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#### RESEARCH ARTICLE

# CLINICAL SPECTRUM ANDETIOLOGY OF CHILDHOOD STATUS EPILEPTICUS IN A TEACHING HOSPITAL, KASHMIR, INDIA

# Syed Muzamil Mehraj<sup>1</sup>, Shafat Ahmad Tak<sup>2</sup> and Suhail Ahmad Naik<sup>3</sup>

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- 1. Post Graduate 3<sup>rd</sup> Year Resident, Department of Pediatrics Government Medical College Srinagar Kashmir India.
- 2. Professor, Department of Pediatrics Government Medical College Srinagar Kashmir India.
- 3. Department of Pediatrics Government Medical College Srinagar Kashmir India.

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# Abstract

**Objective:** The study aimed to ascertain clinicalspectrum and different etiologies of convulsive status epilepticus in children. Methods: Hospital based prospective observational study performed in department of Pediatrics in Children Hospital Government Medical College Srinagar Kashmir India from October 2020 to September 2022. Data were recorded with the help of a pre-formed proforma.

**Results:** In this study, 184 cases of status epilepticus were included. The infants (less than 1-year)account for 23.9% of the total cases (n=184) and 67.4% children were in the age group < 5 years. The total number group >10yrs of cases in the age only 6.5%.Outof184children,malechildrenwere102(55.4%)andfemalechildre nwere82(44.6%).We found that 81.5% of the cases reachedEmergency Room (ER)within30-60minutes after seizure initiation and 18.5% reached after

Themostcommonetiologyassociatedwithstatusepilepticuswasremotecau ses like post HIE or cerebral palsy, seen in 25.54% cases, followed by acute CNS infection in 18.45 cases (pyogenic meningitis 10.3%, viral encephalitis 4.9%, and tubercular meningitis 3.26%).

Conclusion: The outcome was better for patients who had less seizure duration and received early effective standard treatment protocol within a given time frame. The patients who had prolonged seizures or first treatment hadapoor outcome. Our study reveals that though we have successfully decreased the infant mortality rate, still there is large scope for decreasing morbidity by improving the neonatal care services across Kashmir and the intact Neonate intact Nation should be our mission and passion. Furthermore, it seems very imperative that all patients of CSE should receive early effective standard treatment at doorsteps to decrease the associated morbidity and mortality.

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#### Introduction:-

Status epilepticus (SE) is a neurological emergency and is defined as seizure continuous in character for more than five minutes or multiple seizures occurring consecutively during which patients were unable to regain consciousness over a period of 30 minutes [1]. The five-minute window corresponds with the time at which urgent treatment should

### Corresponding Author: - Suhail Ahmad Naik

Address:- Department of Pediatrics Government Medical College Srinagar Kashmir India.

be initiated. At least one study has found that a convulsive seizure lasting more than 5 minutes has a high risk of lasting 30 minutes or more [2].

There are two broad categories of SE: convulsive status epilepticus (CSE)andnon-convulsive statusepilepticus(non-CSE). The identificationofnon-CSE from behavioral signs is difficult and electroencephalography(EEG)is oftenacrucial diagnostictool [3]. InCSE early institution of treatment is essential to avoid irreversible braining in through both metabolic decompensation or systemic complication like respiratory depression which further exacer bates the cerebral metabolic injury through an oxia, and subsequently, profound hypotension [4].

The Non-CSEisnotconsideredamedicalemergencysincepatientsdo not lose consciousness (there may be impairment in consciousness), don't convulse clinically andusually return to normal within minutes of its resolution (either spontaneously or in response to treatment). Some classifications have considered these seizures to be sustained seizures in comatose patients, whether the ictal discharges seen on EEG were accompanied by subtle convulsive activity, such as tonic eye deviation or rhythmic twitching of part of an extremity [5].

There are four phases of status epilepticus. They are classified based onduration as follows: [6-9]

- 1. Early phase or premonitory status: in which the convulsioncontinues for more than 5minutes. Atthis stage, the first-line treatments (benzodiazepines) are used to control these izure either prior to arrival at the hospital, by the patient's parents or paramedics, or at a hospital in the emergency department.
- 2. Established status epilepticus: in which the seizure activity continuesformorethan10andupto30minuteswiththelossofconsciousness between seizures. In this stage second line treatmentssuch as intravenous phenytoin, phenobarbital or levetiracetam areused to try and terminate it. This phase of status epilepticus may betermedbenzodiazepine-resistantstatus epilepticus.
- 3. Refractorystatusepilepticus:inwhichtheseizureactivity(convulsion) lasts for more than 30 minutes or has failed at least onedose of the benzodiazepine and a dose of second-line intravenous AED, or both.
- 4. Theformaletiologyof statusepilepticushasbeenclassifiedbytheInternational LeagueAgainstEpilepsyintofivedivisions:acutesymptomatic,remotesymptomatic,idiopathicepilepsyrelated,cryptogenicepilepsy-related andunclassified [10].
- 5. In 2006, the North London Convulsive Status Epilepticus in ChildhoodSurveillance Study (NLSTEPSS) classified the etiology into 7 groups:prolongedfebrileseizure,acutesymptomatic,remotesymptomatic,remotewithacutecauses,idiopath icepilepsyrelated,cryptogenicepilepsyrelatedand unclassified[11].

**Table I:-** Etiologyofstatusepilepticus.

Etiology	Definition	Causes	
Prolonged	CSEthatoccurredinnormalchildrenwhohadno history of central	Febrileseizure	
febrileseizur	nervous system (CNS)infection and agedbetween 6months and		
e	5yearswithatemperatureatleast38.0C		
Acutesym	CSEthatoccurredinotherwisehealthychildren whohad	MeningitisViral	
ptomatic	neurologicalinsultwithinthepast week	CNSInfection	
		Headinjury	
		Hypoxia	
Remotesy	CSE reported in children who had a pre-	Tuberous	
mptomatic	existingCNSabnormalityformorethan1week	sclerosisEncephalop	
		athy	
Remote	CSE that occurred in children within a weekfrom febrile illness or	CerebralpalsyHy	
withacutecau	acute neurological	drocephalus	
ses	insultandassociatedwithahistoryofpreviousneurologicalabnormalities		
Idiopathicepil	CSEthatoccurredinchildrenwhohadahistoryofidiopathicepilepsywith	Idiopathice	
epsyrelated	nosymptomaticcausesfortheseizure pilepsy		
Cryptogenicepi	CSEthatoccurredinchildrenwhohadahistoryofcryptogenic	Cryptogenice	
lepsyrelated	epilepsywith nosymptomaticcausesfortheseizure pil		

Unclassified	AllotherSE	

The incidence of CSE in children ranges from 10 to 38 in 100,000 peryear. [12]. The higherincidence of CSE isseen inchildrenagedlessthan4years with a peak in first year of life. [13] SE may occur in the setting of underlying, premorbid epilepsy or as the first manifestation of epilepsy [14]. SE may also be an acute symptom of medical or neurologic disease. The more common examples of the latter include [14,15]:

- 1. Central nervous system infections: encephalitis, meningitis,
- 2. Acute hypoxic-ischemic insult
- 3. Metabolic disease (e.g., hypoglycemia, inborn error of metabolism)
- 4. Electrolyte imbalance
- 5. Systemic diseases like renal failure, hepatic failure
- 6. Demyelination
- 7. Isolated CNS vasculitis
- 8. Isolated CNS lymphoma
- 9. Traumatic brain injury
- 10. Drugs, intoxication, poisoning
- 11. Cerebrovascular event

## Studyjustification:

ChildrenwithCSEareathigh

riskofmortalityandmorbidity. Asthisisamedicalemergency, themanagement of CSE must be rapid, effective, and safe. Consequently, there is a risk that the treatment of CSE may be associated with iatrogenic complications, including potentially serious adverse side effects. Even though much research has been carried outto assess the effectiveness and safety in adult patients, less research has been done to evaluate this in infants, children, and young people. This study was undertaken as an attempt to describe the clinical spectrum and etiological profile of convulsive status epilepticus CSE presenting to a tertiary care hospital.

# Aimsandobjectives:-

Toclinical spectrum, etiology of childhood status epilepticus in a teaching hospital in the age group 1month to 18 years.

#### **Inclusioncriteria:**

All children aged between 1 month to 18 years who at presentation orduring the hospital stay had status epilepticus - defined ascontinuous seizure activity or recurrent seizure activity without regainingconsciousness lastingfor >30min.

# **Exclusioncriteria:**

All the patientsinwhomtheinformationregardingseizuredurationwasincompleteorunclear, poisoning, traumatic brain injury, and electrical or non-convulsive status epilepticus.

#### Samplesize:

Totally184cases who presented with status epilepticus in our pediatricem ergency during the study period were included in study.

# Method:-

This was a hospital based prospective observational study performed in department of Pediatrics in Children Hospital Government Medical College Srinagar Kashmir India from October 2020 to September 2022. Ethical approval for this study was obtained from the hospital ethics committee. During this period a total number of 184 cases who were presented to the emergency with status epilepticus were included in study. All children aged between 1 month to 18 years who at presentation orduring the hospital stay had convulsive status epilepticus - defined ascontinuous seizure activity for more than 5 minutes or recurrent seizure activity without regaining the consciousness in between.

#### Procedure:-

Every sick child who was presenting to emergency department with CSE had been assessed and triaged on arrival and a rapidcardiopulmonary assessment was made with immediate monitoring of heart rate, blood pressure, SPO2, signs of

shock, pupil size and reaction to light. Before starting IV resuscitation, a blood sample was taken forbaseline investigations. Then the caseswere managed according to the protocol followed in our emergency room/pediatric intensive unit. After early management and stabilization detailedhistorywasobtainedincludingdurationofseizure,distancefromthe hospital where the fits started, mode of prehospital and transportation, precipitating factors, priorseizures/SE, drughistory and compliance, any chronic medical or neurological illness, developmentalmilestones, and prior neurological status. Demographic and baseline data was recorded with the help of a preformed proforma. Variables included age, sex, type of status epilepticus, cause, duration of convulsions, duration of unconsciousness, precipitating factors, EEG, and number of anti-epileptic drugs required to control the seizures, history of convulsions and fever, any complications occurred and ultimate survival or death. Baseline investigations were also carried out including complete blood count, blood glucose levels, serum electrolytes, serum calcium and magnesium, blood urea and creatinine, urinalysis, comprehensive CSF analysis, MRI and EEG were performed.

Operational definition of status epilepticus used in this study was that a seizure continuous in character for more than five minutes or multiple seizures occurring consecutively during which patients were unable to regain consciousness over a period of 30 minutes.

Data thus collected was subjected to statistical analysis with the help of computer software SPSS version 23. Chi square test was applied and p value less than or equal to 0.005 was considered significant. Therelationshipofvariousdemographic, clinical characteristics and etiology without come was evaluated employing the Chi-square test, Fischer's exact test for categorical data, and independent t-test for continuous data with normal distribution.

**Table 2:-** Agedistribution.

Ageinyears	Noofcases	Percent
< 1	44	23.9
1-5	80	43.5
6-10	48	26.1
> 10	12	6.5
Total	184	100
Mean:4.9years,		
Range:2months-15years		
S.D:41.241		

In this study, Status epilepticus in children < 1year account for 23.9% (44cases)ofthetotalcases(n=184).67.4%(124cases)ofthetotalcaseswerechildren < 5 years. Number of cases in the age group of >10yrs was only12 cases (6.5%). The mean age of the patient in the present study was 4.9yrs.Theyoungestagebeing 2months.Themaximumagebeing15years.

**Table 3:-** Sexdistribution.

SEX	TOTALNO.OFCASES(n=184)	PERCENTAGE
MALE	102	55.4
FEMALE	82	44.6

Out of 184 children, Male children were 102 (55.4%) and female childrenwere82(44.6%).

Table 4:- Prehospitaltherapy.

Prehospitaltherapy	Noofcases	Percentage	
Given	48	26.1%	
Notgiven	136	73.9%	
Total	184	100%	

Prehospital the rapy with AED was given to 48 patients (26%). The remaining 136 (74%) did not receive prehospital the rapy with AED, though 30 of them had been referred. Out of 48 children who had received prehospital the rapy only 32 had proper prehospital the rapy only 32 had proper prehospital the rapy of the remaining 136 (74%) did not receive prehospital the rapy of the rapy of the remaining 136 (74%) did not receive prehospital the rapy with AED, though 30 of them had been referred. Out of 48 children who had received prehospital the rapy of the rapy of the rapy of the remaining 136 (74%) did not receive prehospital the rapy of the rapy o

ltherapy.16childrenhadreceived improper medication or drug dosage. 32 children had receivedinjection diazepam, 12 children had received phenytoin and 4 childrenreceived phenobarbitoneas Prehospital therapyAED.

**Table 5:-** Durationofseizureatthetimeofarrival

Durationofseizureinmin	Noofcases n=184	Percentage	
30-60min	150	81.5%	
>60min	34	18.5%	
Mean: 78.12 minRange: 30 min-10hrs.SD:			
104.938			

The above table shows that 81.5%(150)of casesreachedto ERwithin30-60minsdurationofseizure and 18.5% and (34)reachedwithseizuremorethan60min.Minimumdurationwas 30mins and and duration was 10 hrs.

**Table 6:-** Seizuretype.

Typeofseizure	Noofcases	Percentage
GTCS	154	83.7
FOCAL	26	14.1
MULTIFOCAL	04	2.2
TOTAL	184	100

Theabove table shows that the commonestseizureamongCSEwasGTCS-83.7%(184cases) followed by Focal seizure forabout14% (26 cases). Fourcases (2.2%) were multifocal.

Table 7:- Seizureepisode.

Seizureepisode	Noofcases(n=184)	Percentage
Firstepisodeofseizure as CSE	56	30.4%
Previousepisodeofseizure	128	69.6%

The above table shows that 56 cases (30.4%) had first episode of seizure and 128 cases(69.6%)had previoushistoryof seizure.

**Table 8:-** Feverassociation.

H/OFEVER	Noofcases	Percentage
Present	105	57.1
Absent	79	42.9
Total	184	100

The abovetableshows that 57.1% cases presented with fever and 42.9% cases were afebrile.

**Table 9:-** Demographic, clinical, and etiological spectrum.

CHARATERISTICS				
Median age in years	4.9 years			
Less than 5 years	120	67.4%		
Male	102	55.4%		
History of fever before onset	105	57.1%		
First episode of seizure as CSE	56	30.4%		
Prior history of seizure	128	69.6%		
Drug noncompliance	10	5.4%%		
Patients received pre-referral treatment	48	26.1%		
DURATION OF STATUS EPILEPTICUS				
< 30 Minutes	0	0.0%		
30-60 Minutes	150	81.5%		
>60 Minutes	34	18.5%		
SEIZURE TYPE				
Generalized	154	83.7%		
Focal	26	14.1%		

Multifocal	04	2.2%
Acute symptomatic CSE	•	
Febrile status epilepticus	34	18.5%
Viral encephalitis	9	4.9%
Pyogenic meningitis	19	10.3%
Tubercular meningitis	6	3.26%
Acute demyelinating encephalomyelitis ADEM	2	1.08%
Drug noncompliance	10	5.4%
Hypertensive encephalopathy	1	0.54%
Stroke	2	1.08%
Intracranial hemorrhage	4	2.17%
Systemic illness/metabolic/dyselectrolymia	6	3.26%
Remote symptomatic		
Cerebral palsy /Post HIE	47	25.54%
Neurocutaneous syndromes	4	2.17%
CNS Tumor	6	3.26%
Progressive neurological disorder	4	2.17%
Idiopathic/ Cryptogenic	30	16.3%

#### **Discussion:-**

Status epilepticus is associated with significant morbidity and mortality. It requires a prompt, effective protocol-based treatment in a given time frame with recommended drugs.

In this study, 184 cases of status epilepticus were included within the given study period. The mean age of the patient in the present study was 4.9years. The youngest age was 2 months and the eldest was 15 years. The infants (less than 1-year)accountfor 23.9% ofthetotalcases(n=184) and67.4% childrenwere in the age group < 5 years. The total number of cases in the age group >10yrs was only 6.5%.Outof184children,malechildrenwere102(55.4%)andfemalechildrenwere82(44.6%). The high prevalence of CSE intheyoungeragegrouphasbeen found by various studies in the past (Chin et al. 16, Kumar M et al. 17 and BergamoSetal. 18

In our study we found CSE is more common in the age group less than 5 years with mean age of 4.9 years. Of This finding ourstudy was very much consistent with SachinAdmuntheetal. <sup>19</sup>, MaytalJetal. <sup>20</sup> and RKS inghset al. <sup>21</sup> The predominance the vounger group and for them to present in age asstatusduringthefirstepisodehasbeentheorizedtobeduetotheunderdevelopedmechanismsforcontrolofseizureactivityand with disruptionof these mechanisms minimal abnormalities neuronal function inyoungerchildren. Also, youngerageismore vulnerable to febrile status epilepticus.

Our study findings revealed that outof184cases who had presented with CSE, around 42.4% werereferred from other rural care health centers. Most of the referred patients (57.6%) reached tertiary care hospital without any pre-referral treatment. The pre-referral treatment was given to only 48 patients (26.1%), the remaining 136 (73.9%) didn't receive any prehospital therapy, even though some of them have been referred from rural health care delivery system.

Out of 48 children who have received prehospital therapy, only 32 had been given standard protocol-based therapy.

In a study conducted by Fernandez et al.<sup>22</sup>, out of 64 patients of CSE with out-of-hospitalseizure onset, only 24 patients (37.5%) received AED prior to hospitalarrival. In an Indian study by Gulati et al.<sup>23</sup> at a tertiary care hospital inNew Delhi, 60% had received prehospital treatment. Treatment of SEneeds to be initiated as early as 5 to 10 minutes. The longer the seizureepisode the more chance of it going into refractoriness and developmentof complications. The lag time for receiving the first AED was morethan60minutesin23patients(26.4%)andonlyoneamongthemresponded to first-line AED. Hence the need for early initiation of AEDsand prehospitaltreatment isemphasized.

In our study we found that 81.5% of the cases of CSE reached ER within 30-60 minutes after seizure initiation and 18.5% reached after 60 minutes. This delayed presentation was associated with seizure refractiveness to drugs and adverse outcome.

K. Eriksson et al.<sup>24</sup> in their study have also concluded that there is an association between treatment delay and seizure refractiveness. This association between seizure refractiveness to standard treatment became significant after 30 minutes CSE, when this was analyzed as a single variable (p=0.003)

In our study we found that the most common type of seizures in CSE wereGTCS, seenin154cases(83.7%) followed by focal seizurein around 12% (26cases). Further our study revealed that CSE was first seizure presentation in 35% of cases, and 65% had a previous history of seizure or seizure disorder. Outof184cases, 57.1% (105) cases had fever on presentation. The study by Garzon et al. 25 also depicted that 40.6% of cases of CSE didn't have a previous history of seizures. Similar findings were revealed by Mah J Ketal. 26. in their study they found 43% cases didn't had previous history of seizures.

Themostcommonetiologyassociatedwithstatusepilepticuswasremotecauses like post HIE or cerebral palsy, seen in 25.54% cases, followed by acute CNS infection in 18.45 cases (pyogenic meningitis 10.3%, viral encephalitis 4.9%, and tubercular meningitis 3.26%). The tropical infections like malaria, dengue, Japanese encephalitis, West Nile encephalitis, are not endemic in Kashmir, therefore we didn't report a single case of them.HuiAcetal.'sstudy<sup>27</sup>showsthatacuteCNSinfectionwasapredictorofpooroutcomes.MurthyJMetal.<sup>28</sup>studyshowsCN Sinfectionaccountsforasignificantnumberofcases.

In our study we found that febrile status epilepticus was presenting episode in 18.5% cases. Studies from developed countries report a higher incidence of febrileseizures to be the cause of CSE in children <sup>29</sup>. The difference in the etiological spectrum of SE in children between developed countries and developing countries could be a result of the high incidence of neuro-infection in developing nations. Acute symptomatic etiology (other than febrileseizures) was the most common cause of CSE in children less than 5 years of age and remote symptomatic etiology was common inchildren greater than 5 years. This may be because of a high proportion of children with priorse izures in the older age group.

#### **Conclusion:-**

Among 184 total cases in our study, there were 23.9% infants who presented to emergency department as convulsive statusepilepticus CSE. The highest number of patients around of less than 5 years, therefore CSE is an important reason for under 5 mortality and morbidity in developing nations. Themeanageofthepatientinthepresentstudywas4.9yrs.

The outcome was better for patients who had less seizure duration and received early effective standard treatment protocol within a given time frame. The patients who had prolonged seizures or first treatment hadapoor outcome. Further acute CNS infection, remote causes, noncompliance of AED, IEM, were other etiologies responsible for the CSE. In our study we found that the large number of cases had cerebral palsy a remote cause of CSE in around 25.54% cases. Our study reveals that though we have successfully decreased the infant mortality rate, still there is large scope for decreasing morbidity by improving the neonatal care services across Kashmir and the intact Neonate intact Nation should be our mission and passion. Furthermore, it seems very imperative that all patients of CSE should receive early effective standard treatment at doorsteps to decrease the associated morbidity and mortality.

#### **Limitations:**

First, it is a hospital-based single-center study.

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