio-economic families. Maximum number (88%) of children were malnourished according to ‘Gomez' classification and rate of exclusive breast feeding was low (15%). Only 15% of the families were using mosquito nets during sleep time and 68% children had free movement surrounding the household environment. There was no contact with pigs and patients suffering from encephalitis (Table 3). CSF analysis showed lymphocytic pleocytosis in 35% of cases. CT scanning findings showed generalized or focal oedema of brain in 78% of cases. IgM antibody against HSV, CMV and Toxoplasma gondii were positive in 4% of cases each and in 0.7% cases this was positive for dengue virus (Table 4).
Discussion
The mean age of the children was 4±2.4 years and 71.2% was male children. The children of pre-school age and poor immune status are mostly affected by acute encephalitis. In pre-school years they usually move freely and are exposed and get infection. The immune system against the causative agents remains also poor in this age group and the infection becomes severe. The rate of exclusive breast feeding was low and nutritional status of the subjects was also poor in this study which may produce poor immune response. There were two surveys conducted in USA where the mean age of acute encephalitis was 4 years which goes in favour of this study. In 2001, there was an outbreak of acute encephalitis in Meherpur District of Bangladesh and another similar type of outbreak occurred in Naogaon Districts in 2004. Epidemiological investigation in these two outbreaks revealed evidence of Nipah virus infection and the mean age of the victims in those outbreaks was 12 years which also supports that children are mainly affected by encephalitis.

The death rate was 44.56% in this study. Acute encephalitis is a severe and potentially life-threatening disease. In Malaysia and Singapore in the period of outbreak in 1998-99 due to Nipah virus infection, out of 265 infected cases, the death rate was 40%. In this hospital the death rate in children suffering from encephalitis in 2005 was 51%. In the above mentioned Meherpur and Naogaon outbreaks in Bangladesh out of 47 infected people the death rate was 74% and death occurred in 4-6 days. Though the patient characteristics of this study were a bit different but the mortality rate of this study corresponds to the above figures. The GCS was determined on admission to correlate with outcome of the disease. This study has shown that children having GCS less than 6 on admission had expired. Almost similar finding has also been shown in another studies.

Convulsion, altered consciousness, respiratory prodromal symptoms and fever were the presenting features. Though the antibody detection was not possible, the clinical features suggest infection by Nipah virus. In four outbreaks of encephalitis in Bangladesh during 2001-2004, the main clinical features were respiratory and neurological signs. In a similar outbreak of Nipah virus infection in Siliguri, India, a town close to these Districts, the clinical features were also of respiratory and central nervous system. Endemicity of this virus infection has also been documented by Acute Meningo-Encephalitis Surveillance (AMES) programme conducted in three Medical College Hospitals and laboratory evidence of presence of IgM antibody was found in 1% cases in Bangladesh. There was no history of contact with cases of encephalitis in the locality, rather it occurred sporadically and there was also no history of contact with pigs which are suspected hosts of Paramyxoviruses and no history of travel of children or parents outside the localities in recent past. This indicates that in addition to the modes of transmission described in several studies, there may be human carriers of the virus to transmit the disease to susceptible children. The clinical features also go in favour of Japanese B virus as a cause of encephalitis. Almost all (98%) children came from rural areas and economically poor families. In these families there were inadequate breast feeding, improper weaning practice, low rate of use of safe water and sanitary latrines which aggravated malnutrition as a host factor to be infected by Japanese B virus. Many of the parents were also illiterate and were not careful about their child's health. The use of mosquito nets was also occasional in these families and the children moved freely especially in the dusk which are predisposing factors for Japanese B encephalitis. In the above mentioned Surveillance (AMES) programme, laboratory evidence of Japanese Encephalitis (JE) has been shown in 6% cases in our country. There are also reports of Japanese B encephalitis in the neighboring districts of India.
The findings of 4% positive cases of HSV, CMV and Toxoplasma gondii signifies that other viruses should not be ignored. Because there are reports that the most frequent causes of encephalitis are adenoviruses and herpes viruses in a few countries. There was low yielding of positive results. Actually the aetiological diagnosis of encephalitis in children is very difficult. Glaser et al has stated that there are great variation in the epidemiology of encephalitis globally and in 32-75% of cases of clinical encephalitis confirmed etiology remains unexplained.

Brain oedema either whole brain or focal areas was the commonest abnormal findings in this study. Various types of changes in the brain have been described in encephalitis revealed by CT scanning and MRI. In two studies, brain oedema and low attenuation of the brain and multifocal lesions in thalami, brainstem and cerebellar white matter was present which goes in favour of this study. But this study could not detect other findings by concerned radiologist. The imaging findings may also be normal. A small study conducted by the and published by the 1st author has also shown normal CT findings in encephalitis.

**Limitations of the study**

There were several limitations of this study. Serum examination on admission was not possible. Blood culture was not performed for bacterial causes. Other viral markers were not done due to lack of facilities. Nasopharyngeal swab could not be examined. Special tests for Viral markers such as Enzyme Immunoassay (EIA) and Reverse transcription-PCR were not done. EEG and MRI could not be performed. There may be inclusion of some cases of aseptic meningitis.

**Conclusion**

Encephalitis in children is a dreadful disease with high mortality. It is endemic in this area. It is mainly diagnosed by clinical examination due to lack of special sensitive tests. Still it is an initiation to explore the causes and there is a hope that in future further studies will be able to ascertain the aetiologies of childhood encephalitis in this region. Though we are very concerned about Nipah and JE encephalitis, other viruses should not be ignored.

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**References**


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