INCIDENCE AND ETIOLOGY OF ACUTE SYMPTOMATIC SEIZURES IN CHILDREN IN THE AGE GROUP 1 MONTH TO 6 YEARS IN KASHMIR NORTH INDIA

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ABSTRACT: BACKGROUND: Seizure is one of the common causes of childhood hospitalization with significant morbidity and mortality. Objective of current study was to know the incidence and etiology of Acute Symptomatic Seizures in children in the age group of 1 month to 6 years, in Kashmir, North India. **METHODS:** A prospective randomized hospital based study, carried out in the Department of Pediatrics, G.B. Pant Hospital Government Medical College and Research Institute, Srinagar India from 1 July 2009 to 30 June 2010. Setting: A teaching, Research and tertiary care hospital at Srinagar Kashmir North India. **PARTICIPANTS:** All the hospitalized sick children who had seizure in the age group 1 month to 6 years of the age between 1 July 2009 to 30 June 2010. **PROCEDURE:** All children with seizures in the age group 1 month to 6 years were enrolled in this study. Variables recorded were demographics, clinical presentation, laboratory tests, neuroimaging, electroencephalograph (EEG), Cerebrospinal Fluid (CSF) analysis, and hospital course. **RESULTS:** A total of 897 children in the age group 1 month to 6 years were admitted for seizures with 514(57.3%) males and 365(40.6%) females. Among these patients 545(60.7%) had Febrile Convulsions, 223(24.8%) had seizure disorder, and 129(14.3%) had Acute Symptomatic Seizures. Generalized seizures were most common seizure type (86.5%). CNS infection was the most common cause for Acute Symptomatic Seizures (38%). **CONCLUSION:** The most common etiology for Acute Symptomatic Seizure was Central nervous system (CNS) Infections. Meningitis and encephalitis were common CNS infections associated with Acute Symptomatic Seizures with significant childhood mortality and morbidity. These CNS infections can be prevented by improving the health care facilities and immunizing all infants with available Hib Conjugate Vaccine, Pneumococcal Vaccine and meningococcal vaccine.

KEYWORDS: Seizures, Acute Symptomatic Seizures, Febrile Convulsions, Kashmir India.

INTRODUCTION: Seizures are a common neurological symptom in sick children and are common cause of pediatric admission to hospitals.^(1,2,3) In children they include febrile seizures, acute symptomatic seizures (e.g., in a child with pyogenic meningitis) and seizure in child with epilepsy.⁽⁴⁾ An acute symptomatic seizure is defined as a clinical seizure occurring at the time of a systemic insult or in close temporal association with a documented brain insult.^(5,6,7) A seizure due to acute brain insult be it traumatic, infectious, toxic, metabolic, vascular, or other is called acute symptomatic seizure (ASS).^(4,7,8) These seizures are caused by specific and transient pathophysiological abnormality in central nervous system.⁽⁴⁾ Acute symptomatic seizures as those events occurring within 1 week of acute brain insult such as stroke, traumatic brain injury, anoxic encephalopathy, or intracranial surgery; at first identification of subdural hematoma; at the presence of an active central nervous system (CNS) infection; or during an active phase of multiple sclerosis or other autoimmune

ORIGINAL ARTICLE

diseases.⁽⁶⁾ In addition, a diagnosis of acute symptomatic seizure should be made in the presence of severe metabolic derangements (documented within 24 h by specific biochemical or hematologic abnormalities), drug or alcohol intoxication and withdrawal, or exposure to well-defined epileptogenic drugs.^(6,7) Acute symptomatic seizures must be distinguished from unprovoked seizures and separately categorized for epidemiologic purposes.⁽⁷⁾ Approximately 5% children with infection of CNS have acute symptomatic seizures at the time of infection.⁽⁸⁾

METHODS: This study was conducted in the postgraduate department of pediatrics, G.B Pant hospital, an associated hospital of the Government Medical College Srinagar North India. The hospital is referral tertiary care hospital housing department of pediatrics. It was hospital based prospective non-randomized study conducted from 1 July 2009 to 30 June 2010. Participants were all sick children with history of recent seizure in the age group 1 month to 6 year of the age.

Excluded from the study were all with Febrile Convulsions and Seizure disorder.

Following were the investigations done in children with seizure:

Blood was obtained for complete blood counts, ESR, CRP, blood glucose, kidney function tests, serum sodium, serum potassium, serum calcium, serum phosphorous, and serum magnesium. Blood and CSF cultures, were done in patients who had clinical features of suggestive of sepsis. Other extended biochemical investigations (Tandem mass spectrometry and gas chromatography mass spectrometry) and lumbar puncture were performed according to standard protocols to rule out organic cause of symptomatic seizures. MRI/CT scan and USG of brain was done in relevant patients to rule out intracranial pathology. EEG was done in all patients with seizures.

All children 1 month to 6 years of age with convulsions were evaluated by detailed history, relevant prenatal and postnatal events, and intake of any poison or drug. Detailed clinical examination including signs for neuro-cutaneous syndromes, storage disorders, and chromosomal anomalies were looked for and the findings recorded on predesigned proforma.

The following were the standard case definitions to identify the etiology of Seizures:

1. Febrile seizures were defined as seizures during fever between 6 months to 6 years age in absence of intracranial infection or previous history of unprovoked seizures.
2. Epilepsy was defined as two unprovoked seizures >24 hrs apart.
3. Acute symptomatic seizures were defined as seizures due to acute brain insult be it traumatic, infectious, toxic, metabolic, vascular, or due to other systemic disturbance. Following definitions were used to find etiology of acute symptomatic seizures:
 - a. Acute bacterial meningitis: clinical spectrum with seizures with following CSF findings. Elevated pressure, pleo-cytosis with leukocyte count 100-10,000/mm³ or more, PMN's predominate, elevated protein usually 100-500mg/dl, decreased glucose usually <40 mg/dl (<50% serum glucose), organism usually seen on gram stain and recovered by culture.
 - b. Partially treated meningitis: clinical spectrum with seizures with following CSF findings. Normal or elevated pressure, pleo-cytosis with leukocyte count 5-10,000/mm³, polymorphonuclear cells usual but mononuclear cells may predominate if pre-treated for extended period of time, raised proteins 100-500 mg/dl, normal or decreased glucose, organisms may be seen on gram stain, or may be grown in culture.

- c. Viral meningitis or meningoencephalitis: Clinical spectrum with seizures with following CSF findings: Normal or slightly elevated pressure, rarely $>1,000$ cells/mm³, slightly elevated protein 50-200mg/dl, generally normal glucose, may be decreased to <40 mg/dl in some viral diseases like mumps. Absence of gram stain and routine CSF culture. EEG shows diffuse slow wave activity. CT/MRI shows swelling of brain parenchyma. Focal seizures or focal findings on EEG, CT scan or MRI especially involving temporal lobe suggest encephalitis.
- d. Tubercular meningitis: Clinical spectrum with seizures with or without household contact, raised ESR, positive tuberculin dermal test, elevated CSF pressure, CSF pleo-cytosis with leukocyte count ranges from 10-250 cells/mm³ and rarely exceeds 500 cells/mm³, lymphocytes predominate through most of course with protein concentration 100-3,000mg/dl (may be higher in presence of block), with decreased glucose concentration usually <50 mg/dl in most cases. CSF staining by acid fast technique, CSF culture of large volume of CSF for mycobacterium tuberculosis organism, or CSF PCR, CSF ADA. CT scan or MRI brain may show basilar enhancement or communicating hydrocephalus with signs of cerebral edema or early focal ischemia.
- e. ADEM: Children with motor weakness, acute seizures, encephalopathy, vomiting, headache even delirium and coma with MRI typically shows T2 enhancing disseminated multifocal lesions in white mater, basal ganglia, thalamus, and brain stem consistent with edema, inflammation and demyelination.
- f. Brain abscess: Clinical spectrum with elevated CSF pressure, 5-200cells/mm³ (CSF rarely acellular), lymphocytes predominate, if abscess ruptures in to ventricle, PMNs cells predominate and count may reach to >1000000 cell/mm³. CT/MRI brain showing cerebritis and abscess formation.
- g. Vascular (Acute stroke syndromes): Sudden onset focal neurological deficit with CT/MRI showing recent bleeding or large area of infarction.
- h. Trauma: history of recent trauma with seizures, with CT scan Showing brain swelling or subarachnoid haemorrhage or blood clotting along falx or intracranial hemorrhage.
- i. Poisoning: history of poison ingestion with seizures like organ phosphorous. Gastric aspirate and blood sample were sent for toxicological screening.
- j. Hyponatremia: Serum sodium level less than 135meq/dl. In patients with hyponatremia seizures occurs when serum sodium concentration declines to <125 meq/dl.
- k. Hypernatremia: Serum sodium concentration more than 150meq/dl. Symptomatic hypernatremia develops at serum sodium concentration >160 meq/dl.
- l. Hypoglycemia: Whole blood glucose concentration <50 mg/dl.
- m. Hypomagnesaemia: Serum magnesium concentration <1.2 mg/dl.

The data collected was analyzed and scrutinized by SPSS (Statistical package for social science) and Minitab 11.30. Chi square test and students test were applied to draw the inferences.

RESULTS: A total of 12012 children in the age group of 1 month to 6 year were admitted to GB Pant children hospital during 1-year study period. Among them 897(7.4%) had recent seizure. Febrile seizures were diagnosed in 545(60.75%), Seizure disorder in 223(24.8%) patients and were both excluded from the study. Acute Symptomatic Seizures were diagnosed in 129 of 897(14.3%) patients.

ORIGINAL ARTICLE

Only these 129 patients were included in the study, of which 63(48.8%) were boys and 66(51.1%) were girls. Out of 129 patients 28(21.7%) had Pyrogenic meningitis, 10(7.75%) Encephalitis, 9(6.9%) CNS Tuberculosis, 2(1.5%) Brain Abscess, 17(13%) Poisoning, 11(8.5%) post DPT seizures, 10(7.7%) Hyponatremia, 1(0.78%) Hypernatremia, 4(3.1%) Hypocalcaemia, 9(6.9%) Acute Demyelinating Encephalomyelitis (ADEM), 3(2.3%) Nephritis with hypertensive encephalopathy, 1(0.78%) Hepatic encephalopathy, 1(0.78%) Acute lymphoblastic leukemia with intracranial hemorrhage, 1(0.78%) HIV Encephalopathy, 1(0.78%) Sub-acute Sclerosing panencephalitis (SSPE), 1(0.78%) Stroke, 17(13%) Encephalopathy/inborn error of metabolism.

Hospital incidence of different types of seizures in the age group 1 month to 6 years is shown in table 1.

Diagnosis	Patients with seizure	Males	Females	Patients without disease	Both Sexes n=12012	Males n=6226	Females n=5786	P value	Odds ratio	Relative risk
Febrile convulsions	545	308	237	11467	4.54%	5%	4.1%	<0.03	1.26	1.21
Seizure disorders	223	127	96	11789	1.85%	2%	1.65%	0.14	1.3	1.23
Acute symptomatic seizures	129	62	67	11883	1.15%	0.99%	1.1%	0.45	0.85	0.90

Table 1: Sex specific and cumulative incidence of different type of seizures by 6 years, and p value for differences between sexes

The above table depicts that febrile convulsions are most common seizures up to 6 years of age (4.5%) followed by seizure disorder (1.85%) and acute symptomatic seizures (1.15%) .Both febrile convulsions and seizure disorders are common in males than females. Acute symptomatic seizures are common in females.

Sex Specific and etiology of different types of Acute Symptomatic Seizures in children 1 month to 6 years of age is given in Table 2.

Diagnosis	Males	Females	Total	Percent
Pyogenic Meningitis	12	16	28	21.7
Encephalitis	6	4	10	7.75
CNS Tuberculosis	5	4	9	6.9
Brain Abscess	1	1	2	1.5
Poisoning	9	8	17	13
Post DPT Seizures	6	5	11	8.5
Hyponatremia	4	6	10	7.7
Hypernatremia	1	0	1	0.78
Hypocalcemia	2	2	4	3.1
ADEM	4	5	9	7
Nephritis with severe hypertension	2	1	3	2.3
Hepatic grade 3 encephalopathy	0	1	1	0.78
Acute Leukemia with ICH	1	0	1	0.78
HIV encephalopathy	1	0	1	0.78

ORIGINAL ARTICLE

SSPE	0	1	1	0.78
ICSOL	2	1	3	2.3
Stroke	1	0	1	0.78
Encephalopathy / IEM	6	11	17	13
TOTAL	63	66	129	100

Table 2

CNS (central nervous system), DPT (Diphtheria, Pertusis, Tetanus), ADEM (Acute Demyelinating encephalomyelitis), ICH (Intracranial Hemorrhage), HIV (Human Immune Deficiency Virus), SSPE (Sub acute sclerosing pan encephalitis), ICSOL (Intra cranial space occupying lesion), IEM (Inborn Error of metabolism).

Age Group	Male n	Female n	Total
1 – 12months	5	5	10
13-24 months	4	5	9
25-36 months	2	3	5
37-72 months	2	1	3

Table 3: Sex and age distribution of meningitis

The above table depicts that meningitis with seizures is common before 24 months of and females are affected more than males.

Age Group	Male n (%)	Female n (%)	Total
1 – 12months	5	6	11
13-24 months	0	0	
25-36 months	0	0	
37-72 months	0	0	

Table 4: Sex and age distribution of hyponatremia

The above table depicts that Hyponatremic seizures are common in infancy.

DISCUSSION: Seizures are common in pediatric age group and occur in about 10% of children. Most seizures in children are provoked by the disorders originating outside the brain such as high fever, infection, hypoxia, dyselectrolytemia, toxins, and hypoglycemia. Less than one-third seizures in children are caused by epilepsy. Although the outlook for children with symptomatic seizures or those associated with epilepsy is generally good, seizures may signal a potentially serious underlying systemic or central nervous system disorder that requires thorough investigations and management.

In our study, the total incidence of seizures was 7.4% (897/12012) in the age group 1month to 6 years. Our study revealed the incidence of febrile convulsions was 4.54%, Seizure disorder 1.85%, and Acute symptomatic seizures 1.15%, which is consistent with study of Forsgren et al.⁹

Few epidemiological studies have assessed the incidence and etiology of acute symptomatic seizures in young children who represent one of the most vulnerable age groups for seizures.

ORIGINAL ARTICLE

The cumulative incidence of acute symptomatic seizures in our study was 1.15% (1100.5/100000 per year) with male incidence 0.99% and female incidence of 1.1%. The incidence was higher than found by Chao- Ching Haung et. al¹⁰ in Taiwan, which revealed the incidence of acute symptomatic seizures 0.48% and was lower than found by J. M. K. Murthy et.al¹¹ that reported incidence in 22.5% of patients in south India. Our cumulative incidence of acute symptomatic seizures is also higher than that in the US study by Annegers et al.⁶ The higher incidence of acute symptomatic seizures in Kashmir can be explained by the fact that majority of acute symptomatic seizures in our study were caused by intracranial infections 38%, poisoning 13% and post DPT encephalopathy 8.5%.

The higher incidence of acute symptomatic seizures due to primary CNS infections is due to very low rate of vaccination against streptococcus pneumonia, n. meningitides and H influenza and MMR, poor socioeconomic status, overcrowded families, and poor health and sanitation services. Immunization against Haemophilus influenza b (Hib) has virtually stopped this organism from causing severe childhood illness in western countries and significant progress has already achieved with streptococcus pneumonia. The poisoning contributing to 13% incidence of acute symptomatic seizures in Kashmir, because 80% population of Kashmir is associated with agricultural and horticulture sectors and hence there is easy availability of the pesticides that makes them their children prone to poisoning. As the conventional DPT vaccine is still used in national immunization program in Kashmir India, so incidences of post DPT encephalopathy/seizures are quite high.

The 22.5% incidence of acute symptomatic seizures in south India as found by Murthy et.al⁽¹¹⁾ was because of high prevalence of neurocysticercosis in that part of India of which we found no case in our study.

Our study revealed that acute symptomatic seizures are more common in females 48% vs. 52%. This was in contrary to Lee et.al,⁽⁸⁾ which revealed male to female ratio was 1.18:1, and Haung Chao et al⁽⁷⁾ that revealed male to female ratio of 1.6:1. The higher incidence of acute symptomatic seizures in our study can be due to social factors with bias in gender and maximum rate of vaccination in males.

Our study revealed the cause of acute symptomatic seizures in order of frequency as intracranial infections 38%, poisoning 13%, dyselectrolytemia 8.5%, acute Demyelinating encephalomyelitis 3%, ICSOL 2.3%, Nephritis with hypertensive encephalopathy, hepatic encephalopathy, hematological malignancy, HIV encephalopathy, SSPE each constituting 0.8%. Infections were the predominant precipitant of acute symptomatic seizures. Our study was consistent with findings of Murthy et al⁽¹¹⁾ and Richard Idro et al,⁽¹²⁾ which revealed CNS infections as most common cause of acute symptomatic seizures. J. M. K Murthy et al⁽¹¹⁾ found that the most common CNS infection associated with acute symptomatic seizures was neurocysticercosis in south India and Richard Idro et al⁽¹²⁾ revealed that most common cause of acute symptomatic seizures in rural Kenyan village was malaria. However, both these parasitic infections of CNS do not occur in Kashmir. Hence, in our study, the most common etiology for Acute Symptomatic Seizures found was meningitis/encephalitis and tuberculosis of brain accounting for 38% of cases.

The age specific incidence for meningitis presenting as seizures was highest in first year of life and is consistent with Haung Chao et al,⁽⁷⁾ and Akpede GO et al⁽⁵⁾ who revealed that prevalence of meningitis was significantly higher in 1-6 months old infants when compared to older children. This finding was also consistent with the study of Joshi Batjoo,⁽¹³⁾ which revealed that in the age group of 6

ORIGINAL ARTICLE

months to 12 months, 30% of the children had meningitis as compared to 20 % and 5% in other age groups of 12- 18 months and above 18 months respectively.

The high incidence pyogenic meningitis and its associated mortality and morbidity can be decreased by using available vaccines against bacterial infections. We concluded that the introduction of vaccines against H. influenza type b and streptococcus pneumonia could produce a major change in the epidemiology not only of bacterial meningitis but also of provoked seizures in children. In United States, because of the vaccine related decline in meningitis due to H. influenza type b, bacterial meningitis is now disease predominantly of adults.

The incidence of acute symptomatic seizures attributed to metabolic insults was highest in the age group 1-12 months, largely due to Hyponatremia. This finding was consistent with Haung Chao et al³⁰ and Robert C Bruce et al.^{5,3} In our study, all Hyponatremic seizures were caused by water intoxication, not by dehydration. This was consistent with studies done by Haung Chao et al⁽⁷⁾ and Keating JP Et al.⁽¹⁴⁾ In our study hyponatremia, resulting from water intoxication was etiology in 10 infants and all were less than 12 months of age. This finding was consistent with Haung Chao et al⁽⁷⁾ and Robert C Bruce et al.⁽¹⁵⁾

Poisoning was another major and unique cause of symptomatic seizures in Kashmir contributing to 13% of acute symptomatic seizures. Because 80% population of Kashmir is associated to agricultural and horticulture sectors, hence there is an easy accessibility to pesticides.

Limitations of the Study: The details of other causes contributing for seizures like inborn error of metabolism could not be specified due to lack of investigations in a resource poor set up like ours. Multi centric prospective study is needed to find out details regarding these problems.

CONCLUSION: Acute episodes of seizures are one of the common causes of hospitalization with high mortality and morbidity. Febrile convulsions are common cause of seizures in this age group. The most common condition responsible for acute symptomatic seizures during our study was primary central nervous system infections followed by metabolic and toxic causes. Furthermore, many symptomatic seizures are preventable by improving public health service, sanitation. Public education as well as nationwide vaccination against bacterial meningitides in young infants is necessary to decrease the incidence of acute symptomatic seizures and their associated mortality and morbidity.

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ORIGINAL ARTICLE

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