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ORIGINAL ARTICLE

FREQUENCY, ETIOLOGY AND IMMEDIATE OUTCOME OF CHILDREN ADMITTED TO PEDIATRIC INTENSIVE CARE UNIT (PICU) WITH CONVULSIVE STATUS EPILEPTICUS IN KASHMIR NORTH INDIA

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ABSTRACT: BACKGROUND: Convulsive status epilepticus (CSE) is one of the common causes of childhood hospitalization to PICU with significant morbidity and mortality. Objective of current study was to know the Frequency, etiology and immediate outcome of children admitted to Pediatric Intensive Care Unit (PICU) with convulsive Status Epilepticus in Kashmir North India. **METHODS:** A prospective 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 2013 to 30 June 2014. **SETTING:** A teaching, Research and tertiary care hospital at Srinagar Kashmir North India. **PARTICIPANTS:** All the sick children admitted to PICU who had convulsive status epilepticus in the age group 1 month to 15 years of the age, between 1st July 2013 to 30th June 2014. Variables recorded were demographics, clinical presentation, laboratory tests, neuroimaging, electroencephalograph (EEG), Cerebrospinal Fluid (CSF) analysis, and hospital Course. **RESULTS:** During this period, 120 children aged 1 month to 15 years were admitted to PICU with status epilepticus. Twenty-eight of the 120 children (23.3%) were admitted following a prolonged febrile seizure. Thirty-six of the 120 children (30%) had a remote symptomatic cause for the CSE, twenty two of 120(18.3%) were admitted for an acute symptomatic cause and seventeen of 120(14.2%) were admitted with an acute exacerbation of a pre-existing idiopathic epilepsy. seven children had a progressive encephalopathy and no cause was identified in the remaining 10 of the 137 children (8.3%). Twenty of the 120 children (16.7%) died and ten (10%) had gross Neurodefecit on discharge CONCLUSION: The most common etiology for convulsive status epilepticus was remote symptomatic (30%). Cerebral palsy was common etiology for remote symptomatic CSE. Intracranial infections were commonly associated with Acute Symptomatic CSE with significant childhood mortality and morbidity. Improved perinatal and neonatal care and immunizing all infants with available Hib Conjugate Vaccine, Pneumococcal Vaccine and meningococcal vaccine can decrease the frequency of CSE.

KEYWORDS: Convulsive status epilepticus, prolonged Febrile Convulsions, Remote symptomatic convulsive status epilepticus, Kashmir India.

INTRODUCTION: Status epilepticus (SE) is a serious neurological problem in children. Both convulsive and non-convulsive SE affects people of all ages, though it is more common and causes greater morbidity and mortality in infants.[1,2,3,4,5] Age, etiology, and the duration of seizure activity correlate with mortality.[6] Status epilepticus (SE) is an epileptic seizure of greater than five minutes or more than one seizure within a five-minute period without the person returning to normal between them.[7] However the current definition of 30 min is not universally accepted and several clinical studies have been published using duration of 10 or 20 min.[6,8,9]

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It has been reported that the mortality is nearly 10-fold higher for seizure lasting 30 min or longer than for those lasting 10–29 min.[9] Status epilepticus (SE) is a medical emergency associated with high morbidity and mortality.[10] It has numerous subtypes, but generalized convulsive status epilepticus and non-convulsive status epilepticus (NCSE) are the important clinical types. The diagnosis is difficult on the basis of clinical semiology alone and requires investigation like electro-encephalogram (EEG), especially in-patients having NCSE.[11]

The recognition and rapid treatment of seizures is important during acute illness.[12,13,14] The failure to diagnose status epilepticus leads to high mortality Lately it is becoming increasingly recognized that seizure duration of more than 10 minutes can lead to brain damage and duration of seizure activity in definition of status epilepticus is being decreased.[15,16] The longer the SE is present, more difficult is the control and more is the risk of permanent neurological damage. Immediate intervention is important whenever the patient has SE.[16] It is important to consider SE whenever a seizure activity or a series of seizure activity persist for more than 10minutes or and to consider therapy.[17]

Increasing number of studies from India and around the world, have tried to systematically examine trends in incidence, precipitants and outcome in patients with SE with an aim to look at potentially reversible factors.

MATERIAL AND 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 1st July 2013 to 30th June 2014. Participants were all sick children admitted to pediatric intensive care unit (PICU) with Convulsive Status Epilepticus (CSE) in the age group 1 month to 15 year of the age.

Following were the Investigations done in Children with Convulsive Status Epilepticus: 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 status epilepticus. 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 15 years of age with convulsive status epilepticus (CSE) 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: Convulsive status epilepticus was classified using a modification of an earlier classification into five etiological categories: prolonged febrile convulsion (PFC), acute symptomatic (AS), remote symptomatic (RS), idiopathic epilepsy-related (IE-R), progressive encephalopathy (PE) and unclassified (U).

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These were defined as follows:

Prolonged Febrile Convulsion (PFC): CSE during a febrile (temperature above 38°C) illness in a previously neurologically normal child aged between 6 months and 6 years, and in the absence of defined central nervous system (CNS) infection.

Acute Symptomatic (AS): CSE in a previously neurologically normal child, within a week of an identified acute neurological insult including head trauma, CNS infection, encephalopathy, cerebrovascular disease, and metabolic or toxic derangements.

Remote Symptomatic (RS): CSE in a child, with previous neurological abnormality. This category included children with cerebral palsy with a febrile illness not of CNS origin and children with obstructed ventriculo-peritoneal shunts for post-hemorrhagic hydrocephalus.

Idiopathic, Epilepsy-Related (IE-R): CSE in a child, with a prior diagnosis of idiopathic or cryptogenic epilepsy or when the episode of CSE is the second unprovoked seizure that has led to a diagnosis of epilepsy.

Progressive Encephalopathy (PE): CSE in a child with progressive neurodegenerative disease (e.g., late infantile neuronal ceroidlipofuscinosis, subacute sclerosing panencephalitis [SSPE], mitochondrial disease).

Unclassified (C): CSE that could not be classified into any of the above category**.**

The data collected was analyzed and scrutinized by SPSS (Statistical package for social science) and Stata.

RESULTS: A total of 1800 children in the age group of 1 month to 15 year were admitted to PICU GB Pant children hospital during 1-year study period. Among them 120(6.6%) had convulsive status epilepticus. Generalized tonic clonic status epilepticus was most common presentation 102/120(85%), myclonic in 12/120(10%), tonic 5/120(4.1%), complex partial status 1/120(83). Prolonged febrile convulsion (PFC) was diagnosed in 28/120(23.3%), Remote symptomatic (RS) in 36/120(30%), Acute symptomatic (AS) (including meningitis, encephalitis, trauma and anoxia) in 22/120(18.33%), Idiopathic-Epilepsy Related (IE-R) in 17/120(14.2%), Progressive encephalopathy (PE) in 7/120(5.8%) and Unclassified (U) in 10/120(8.3%) of patients. The convulsive status epilepticus was more common in age group 1month to 36 months of age 42/120(35%) and 36 months to 72 months of age group 36/120 (30%).

	PFC	AS	RS	IE-R	PE	U	Total
1 to 36 months	22	12	4	4	5	2	49/120(40.8%)
36 to 72 months	5	7	10	6	2	4	34/120(28.4%)
72 to 108 months	1	2	8	4		3	18/120(15%)
108 to 144 months		1	6	2		1	10/120(8.34%)
144 to 180 months			8	1			9/120(7.5%)

Table 1: Age distribution of convulsive status epilepticus (CSE)

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PFC=Prolonged febrile convulsion, AS=Acute symptomatic, RS=Remote Symptomatic, IE-R= Idiopathic epilepsy related, PE= progressive encephalopathy, U=Unclassified.

The above table depicts that Status epilepticus is more common in age group 1 month to 36 months (40.8%) and 36 to 72 months (28.4%).

Sex	PFC	AS	RS	IE-R	PE	U	
MALE	15	8	23	11	4	8	69
FEMALE	13	14	13	6	3	2	51
TOTAL	**28/120 (23.3%)**	**22/120 (18.3%)**	**36/120 (30%)**	**17/120 (14.2%)**	**7/120 (5.8%)**	**10/120 (8.3%)**	**120**

Table 2: Sex distribution of convulsive status epilepticus (CSE)

PFC=Prolonged febrile convulsion, AS=Acute symptomatic, RS=Remote symptomatic, IE-R= Idiopathic epilepsy related, PE= progressive encephalopathy, U=Unclassified.

The above table depicts that the Convulsive status epilepticus is overall more common in males than females.

Etiology	Males	Females	Total	Percent N=22
Meningitis	1	3	4	18.18
Encephalitis	1	3	4	18.88
CNS tuberculosis	1	1	2	9.09
Hypoglycemia	1	2	3	13.64
Hypernatremia	2	0	2	9.09
Hyponatremia	1	1	2	9.09
Hypocalcemia	1	0	1	4.55
Acute hypoxia	1	1	2	9.09
Stroke (CVA)	1	0	1	4.55
Trauma	0	1	1	4.55
Total	**10**	**12**	**22**	**100%**

Table 3: Etiology of different types of acute symptomatic CSE

CSE=Convulsive status epilepticus, CVA = cerebrovascular accident.

The above table depicts that most common etiology for acute symptomatic CSE is intracranial infection.

Etiology	Male	Female	Total	Percent N=36
Cerebral palsy	14	6	20	55.6%
Anatomical malformations ofbrain	5	4	9	25%
Neuro- cutaneous syndromes	4	2	6	16.6%%
Post traumatic	0	1	1	2.78%
Total	**23**	**13**	**36**	**100%**

Table 4: Etiology for Remote symptomatic CSE

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The above table depicts that cerebral palsy is most common cause for remote symptomatic convulsive status epilepticus and males are affected more than females.

Diagnosis	TOTAL	Mortality	Gross Neurodefecit
Meningitis	4	1	1
Encephalitis	4	2	2
CNS tuberculosis	2	2	
Hypoglycemia	3	0	1
Hypernatremia	2	1	1
Hyponatremia	2	1	0
Hypocalcemia	1	0	0
Acute hypoxia	2	0	1
Stroke (CVA)	1	0	1
Trauma	1	0	0
Cerebral palsy	20	5	*
Anatomical malformations of brain	7	2	*
Neuro- cutaneous syndromes	4	1	*
Post traumatic	1	0	0
Developmental Delay	4	0	1
PFC	28	0	0
PE	7	3	*
IE-R	17	1	2
U	10	1	2
Total	**120**	**20/120(16.7%)**	**12/120(10%)**

Table 5: Diagnosis and poor outcome in children with CSE

PFC=Prolonged febrile convulsion, IE-R=Idiopathic epilepsy related, PE=progressive encephalopathy, U=Unclassified.

*Neurodefecit was already present.

	Died	Gross neurological deficit
1 to 36 months	8	4
36 to 72 months	5	3
72 to 108 months	4	2
108 to 144 months	2	2
144 to 180 months	1	2

Table 6: Age specific immediate outcome of convulsive status epilepticus

The above table depicts that outcome is poor in younger age group.

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		Died	Alive	p	95% CI	Odds ratio
Seizure duration	>45minutes	13	37	0.0140	1.11 10.77	3.36
	<45minutes	7	63			
Lag time for treatment	>1hour	14	40	0.9	0.435 2.48	1.05
	<1hour	6	60			
Response to treatment	>1hour	18	30	<0.001*	4.46 192.7	21
	<1hour	2	70			
	Absent					
Pre-hospital treatment received	No	16	55	0.0379	0.955 14.3	3.27
	Yes	4	45			
Ph	<7.0	15	30	0.0001*	2.134028 26.42627	7
	>7.0	5	70			

Table 7: Risk factors for immediate mortality in convulsive status epilepticus

*P value less than 0.001 significant.

The above table depicts that prolonged seizure duration, lag in referral time, delayed response to treatment; presenting Ph less than 7.0 are risk factors for immediate mortality.

DISCUSSION: Children living in this part of India experience a very high burden of convulsive status epilepticus. The incidence of SE in Indian subcontinent is not known. Our study revealed 120/1800 (6.6%) patients had SE. The incidence of SE varies from 3.7%-9.1% as per western literature and our results are corroborative to the reports.[15] The incidence rate is age dependent and is highest in the age group less than 36 months of age. 69% of patients were less than 6 years of age in our study. Predominant involvement of younger age group has been reported previously.[18,19] the two most common causes of CSE in our study were a remote symptomatic (30%) and prolonged febrile convulsion (23.3%) and are in concordance with Nahin Hussain.[20] Most children in the RS group in our study had pre-existing cerebral palsy. This was in discordance with most of the previous studies. The poor perinatal and neonatal care services and low rate of vaccination against pneumococus, H. Influeza and Meningococus explain the higher incidence of cerebral palsy in this part of world.

Immunization against Haemophilus infleunzae type b (Hib) has virtually stopped this organism from causing severe childhood illnesses in Western countries and significant progress has already been achieved with Streptococcus pneumoniae. Improved antenatal, perinatal (Delivery by competent personnel and neonatal resuscitation programs) and postnatal care (Cord care) can decrease the number of neonates exposed to seizures.

In our study CSE occurred in 14.2% patients who had established diagnosis of epilepsy which was in concordance with Herdorffer et al. They also reported 18% of unprovoked SE occurred in people with established epilepsy.[19]

In our study 20 children died (16.6%) while 12(10%) of the surviving children developed gross neurodefecit. These results are very dissimilar to those published recently from Nahin Hussain.[20] and Finland.[21] No child died in the study from Finland, four children (2.2%) developed permanent neurological sequelae. In contrast, an earlier 10-year study from the USA undertaken in

147 children (Aged three days to 18 years) admitted in status to a PICU found that nine patients (6%) died on PICU, usually due to the underlying cause of the status, rather than the status itself.[22]

Significant association was seen in-patients having seizure activity lasting for more than 45 minutes, delayed response to treatment and presenting Ph less than 7.0. The other risk factors for immediate mortality were age less than 36 months, lag time in the treatment of more than equal to 1 hour and patients responding after 1 hour of treatment. These findings were in concordance with Sheffali Gulati.[23]

Mortality in SE varies from 11%-53%,[24,25] Most of these patients were acute symptomatic and this was not purely a pediatric study. Logroscino et al.[25] reported 1% mortality (2/37) in age group 1-19 years. They studied risk factors as a whole but did not analyze risk factors in pediatric age group as it was mainly adult based study.

In summary, this prospective study in patients with convulsive status (CSE) in PICU has suggested that the current emergency and intensive care management of CSE in children appears to be associated with a good outcome, similar to recent data, and represents a marked improvement when compared to findings published over 30 years ago. Meanwhile improving peripheral health care delivery system, treatment of CSE before referring to tertiary care, improving PICU care, increasing rate of vaccination and perinatal and neonatal care services will decrease both incidence and poor outcome of convulsive status epilepticus.

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