IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 6 Ser.3 (June. 2022), PP 25-41
www.iosrjournals.org

Clinical Profile, Immediate Outcome and Risk Factors Determining Adverse Outcome of Status Epilepticus in Children–Managed In an Urban Tertiary Level Referral Centre

Dr. N. Kumar, MD,
Associate Professor of Pediatrics, Government Medical College, Dindigul

Abstract: Objective: *Clinical Profile and immediate outcome, risk factors determining adverse outcome of Status Epilepticus in children between 2months to 12 years,* ***Design:*** *Descriptive study done from Jan 2018 to Dec 2020.* ***Setting:*** *Urban tertiary level referral Hospital in western Tamil Nadu, India.* ***Patients:*** *SE is defined as seizures lasting for > 5 minutes. Children from 2 months to 12 years with SE on arrival to ER managed with ACD were included. Seizures stopped before ACD and simple partial seizures without LOC were excluded.* ***Main outcome measures:*** *Death and AMA were considered as poor outcomes. All cases followed up for one month to determine the immediate outcome. Survivors either with intact neurological status or with sequele were taken as good outcome group. Risk factors in poor outcome group (cases 23) were compared with good outcome group (controls 104). Univariate and multivariate analysis were done to determine predictors of adverse outcome.*

Results: *Among 131 cases, 4 dropouts. So 127 completed the study. Males were 70& Females 57. M: F ratio was 1.22:1. There was no significant sex difference. 29.1% cases (37/127) were < 1 year. 58.3% (74/127) of cases were less than 3 years and 81.2% (103/127) cases were <6 years. Mortality is 15.7%. 30% deaths were in <1 year of age. 85% of deaths were in <3 years. Commonest seizure type is GTCS. NCSE also accounts for 26% of the cases. All required supplementary oxygen at arrival and most of them were apneic, hypoxic and shocky. 9% of the children had hypoglycaemia and 11% had hyperglycaemia at arrival but all of them received 25% dextrose. Common causes of SE were acute CNS infection; septic shock, idiopathic epilepsy, febrile SE and CNS co morbidity like CP. Febrile SE and idiopathic epilepsy were associated with good prognosis. All the children in FSE group recovered completely without any sequele. CNS infection and septic shock were associated with poor outcome. New neurological sequele occurred in 2 cases both of them had acute CNS infection as the underlying aetiology. Acute CNS infection, duration of SE, distance travelled to seek medical advice and respiratory failure requiring IPPV, were independent risk factors that influence the outcome adversely. 109 /127 cases responded to I line ACDs. 18 cases diagnosed as RSE and out of them 10 survived. Refractory SE is associated with poor outcome and prolonged hospital stay. Most of them responded to midazolam and only 2 cases required thiopentone but not controlled with thiopentone also. All cases of RSE were intubated using midazolam IV as the sedative and neuromuscular blockade avoided. Common complication of midazolam infusion was shock and noted only with higher doses >6 mcg/kg/min and managed with ionotropes.* ***Conclusion:*** *Common cause of SE is acute CNS infection and this results in higher mortality, morbidity and later neurological sequel and is one of the independent risk factor for poor outcome in SE. Duration and distance travelled to seek medical advice is also important independent risk factors influencing poor outcome. Many of the complications and consequences like shock, respiratory failure, aspiration pneumonias, hypo/hyperglycemias, dyselectrolytemias can be managed successfully with anticipation and early intervention, protocol based management. Management of vital signs and underlying cause of SE along with specific ACD therapy are the priorities in the management of SE. Midazolam is safe and effective for the treatment of RSE in children.*

Keywords: Convulsive Status Epilepticus, Outcome, Predictors

Date of Submission: 01-06-2022 Date of Acceptance: 13-06-2022

I. Introduction

Status Epilepticus (SE) is one of the most critical medical emergencies that may result in significant morbidity and mortality if not addressed in a timely and effective manner[1]. Currently SE has 1/5 the morbidity and 1/3 the mortality of pre -1970[2]. But still mortality is around 11-53% [3, 4, 5]. Although most seizures in children stop prior to arrival at a hospital, an estimated 60,000 US children are treated each year for SE. 1/3 of

the episodes will be initial event in a patient with new onset epilepsy and an additional third occur in children with established epilepsy. Up to 70% of children with epilepsy beginning before age 1 will experience an episode of SE in their life time. Incidence is about 50000-2.5 Lakhs times/year in US. 21% were <1year and 64% were <5 years. <50% of SE has h/o epilepsy. 15% of the epileptics will have SE at one time. 10% of the epileptics will present with SE at I time itself[2]. Acute causes are CNS infections, SOL, febrile convulsions, trauma, metabolic derangements, toxins, drugs overdose, vascular, hypoxia etc. Static causes are Idiopathic epilepsy (here SE may be the first manifestation or may be precipitated by drug default /poor compliance, irregular drugs sudden withdrawal of AED, change of drugs, inadequate AED level in serum, fever, stress, sleep deprivation), structural brain lesions either developmental or acquired. Progressive causes are Degenerative cerebral disorders.

SE is a medical emergency and must be treated immediately. Cardio respiratory dysfunction, hyperthermia, metabolic derangements, irreversible neuronal injury can develop as a consequence of prolonged SE [9]. CNS injury can occur even when the patient is paralyzed with neuro muscular blockade but continues to have electrographic seizures[6]. About 70-80% of cases of CSE throughout all age groups will have a focal onset but be secondarily generalized. CSE starts with localized epileptic activity followed by isolated generalized bursts of seizure activity with a normal EEG in between. If the patient does not regain consciousness between these episodes, then they meet the clinical criteria for CSE. The isolated ictal discharges merge and become a continuous discharge after about 30 minutes. Discharges then fragment and are interspersed with flat periods. Ultimately, periodic epileptiform discharges, which may reflect underlying metabolic failure, will occur [7]. The motor phenomena associated with CSE follow a similar pattern to the EEG changes. Recurrent seizures will merge into continuous motor activity, followed by fragmentation of the motor activity and myoclonus. If the seizure persists, then electromechanical dissociation will ensue. The prognosis for a good neurological outcome decreases the further the patient moves through this continuum.

Excitotoxic amino acids are important in causing structural brain damage secondary to CSE. Mesial temporal sclerosis is the most common acquired brain lesion following CSE and may result from excitotoxicity. Most work in this field has been directed at the effects of glutamate. CSE can itself cause hippocampal damage and resulted in neuronal loss in the hippocampus, neocortex, amygdala, thalamus, and cerebellum. Bilateral hippocampal damage may occur even with unilateral stimulation with excitatory neuro transmitters. The implication is that prolonged seizures may need to occur in epilepsy human patients for mesial temporal sclerosis to develop, and that once it has developed further episodes of CSE may not worsen the mesial temporal sclerosis [8].

Patho physiological consequences following SE is extensively studied in animal models. There is no deficit in brain energy state until later around 1 hour, when parenchymal oxygen falls. Then brain damage occur[9]. Several investigations have shown that seizures become more difficult to stop and the chances of neuronal injury increase when seizures persist beyond a transitional period that varies between 20 and 60 minutes in animals during constant seizure activity. Treatment in children should be directed to supporting vital functions and to controlling the convulsions as expeditiously as possible, because the precise transitional period in humans is not known.

The systemic effects of CSE are initially dominated by the body's attempt to maintain homeostasis. Blood pressure and central venous pressure increase, blood glucose increases, and the patient become tachycardic. CSE may also results in electrolyte imbalance and hyperthermia. Cerebral blood flow, blood glucose, and oxygen utilization increase in the initial phases of a seizure to maintain cerebral homeostasis. After 30 minutes homeostatic failure begins and the patient may need systemic support. Cerebral blood flow, brain glucose, and parenchymal oxygenation all decrease and potentially play a part in the cell damage associated with CSE. Respiratory and metabolic acidosis, electrolyte imbalance (for example, hyperkalemia), hyperthermia, and rhabdomyolysis may all occur. Treatment with drugs with depressant cardio respiratory side effects (for example, benzodiazepines and barbiturates) may worsen the systemic complications of CSE [9]. Hypoxia associated with SE is multi factorial. Impaired mechanical ventilation secondary to tonic clonic activity, increased salivation and tracheo bronchial secretions obstructing the airway, increased O2 consumption resulting from the seizure, drugs to terminate SE are respiratory depressants that cause hypoventilation are some of the factors. Acidosis of SE is of both respiratory and metabolic in origin as seizure activity results in increased metabolic needs unmet by tissue oxygenation and perfusion, causing lactic acidosis. In first 30 minutes of seizure activity, catecholamine release results in an increase in heart rate, blood pressure, central venous pressure, cerebral blood flow and serum glucose. After 30 minutes of GTCS, Blood pressure begins to drop and cerebral blood flow although still increased above base line, drops to the point where it may be unable to supply adequate substrate and oxygen to meet increased cerebral metabolic demands. This results in impaired cortical oxygenation [9]. Other effects are ↑ CPK, Myoglobinuria, ATN, trauma, tendon rupture. Seizure duration greater than 1 hour, especially with hypoxia, has been associated with permanent neurologic injury. During SE cerebro vascular resistance falls due to hypoxia resulting in severe derangement of cerebral auto regulation.

Cerebral perfusion becomes directly dependent on systemic blood pressure. Within the first 30 minutes of SE hypertension occurs. Later, BP either becomes normal or low. This circulatory shock which follows ongoing SE severely deranges cerebral physiology. Convulsions are easily identified as the source of altered mental status if typical tonic clonic movements are witnessed. However, children may also present in a post ictal state, without a clear history of a seizure, thus making the diagnosis more difficult to determine. Furthermore, seizures may be followed by a period of transient paralysis (Todd's paralysis) that is often present on one side of the body. This may lead to the clinician to suspect a structural aetiology rather than seizures. NCSE should be considered in comatose children without signs of seizures activity, an EEG, will help to diagnose this condition[11].

If the patient stops overt convulsions yet remains comatose an EEG should be performed to rule out ongoing S.E. Up to 20% of children with SE have non - convulsive SE after tonic - clonic SE[12]. Neurologic signs after termination of SE are common: pupillary changes, abnormal tone, abnormal Babinski reflex, posturing, clonus, may be asymmetrical. They should not be misinterpreted as NCSE. NCSE is commonly diagnosed in children, where as acute delirium status is frequent in adults ED diagnoses. NCSE is usually entertained only when the child is unresponsive and rigid or has a known seizure disorder. But PCSE and ASE both can present with subtle findings erroneously ascribed to other etiologies and may occur in patients without a known seizure history[13]. NCSE accounts for almost 20% of SE [13]. PCSE has been associated with neuronal damage and stroke[14] and is more likely caused by primary pathology of the cortex such as an infection or bleed. In contrast ASE probably has a different and less harmful origin, seemingly resulting from vacillating thalamo cortical excitation and excessive synchronous neuronal inhibition, which could explain the absence of tissue injury following its resolutions[14]. In PCSE, as in GTCS excessive excitatory neuro transmitter release leads to depolarization and increased intracellular calcium. When GABA inhibition is overwhelmed, calcium triggered proteases and lipases leads to cell injury and death[14].

RSE is defined as seizures that do not controlled with adequate does of BZD, Phenytoin or Phenobarbital and require more aggressive treatment[15]. Complications are more and outcome poor in RSE. Continuous IV infusions of anesthetic doses of midazolam, propofol, or barbiturates are the most useful treatments[16]. Children with prior, new, progressive CNS injury are more prone to have RSE.

Types are[7] convulsive SE (CSE), primary/secondary generalized, Hemi convulsive SE, Tonic SE, Clonic SE, Simple PSE/ Epilepsia partia continualis, Non convulsive SE (Subtle SE), Neurological EMD (Electrical SE), CPSE, ASE, Myoclonic SE +/- salaam attacks

Complications due to SE are Epilepsy subsequently (77%), Hemi convulsion Hemiplegia (HH), Inter ictal coma, Airway obstruction, Cumulative anoxia, Bradypnea, Tachypnea, Apnea, Chyne stokes breathing, Tachycardia, Bradycardia, Hypertension, Hypotension, Cardiac arrest, Cardiac failure, Cardiogenic shock, Neurogenic pulmonary edema, Aspiration pneumonia , Respiratory acidosis, Cyanosis, Oliguria, Uremia, ATN, Rhabdo myo lysis, Hyperpyrexia, Excessive sweating, vomiting , Hyper secretions (salivary, tracheo bronchial), Acidosis (metabolic, lactate, Hypernatremia, Hyponatremia, Hyperkalemia, Hypoglycemia, Hepatic failure, Dehydration, Acute Pancreatitis, Leucocytosis, Altered auto regulation of CBF, Increased cerebral metabolic rate of O2 (CMR O2), DIVC, MODS, Fractures, Thrombo phlebitis .

Longer the duration of seizures, the lower is the likelihood of spontaneous cessation, the harder it is to control and the higher is the risk of morbidity and mortality[16], greater the risk of complications, so, every attempt should be made to control epileptic activity (clinically and electrically). Convulsive Status Epilepticus is one of the most critical neuro emergencies and every physician confronted with these patients in the emergency department should have a protocol in mind how to terminate seizure. Therapy must be aggressive because neuronal excitability can be reversed only early in the course and quick intervention may decrease the risk of seizures generated neuronal damage. GCSE is a condition which most likely will not terminate rapidly and / or spontaneously and requires prompt intervention[17].

Goal of management is, to maintain adequate vital function and oxygenation, to terminate seizure activity as quickly as possible, to evaluate and treat the underlying cause of SE. Ventilation is to be anticipated. Use of ACDs to stop seizures and to stop respiration for intubation is better than giving neuromuscular blockade alone. Use correct and adequate anti-seizure drug doses. Epileptics and non-epileptics in status require the same drug doses. It should be remembered that outcome is determined by aetiology, age, duration and treatment. We can affect only the treatment. Most easily missed causes of Status Epilepticus are bacterial meningitis, encephalitis, abuse/unsuspected trauma, drug ingestion.

Benzodiazepines are the initial drug of choice in terminating SE. Lorazepam, Diazepam, Midazolam are the recommended drugs. Though diazepam and lorazepam are equally effective in controlling seizures lorazepam is preferred because if it's longer duration of action [18, 19]. If diazepam is given it should be followed by a long acting drug ACD such as phenytoin to prevent recurrences [110]. Midazolam has no more advantage over diazepam or lorazepam in efficacy, onset and duration but can be given as IM injection. So, ideal for pre hospital therapy and it can be given if IV access could not be obtained [20, 21]. Intramuscular midazolam is given as 0.2 mg/kg and it is an aqueous solution and rapidly absorbed, anticonvulsant effect begins after 2 minutes.

Next line drugs are Phenytoin/Fos Phenytoin,, Phenobarbitone, Leveteracetum, Sodium valproate. Depanding upon clinical condition and availability these drug are given one by one. Phenytoin is avoided in Shock, cardiac dysfunction. Valproate is avoided in liver diseases, IEM, young infants where phenobarbitone is safe. Leveteracetum can be used in all ages with fewer side effects.

In RSE, midazolam given as 0.2mg/kg IV bolus followed by 0.75 to 10 mcg/kg/min infusion [41-45]. Propofol is given as 1to2 mg/kg loading followed by 2 to 10 mg/kg/hr [46-50]. Both drugs have the substantial advantage over barbiturates of rapid clearance and midazolam has less pronounced hypotensive effects. Midazolam infusion is typically maintained for 12 to 24 hours and is then withdrawn gradually while the patient is observed for clinical and EEG evidence of seizure termination. If seizure continues the therapy should be resumed for prolonged periods. Midazolam may be associated with tachyphylaxis leading to the need for exceedingly high doses. Propofol is a pro convulsant. Seizure during induction and termination was reported but, these effects in the management of SE are unknown.

Thiopental and pentobarbital are potent anti seizure drugs that have potential though unproved cerebral protective effects in the management of SE [51-59]. In adequate doses these drugs will always control seizures, but severe hypotension requiring pressor therapy limits their safety. So, these are reserved for failed midazolam / propofol. In resistant cases, Inj. Sodium valproate 20-40 mg/kg IV bolus as well as infusion may be used [60-78].

In a child with a new onset of seizures, an EEG may help to differentiate ictal from non ictal events, to determine seizures type or epilepsy syndrome and to better define the risk for recurrence. For most children it is not necessary to perform the EEG as part of the initial emergency department evaluation. In fact if it is performed shortly after the seizure (<48 hours) the EEG may show diffuse post ictal slowing without prognostic significance [79, 80, 81]. All children with persistent altered mental status after a seizure, an emergent EEG is helpful to identify subtle or NCSE [82]. CT Brain may be necessary to evaluate safety of LP and to rule out haemorrhage or large mass lesions. MRI will almost always be performed later, even if CT is normal. LP should be done if SE presented in febrile children. And it should be done only after stabilizing the child not at arrival.

Outcome is determined by, *Etiology, Age, Duration, Treatment*[3, 4, 5]. Ultimately mortality related to, damage to the CNS caused by the acute insult precipitating SE, systemic stress from SE (major cause because of anoxia, acidosis, shock), injury from repetitive epileptic discharges within the CNS (minor but cognitive impairment later). Mortality increases from 3% to 32% if the duration of seizures becomes >1 hour. Normal children and children with febrile status have a favourable prognosis. Improved outcome is a result of timely and approximate evaluation and treatment. Most favourable for patient who respond to first line agents, but obviously the underlying cause of status, determine the outcome. Cognitive function may be impaired (particularly memory) in patients with prolonged S.E. and is more common when significant hypoxemia (aspiration) intervened. Outcome may be worse when S.E. is managed inappropriately. Most common mistakes seen are, inadequate dosing, Failure to order maintenance therapy. Failure to do the latter will result in recurrence. AED should be continued particularly if a structural lesion resulted in S.E.

Status epileptics definition [101,102,103,104]: International Classification Of Epileptic Seizures/ Conventional "Textbook" Definition Of Status Epilepticus [110]: Continuous seizures activity lasting for 30 minutes or longer, or Intermittent seizures activity lasting for more than 30 minutes, from which the patient does not regain consciousness[105, 106]. This definition has been repeated in most articles and textbooks. However, there is nothing magic about 30 minutes. In fact, the likelihood for a tonic-clonic seizure to stop spontaneously decreases dramatically after 5 minutes. Where did the initial definition of 30 minutes come from? Animal experiments in the 1970s and 1980s had shown that, neuronal injury could be demonstrated after 30 min of seizure activity, even while maintaining respiration and circulation [6].Here the concepts of potential neuronal injury related solely to the duration of SE, is based in part of animal studies. Despite optimal circumstances during SE, with animals paralyzed and ventilated, neuronal damage may occur after 30 minutes in pars reticularis of substantia nigra, and after 45-60 minutes in hippocampus, thalamic nuclei, cerebellum purkinji cells, layer IV, V of the neocortex, and other parts subsequently. In 1999 Lowenstein, Bleck, Macdonald [17] proposed an operational definition for GCSE in adults and older children (>5 years old) to incorporate the practical consideration of patient management. GCSE in adult and older children (>5years old) refers to > or = 5 minutes of a (a) Continuous seizure or(b) Two or more discrete seizures between which there is incomplete recovery of consciousness. This determination was based in part of a study completed by Theodore et al[107] that analyzed 120 GTCS recorded during inpatient monitoring and reported mean seizure duration of 62 seconds. Because no seizures lasted for more than 2 minutes, more prolonged seizures encourage the development of SE and the need for IV therapy. This determination excludes children <5 years because relatively little is known about the typical single seizure in this age group. Initial febrile seizures [108] and acute symptomatic seizures in children can be prolonged but do not result in the same morbidity seen in adult with prolonged seizures. Further work needed in this age group, before an operational definition can be formulated and treatment strategies developed. But majority of SE occurs in the age group <5 years and we see more morbidity and mortality in younger age group (infants and young children). This operational definition is accepted worldwide[16] in the emergency department for the

management of SE. So, this definition is followed for selection of cases in this study. But because of paucity of reports for SE in younger children and infants and no operational definitions at present formulated, we have taken this definition for children of <5 years also for epidemiological purpose.

Practical Definition: SE refers to the seizures lasting longer than 5 minutes or seizures on presentation to ER or recurring in the ER[2]. SE refers to continuous seizures or repetitive discrete seizures with impaired consciousness in the inter ictal period. The duration of seizure activity sufficient to meet the definition of SE has traditionally been specified as 15 to 30 min. However, a more practical definition is to consider SE, as a situation in which, the duration of seizure prompts the acute use of anticonvulsant therapy, typically when seizures last beyond 5 minutes [109]. Typical seizure duration: Children > 5 years: Typical, generalized tonic-clonic seizure lasts < 5 minutes, Young children and infants: Paucity of data. Suggested time frame for typical tonic-clonic seizure, may be < 10-15 minutes. Patients with generalized seizure activity at arrival in the ER are treated promptly regardless of prior duration. The fact that infants with SE have a higher mortality is likely due to the different etiologies of SE in infants, when compared to older children[17].

Data on outcome in SE is sparse in India. SE is one of the most common emergencies, we managed in our hospital and we see the largest number of SE in children, in our part of the country. As a tertiary level referral hospital, we managed those cases that were referred as refractory seizures. Many children come from long distances with prolonged SE. They do not have effective pre hospital therapy, proper referral and transport services. Though we managed many SE successfully, we do come across poor outcome in SE. If the risk factors influencing poor outcome are identified, some of the factors can be modified and the high risk groups, who are going to have poor outcome can be managed aggressively and with better care to improve their outcome.

II. Methodology

STUDY DESIGN: Descriptive study. STUDY PEROID: Jan 2016 -to –Dec 2016. STUDY POPULATION: Children from 2 month to 12 years of age, who have been managed as SE were studied. STUDY PLACE: Coimbatore Medical College Hospital, Coimbatore. INCLUSION CRITERIA: All children presented with SE (including non convulsive SE and secondary generalized), managed with anti convulsion as per the protocol in the above age group in ER. EXCLUSION CRITERIA: Seizures controlled before arrival to the hospital or before starting IV therapy, Simple partial SE and other NCSE like myo clonic SE with normal vital signs and without loss of consciousness, Seizures occurred during hospital stay, not at arrival were excluded. SAMPLE SIZE: Sample size was calculated based on a pilot study of 49 patients. Here the mortality was 20%. From review of MRD records average cases of SE were 25-30 per month and the precision was fixed as 7%. Hence with the α error of 5% the required sample size statistically calculated for the least expected risk factor was 126. SAMPLING TECNIQUE: All cases included over that period. DROP OUTS: Totally 131 cases were included. 4 drop outs (2 lost follow up, 2 absconded). 127 cases completed the study.

MANOEUVRE

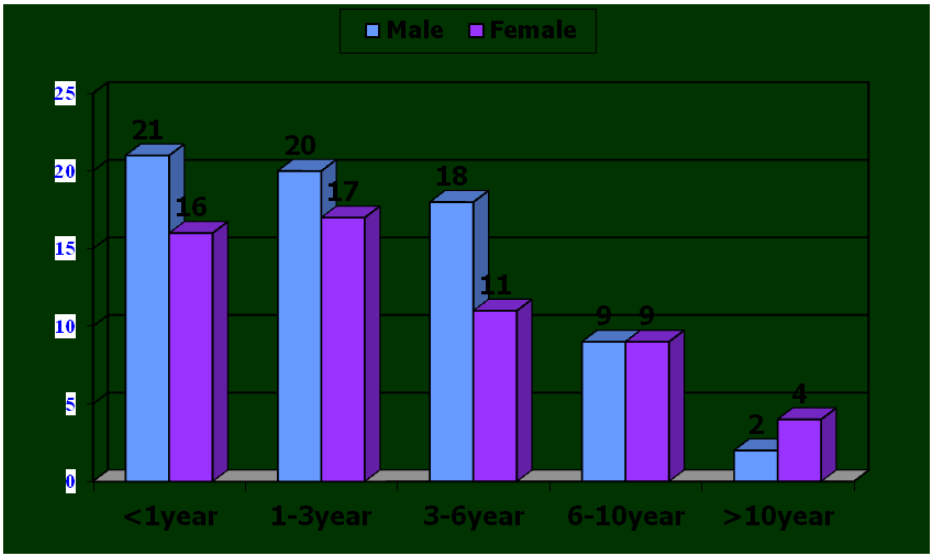
Institutional consent and parental consent were obtained. First the cases were selected as per the inclusion criteria. Each child had been assessed on arrival and a preliminary history was obtained and documented in a pre formed proforma. Rapid cardio pulmonary assessment was made at ER. Preliminary clinical assessment was made. It included Sa02 at arrival, BP, presence of shock, pupil etc. Before starting IV therapy, blood sample was taken for baseline investigations (sugar, calcium, and electrolytes). Then the cases were managed according to the protocol followed in our ER and admitted in wards/PICU. There, the cases were reassessed and detailed history were obtained including duration of seizure, distance from the place where the fits occurred, mode of transport, pre hospital therapy, precipitating factors, prior seizures/SE, drug history and compliance developmental miles stones, prior neurological status. Complete clinical examination was made including neurological examination. Relevant investigations were done like CSF analysis, CT brain/USG cranium, EEG etc. Course of illness and therapy were monitored regularly till discharge. Time taken for control of refractory SE, time taken for full recovery of consciousness, requirement for prolonged ventilatory support (manual/ mechanical), refractory shock or subsequent shock following midazolam or due to complications like sepsis, maximum dose and duration of ionotropes and midazolam / thiopentone infusions, recurrence of fits, complications were noted.. Status of the child at the time of discharge was noted. They were followed for 1 month then the neurological status at the end of 1-month was re assessed. Their neurological status was compared with the previous neurological status. Outcome was determined by the following variables: Death, AMA (persistent ALOC and unstable vitals till AMA), and new neurological sequele, complete recovery, no new neurological sequele (already existing). Observations were entered as tables and percentage charts. According to the final outcome the children were divided into two groups. Death, new neurological sequele, AMA were taken as poor outcome group and those children recovered completely or recovered without any new neurological sequele were taken as good outcome group. Predictors of poor outcome were analyzed for the following risk factors compared with good outcome group using Univariate analysis and Multivariate logistic

regression. P value of < 0.05 is taken as statistically significant. Odds ratio and 95% confident interval were also calculated for statistical significance. Age (<12 months), Duration of seizure (>60 minutes), Increasing distance, Type of seizure, Fever, Prior SE, Poor drug compliance, Developmental delay, Prior neurological abnormality, No pre hospital therapy, Hypoxia at arrival, Refractory Shock, RSE, Prolonged respiratory failure (IPPV), Inter ictal EEG abnormalities, Underlying cause of SE, CNS infections, Abnormal neuro developmental status before SE, Acidosis, Hypoglycaemia at arrival were the risk factors taken for analysis

III. Results And Analysis

Totally 131 cases were included in this study. 4 drop outs (2 absconded, and 2 lost follow up after discharge). So, 127 cases completed the study. Out of 127, male children were 70 and female children were 57. The incidence of SE was more in male than female in this study (1.22:1) but it is not statistically significant. Nearly 81 % of the total cases were < 6 years of age. Around 30 % of the cases were < 1 year and 30 % of the total deaths were occurred in that age group. 85% of deaths were occurred in the age group of <3 years. So, most of the cases of SE were younger children and mortality is also high in this group reflecting the underlying causes like acute CNS infection and septic shock are responsible than the seizures them selves.

	Male		Female		Total		
	Frequency	%	Frequency	%	Frequency	%	Cum.%
<1year	21	16.5%	16	12.6%	37	29.1 %	29.1%
1-3	20	15.7%	17	13.4%	37	29.1 %	58.3 %
3-6	18	14.2%	11	8.7%	29	22.9 %	81.2 %
6-10	9	7.1 %	9	7.1%	18	14.2 %	95.3 %
>10years	2	1.5%	4	3.2%	6	4.7 %	100 %
total	70	55%	57	45%	127	100 %	



DURATION OF HOSPITAL STAY:

No. of hospital days (d)

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 5 days	54	42.5	42.5	42.5
	5 - 9 days	41	32.3	32.3	74.8
	10 to 14 days	21	16.5	16.5	91.3
	15 -19 days	6	4.7	4.7	96.1
	> 19 days	5	3.9	3.9	100.0
	Total	127	100.0	100.0	

Mean duration of hospital stay was 6 days and 18 hours and maximum duration was 27 days, which was observed in one child who had RSE with prolonged respiratory failure and died on 27th day.54 children (42.5%) were discharged within 5 days after admission. 95 children (74.8%) were discharged within 10 days after admission. Prolonged hospital stay of >19 days observed in 5 cases. All were diagnosed to have RSE. Prolonged hospital stay >19 day observed in 5 cases. All were diagnosed to have RSE. Mean duration of hospital stay was 6 days and 18 hours and maximum duration was 27 days, which was observed in one child who had RSE with prolonged respiratory failure

ONSET OF SEIZURES:

Fits started in their home for 116/127 cases (91.3%). Fits started in OPD for 9 children (7%) and for 2 children had fits while travelling towards hospital. Out of 7 cases in which fits started at OPD, 6 had survived and one child died due to prolonged respiratory failure and refractory septic shock. Seizure duration of 8-15 minutes was noted in those cases from OPD before starting IV therapy.

REFERRAL AND TRANSPORT:

75/127 children (59.1%) were coming directly without any referral or treatment before arrival to ICH. 30/127 children(23.8%) were referred by practicing private practioners.11 cases referred by private hospitals for varies reasons (financial containments, for further management, AMA discharge etc). Out of 11, 9 children had survived. Only 10 children (7.9%) were referred from government set up (GH,PHC). 73 children (57.5%) were taken by Auto, 26 (20.5%) children by Bus, 8 children (6.3%) by Train& Auto, 2(1.6%) children by two wheeler, 10 cases (7.9%) by attenders directly and only 7 children were transported by Ambulance with O2.

DISTANCE AND DURATION:

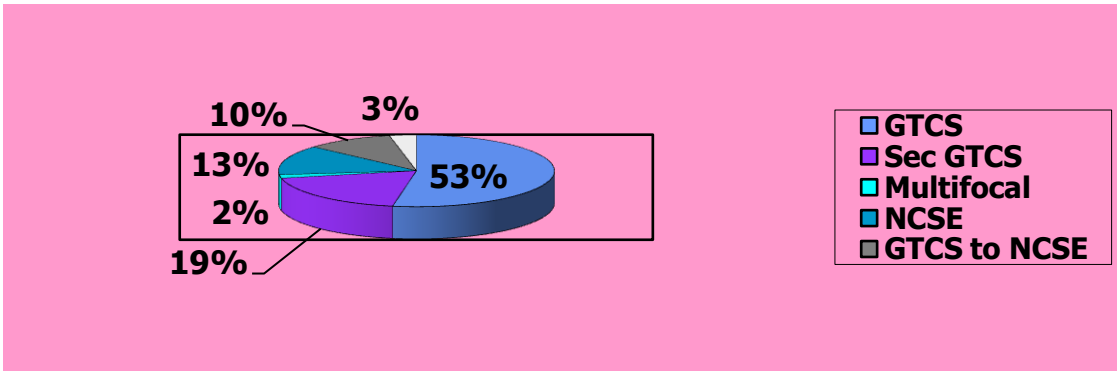
15 children (11.8%) were coming from <1 km distance from ICH. 93 children (73.2%) were from Chennai surroundings within 50 kms distance. 25 cases (19.7%) were coming from very long distance that is >100 km. Out of them 20 children (80%) had seizure duration of more than or = 24 hours and 15 children (60%) had poor outcome (13 children died, 1 went AMA and 1 had new neurological sequele).Out of 20 deaths 13 cases (65%) were from >100 km distance.

DURATION:

Mean duration was 16 hours and 44 minutes. Maximum duration of 10 days observed. 26 cases (20.5%) attended ER within 30 minutes of onset of fits. 46 cases (31.5%) had seizure of < 60 minutes duration before arrival. 65 children had seizure duration <2 hours before arrival. 40 children had seizure of > 2 hours but < 1 day duration. Remaining (22children-17.3%) had seizure of > 1 day duration and out of them, 9 cases were admitted in private hospitals and treated with more than 1 anti convulsant drugs before arrival to hospital. Out of 20 deaths 18 deaths occurred in children who had seizure of > 1 hour duration. Only 2 deaths occurred in children with seizure of < 1 hour duration and both of them had pneumonia, acidosis, shock and hypoglycemia at arrival prolonged respiratory failure and septic shock was the cause for death in both children. No deaths or new sequele observed in FSE (19 cases), though 9 FSE had seizure duration of more than 30 minutes. Nearly 50 % of the children had seizure duration of < 2 hours prior to arrival to hospital. Most of them were coming from near by places. 20% came from long distance >100 km and they spent a lot of time in traveling and in pre hospital management. In nearly 80% of the cases long distance was responsible for prolonged duration of seizure and in remaining cases management of seizures in private hospital and other clinic or PHC was responsible. Out of them 20 children (80%) had seizure duration of more than or = 24 hours and 15 children (60%) had poor outcome (13 children died, 1 went AMA and 1 had new neurological sequele).

TYPE OF SEIZURES:

Convulsive SE accounts for 73.3% (93) of the total cases. GTCS was the commonest type seen in 91 cases (72%). Out of them 67 cases had primary GTCS and 24 cases had initially focal onset with secondary generalization (18.9%). 2 cases of multifocal clonic SE noted. This was seen in younger infants of <6 months of age. 34 cases (26.7%) were in NCSE at arrival to ER. In this 17 cases (13%) were in NCSE from the beginning and 17 cases initially convulsing and later became non convulsive (13 cases GTCS to NCSE and 4 cases Focal to NCSE).

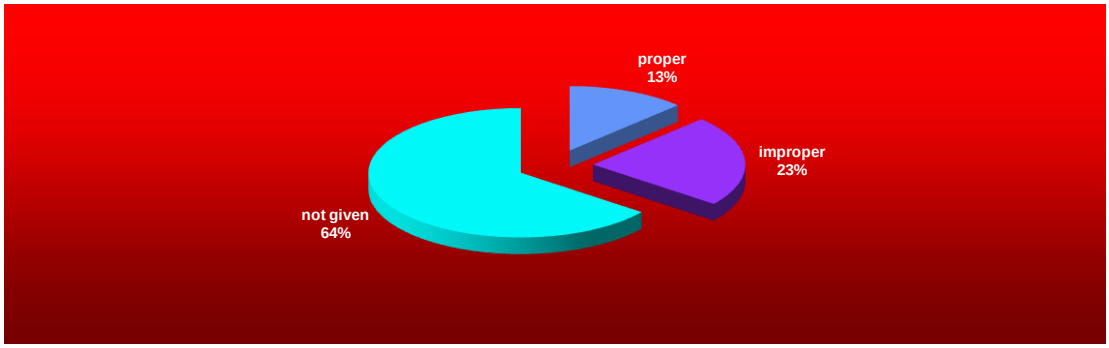


NUMBER OF FITS:

63 cases had single seizure (49.6%), 22 cases had two episodes, 9 had three and 33 had many episodes with impaired alert ness in between. Longest duration of a single episode noted was 400 minutes. Mean duration of a single episode was 22 minutes.

PRE HOSPITAL THERAPY:

Pre hospital therapy was given in 45 children (35.4%). Remaining cases were not given any ACDs prior to arrival, though some of them were referred. Out of 45 children those who received pre hospital therapy only 16 children were given proper drugs and in proper route. Proper means IV/PR diazepam, IV lorazepam, IM /IV /PR midazolam, IV phenytoin infusion, IV phenobarbitone infusion. Here 14 children received IV diazepam with phenytoin (9 cases) or without phenytoin (5 cases) then. One child had IM Midazolam and one infant had IV Phenobarbitone. Where as 29 children (22.8%) received improper drugs or improper route or inadequate doses. Most common drug given was IM diazepam (7 cases) and next was IM phenytoin (4 cases). 6 cases received some IM injections which were not documented. 2 cases received dexamethasone and one child received glucose water orally. Two cases received rectal ACDs (one was clobazam and other was phenobarbitone). None of the children received rectal diazepam.



PRECIPITATNG FACTORS:

11 children (8.7%) had ALOC prior to seizures and out of them 9 had acute CNS infection. Fever was present in 80 cases (63%) out of which 19 cases diagnosed as febrile SE and fever precipited seizures in 27 known seizure disorder children. Causes of fever include, pneumonia/LRI, sepsis, AWD, etc. Other precipitating factors were vomiting 37, trauma 4, toxin 5 (camphor 2, neem oil 3), drugs 3 (carbamazepine 1, unknown 2), hypocalcemia /hypoglycemia 2, shock 6, hypoxia 6 and unprovoked seizures seen in 21 cases (16.5%). In FSE 9 children had seizure of > or = 30 minutes.

Fever	**80(63%)**	Trauma	4
Vomiting	37	Toxin-neem oil, camphor	5
AWD	17	Drug over dose	3
LRI/ URI	14	Pneumonia	10
Poor drug compliance	14	Stress/sleep deprivation	-
Unprovoked	21		

HISTORY OF SEIZURES:

Present in 70 cases (55.1%). 57 cases (44.9%) presented as SE in their first episode of fits. Out of 70 children who had h/o prior seizures, 55 children (43.3%) had afebrile seizures and 15 children (11.8%) had febrile seizures. Out of 55 afebrile seizures 39, had idiopathic epilepsy and 16 had structural neurological disorder that is CP, MR, PMS, PES, CVA, neuronal migration disorder, neurocutaneous syndromes etc. 22 had previous SE and treated with ACDs. Totally 33/127 had CNS co morbidity. 36/127 had delayed miles stones. 47/127 cases, including both febrile and afebrile seizures (6 febrile, 41afebrile) were on AEDs. 16 children were on mono therapy and 31 children had > one drug to control fits. H/o poor drug compliance was present in 14 cases and that could be the cause of SE in them.

CLINICAL STATUS AT ARRIVAL:

122/127 cases were apneic at arrival and needed BVM with 100% O2. 5/127 had regular respirations and all the 5 were in NCSE and, so, O2 through non rebreathing mask was given. All children received supplementary O2 at arrival. Mean duration of BVM was 29.5 minutes and maximum was 75 minutes. 44/127 children (35.4%) needed intubation and IPPV. Minimum of 2 hours to maximum of 560 hours (26days) ventilatory support was given either by manual or by mechanical ventilator. Mean duration was 64 hours. 7 children needed IPPV for <7 hours and rest of them ventilated for >12 hours. 25 had poor outcome and 19 had good outcome in this group. 58 children had SaO2 of >92% at arrival and in remaining cases SaO2 was <92% and in 22 cases it was not recordable. 125/127 children had normal or high BP at arrival and 2 cases were brought with hypotensive shock and both of them died.

Shock was identified in 92/127 cases (72.4%). It was corrected with RL only in 54 cases (42.5%) and inotrope support needed in 38 cases (29.9%). Shock corrected at ER in 12 cases those who needed inotropic support and refractory shock seen in 26 cases (20.5%).

PUPIL

Pupil was normal in 81 cases (63.8%). Dilated pupil and reacting to light was seen in 36 children and pupil was constricted and reacting to light in 1 case. Sluggishly reacting dilated pupil seen in 3 cases and pupil was unequal (raised ICP) in 6 cases (4.7%). DEM defective in 118/127 children and DEM present in 9 case**s.**

PUPIL	**Frequency**	**%**	**Cumm %**
PERL	81	63.8%	63.8%
Dilated reacting	36	28.3%	92.1%
Sluggishly reacting	3	2.4%	94.5%
Constricted	1	0.8%	95.3%
Unequal	6	4.7%	100%
Total	127	100%	

MANAGEMENT OF FITS:

2 cases received IM midazolam as the IV access could not be obtained and fits controlled with midazolam in one case and with subsequent IV lorazepam in one case. None of the fits controlled with 25% dextrose alone though 13 cases had documented hypoglycemia at arrival. In 32 children (25.3%) fits controlled with I dose of lorazepam and 26 cases (20.5%) fits controlled with II dose of lorazepam. In 26 cases fits controlled with lorazepam + phenytoin and in 19 cases with lorazepam + phenytoin + phenobarbitone. 2 children received calcium gluconate as they were known cases of hypocalcemic seizures and in 2 children phenytoin was withheld, one child already received adequate dose (30 mg/kg IV infusion) of phenytoin before

arrival to CMC and one child had hypotension. So, in 109/127 cases (85.8%) fits controlled with I line drugs and 18/127 cases needed midazolam infusion.

Controlled With Drugs	**Frequency**	**%**
Midazolam. IM.	2	1.6%
25% dextrose alone	0	0%
+Lorazepam I dose	32	25.3%
+Lorazepam II dose	26	20.5%
+Phenytoin I dose	15	11.9%
+Phenytoin II dose	11	8.6%
+Phenobarbitone	19	15%
+midazolam infusion	18	14.2%
Phenobarbitone/lorazepam+ phenobarbitone	2	1.6%
Calcium gluconate+Lorazepam	2	1.6%
Total	127	100%

RSE:

18 children were considered to have RSE and out of them 10 survived (55.6%), 8 died (44.4%). All children were started on midazolam infusion within 2 hours of hospitalization. Fits controlled with midazolam in 16 cases. Fits controlled in < or = 3 mcg /kg/ min in 10 cases and in < or = 6 mcg /kg /min in 12 cases (66.67%). 6 cases (33.33%) needed higher doses of midazolam (9 mcg /kg /min to 25 mcg/ kg/ min). Minimum dose was 1 mcg/kg/min and maximum dose was 25 mcg/kg/min. Mean dose was 6.22 mcg/kg min. 2 children needed thiopentone infusion to correct refractory SE. But for both of them fits not controlled with thiopentone also and subsequently died.

MIDAZOLAM DOSE AT WHICH SEIZURES WERE CONTROLLED

DOSE	**NUMBER OF PATIENTS**	**%**
1-3 mcg /kg/ min	10/18	55.56%
4-6 mcg /kg /min	2/18	11.11%
> 6 mcg /kg/ min	6/18	33.33%
TOTAL	18	100%

Mean duration to control fits in those children was 4 hours 35 minutes. In 15 children (83.33%) fits controlled within 8 hours of starting midazolam infusion. In 13 cases (72.22%) midazolam given for < 2 days and in 17 cases (94.44%) it was given for <4 days. Maximum duration of midazolam infusion was 500 hours but that child did not respond. Mean duration was 61 hour and it was usually tapered after 12 to 24 hours of seizure free period. No cases observed recurrence of seizures on tapering midazolam. Shock was noticed in 11/18 cases of RSE. 8 cases had shock after starting midazolam infusion and 6 needed ionotropes and 2 cases corrected with fluid boluses.

DURATION OF MIDAZOLAM INFUSION

NUMBER OF DAYS	**NO.OF PATIENTS**	**%**
<2 DAYS	13/18	72.22%
2-4 DAYS	4/18	522.22%
>4 DAYS	1/18	5.56%
TATAL	18	100%

All children needed IPPV before starting midazolam infusion, intubated with atropine 0.02 mg / kg and midazolam IV 0.2 mg/ kg. Neuro muscular blockade avoided as they may interfere with the clinical signs of recovery.

Time Taken To Control Seizures Completely After Midazolam

TIME	**NO.OF PATIENTS**	**%**
< 30 MIN	9/18	50%
30 MIN-2 HOURS	3/18	16.66%
2-8 HOURS	3/18	16.66%

>8 HOURS	3/18	16.66%

RECURRENT SEIZURES

Observed in 35 cases (27.6%). 21 cases had single recurrence (16.5%) and 14 children had multiple recurrence. Most of them were managed with IV diazepam (13 cases) and by increasing the dose of midazolam infusion. Recurrence was seen in 5 children with RSE and 10 children those who died. 2 cases we used thiopentone and developed profound hypotension managed with inotropic support. That child died.

CONSCIOUS REGAINED

Consciousness regained in 104 cases. Mean duration for complete recovery of consciousness was 40 hours. Minimum 1 hour to maximum 12 days observed. 47 children (37%) had regained full consciousness within 10 hours of hospital stay.

COMPLICATIONS

Respiratory failure necessitating prolonged ventilation was seen in 44 children (34.8%). Pneumonia at arrival was noticed in 10 cases and 6 developed pneumonia subsequently. DIVC was seen in 4 cases, raised ICP was in 6 cases, acute renal failure was in 3 cases, phenytoin toxicity even with the therapeutic doses was in 8 cases, persistent and recurrent shock in 48 cases (37.8%) were some of the complications encountered. 2 children with normal lung before had pneumo thorax and it could be due to manual IPPV. No cases of hyperthermia, rhabdomyolysis or diabetes insipedus were encountered.

Hypoglycemia at arrival was noted in 13 children and hyperglycemia in 11 cases. Low HCO3 was seen in 19 cases and hypocalcemia in 11 cases. No case of hyper calcemia or hyper natremia was seen. 3 hypo natremias, 14 cases of hypokalemias, 1 case of hyper kalemia were observed.

DIVC	4
Pneumonia at arrival	10
Later	6
ICP	6
ARF	3
Phenytoin toxicity	8
Pneumo thorax	5
Hyperthermia/ Rhabdomyolysis /DI	-
Hypo natremia	3
Hypokalemia	14
Hypoglycemia	13
Hyperglycemia	11
Hyperkalemia	1
Low HCO3	19

CSF:

LP and CSF analysis was done in 70 cases either antimortum or post mortum in case of death. Out of them, 54 children had normal CSF, 16 cases had abnormal CSF (elevated protein, decreased sugar, pleocytosis). 2 children had organisms in CSF.

CT/USG/MRI:

CT brain was done for 56 cases and found to be normal in 35 cases and abnormal in 21 cases. USG cranium was done in 39 cases and found to be normal in 31 cases. MRI was done in 4 cases to confirm the CT

findings. CT brain was usually done in all cases of SE with focal onset of seizures (28 cases) and found to be abnormal in 25 cases (89.2%)

EEG:

We were not able to do bedside EEG or EEG during seizures. Inter ictal EEG was done for 54 children. All cases of febrile SE were undergone for EEG (19 cases) and found to have normal EEG. 40 cases had normal EEG and 14 had abnormal EEG.

FINAL DIAGNOSIS:

42 children were diagnosed to have acute symptomatic SE (toxic encephalopathy-5, drug over dose -3, metabolic SE-2, Trauma-3, Acute CNS infection- 19, poorly identified acute encephalopathy- 1, septic shock-9). 19 children were diagnosed as FSE and 22 children had idiopathic epilepsy . 43 children fall in to remote symptomatic group (structural brain lesions, CP-34, PMS-1, CVA-1, neurocutaneous -3, others-4). One child had progressive degenerative disorder.

Diagnosis	Frequency	%	Deaths	AMA	New sequele
FSE	19	15.%	0	0	0
Idiopathic	22	17.2%	0	0	0
Remote symptomatic (CP /MR /DD/PMS/PES/FND)	43	33.8.%	5	1	0
Progressive CNS degenerative conditions	1	0 .8%	0	0	0
Acute CNS infection	19	15.%	7	0	2
Toxic encephalopathy	5	3.9%	1	1	0
Trauma	3	2.4%	0	0	0
Septic shock	9	7.1%	5	1	0
Drug over dose	3	2.4%	0	0	0
Metabolic seizures (hypo calcemia)	2	1.6%	1	0	0
Acute encephalopathy	1	0.8%	1	0	0
Total	127	100%	20	3	2

FINAL OUTCOME

Final Outcome	Frequency	%	Cum%
Recovered	76	59.8%	57.5%
No new sequele	26	20.5%	80.3%
New sequele	2	1.6%	81.9%
Death	20	15.7%	97.6%
AMA	3	2.4%	100%
Total	127	100%	

Out of 127 children 76 children (59.8%) recovered completely without any neurological sequele at the end of 1 month and they were on regular follow up in neuro OPD. 26/127 children (20.5%) recovered no new neurological sequele as compared to their previous status. So, totally 92 children were (80.3%) classified into good outcome group. 20 deaths (15.7%) observed during this study. 3 AMA discharges (2.4%) noted. They were all on ventilator support and ALOC till discharge. So they were also included in the poor outcome group. 2 children had new neurological sequele at the end of 1 month, one had hydrocephalus and other had hemi paresis which were not present already. No deaths observed in FSE (19 cases), though 9 FSE had seizure duration of more than 30 minutes.

Out of varies risk factors analyzed for predicting poor outcome, Age < 1 year, increasing distance from the place of onset, duration >1 hour, no proper pre hospital therapy, SaO2 of <92% at arrival, refractory shock in ER that is uncorrected even after starting ionotropes, on IPPV, refractory SE, acidosis at arrival that is low HCO3 and supported by academia in ABG, acute CNS infection as the underlying cause if SE were some of the

risk factors we found. Odds ratio, 95% confident interval, P values were calculated for poor outcome group comparing with good outcome group and Univariate analysis was done for all these risk factors. Of all the risk factors above mentioned age <1 years and < 6 years (p=0.05), refractory shock (P=0.07) were not statistically significant to influence the outcome adversely. Increasing distance (that is each Km increase in distance increases the odds ratio by 1.7), duration of > 1 hour, no proper pre hospital therapy, SaO2 < 92% at arrival, acidosis at arrival, need for IPPV, refractory SE, acute CNS infection were significant risk factors.

Univariate Analysis	O.R	95% C.I	p- value
Age			
< 1 year	7.4	0.8 , 62.3	0.05
1 to 3 years	12.4	1.5, 102.3	
3 to 6 years	3.7	0.3, 35.1	
> 6 years	1.0	Reference	
Distance	1.7	1.3, 2.4	0.001
Duration from onset of first fits ≤ 1 hrs > 1 hrs	 1.0 5.5	 Reference 2.0, 14.8	0.001
Pre hospital therapy **NO** **Yes**	 3.5 1.0	 1.2, 10.6 Reference	0.02
SPO2 **> 92%** **< 92 % + Not recorded**	 1.0 3.0	 Reference 1.2, 7.7	0.02
Uncorrected shock **Yes** **No**	 2.4 1.0	 0.9, 6.3 Reference	0.07
IPPV **No risk(0)** **Risk (1)**	 1.0 4.6	 Reference 1.9, 11.3	0.001
Refractory SE **No** **Yes**	 1.0 5.0	 Reference 1.7, 14.3	0.003
Acidosis **Yes** **No**	 3.4 1.0	 1.2,9.6 Reference	0.02
Infections **No** **Other** **CNS infection**	 1.0 2.4 9.1	 Reference 0.6, 8.9 2.1, 39.3	0.006

Finally at the end of multiple logistic regressions of all the risk factors, only 4 factors namely increasing distance from the place of onset of seizures to CMC, duration of seizures, need for IPPV, acute CNS infection as the aetiology are statistically significant risk factors. They are independent risk factors influencing poor outcome.

Multiple Logistic Regression	**O.R**	**95% C.I**	**p- value**
Distance	1.8	1.73, 2.6	0.001
IPPV No risk **Risk**	1.0 6.2	Reference 2.2 , 17.6	 0.001
Infections **No** **Other** **CNS**	 1.0 2.3 6.8	 Reference 0.6, 9.6 1.4 , 34.6	 0.04
Duration **<1h** **>1h**	 1.0 4.4	 Reference 1.6,.13.6	 0.001

IV. Discussions

Incidence of SE among male children is more (55%) than female children (45%) in this study and the male predominance is not statistically significant (p>0.05) and male, female distribution is equal in other studies also. Mean age is 3 years and 5 months observed in this study where as mean age of SE is 2 years and 4 months noted in **Mah JK et al** [89] study, and Mean age of 56.6 ± 46.5 months observed in **Kalra Veena et al** [97] study. Most of the cases of SE in children occurred in younger age group.

In our study nearly 60% of the cases were < 3 years and 82% were < 6 years. **Garzon E** [84] observed that SE incidence peaked in the first years of life, and 56.7% cases were < 5 years in **Kalra Veena** [97] study. Mortality is also high in this age group. 85% of mortality occurs in the age group of < 3 years.

Outcome is determined by age, duration and underlying cause. Age < 1 year, duration of >1 hour, acute CNS infection as the underlying cause are predictors of poor outcome seen in varies studies. Young age <12 months and duration >60 minutes associated with adverse outcome concluded in **Kwong et al** [83] study**,** deaths were correlated to etiology and patient's age concluded in **Garzon E** [84] study**,** the group with SE lasting <1hr had a lower mortality as compared with seizure duration > or = 1 h observed in **Towne AR et al** [85] study. **Sahin et al** [87] concluded that the mortality in RSE was related to etiology age and EEG findings and predictors of poor outcome were older age (OR = 1.04,95% CI 1.01 – 1.07), delay in treatment (OR = 9.73,95% CI 1.58 – 59.96) and CNS infection 9 OR = 30.27 95% C 3.14-292.19) seen in **Hui AC et al** [88] study. Outcome related to etiology, duration, and age is a minor factor observed in **Dunn DW** [90] study, mean seizure duration was 1.5 ± 2.8 hours in those children with a normal outcome, 1.7 ± 1.2 hours in those survivors with an abnormal neurological outcome (P > 0.05), and 6.8 ± 12 hours in those who died (P < 0.05) and both the duration and etiology of status epilepticus affect outcome concluded by **Simon J et al** [92]**.**

Singhi S et al [94] concluded that the morbidity and mortality are highest with SE that associated with CNS infections which is the most important cause of SE in our country and the outcome depends on the underlying etiology, age, rapidity of SE and adequacy of care. He also opined that adherence to a time framed protocol in the ED helps in improving the final outcome. Seizure duration >45 min (p.0.001),and presence of septic shock (p-0.001),were associated with significantly more mortality observed in **Kalra veena et al** [97] study. Young age < 12 months duration of seizure > 60 minutes are associated with adverse outcome seen in **Horn drop** study where as risk factors were age< 36 months and refractory SE concluded by **Shinner et al.**

In our study also duration > 1 hour, increasing distance from the place of seizure onset, acute CNS infection, need for IPPV were significant independent risk factors that predict poor out come. Commonest seizure type is GTCS and NCSE accounts for 20 % of SE. In our study also commonest seizure type is GTCS and NCSE account for 26% of SE. This may be because prolonged CSE in many cases (13.3%) resulted in NCSE due to neuro electro mechanical dissociation.

Proper pre hospital therapy is associated with good out come observed in this study. No or improper pre hospital therapy is a significant risk factor for poor outcome in univariate analysis. **Kwong et al** [83] concluded that Pre hospital Rx with BZD reduces adverse outcome. **Allredge BK et al** [92] also concluded that, Pre hospital therapy was associated with shorter duration of SE (P=0.007), reduced likelihood of recurrent seizures in ER (P=0.045), no significant difference between PR and IV and simplify the subsequent management of these patients.

In this study, 57 cases (44.9%) presented as SE in heir first episode of fits which is comparable with other literatures [2] and out of them, H/o poor drug compliance was present in 14 cases and that could be the cause of SE in them where as 59.4% of the individuals had pervious epilepsy while 40.6% had not **in Garzon et al** [84]

study and 43% has no prior SE in **Mah JK et al [90]** study, 28/60(46.6%) were no h/o prior fits in **Dunn DW et al [91]** study, 16 patients (53.3%) had SE I episode without prior H/o fits in **Kalra veena et al [97]** study.

Most of them were apneic (122/127) at arrival and 100% needed supplementary O2 either BVM with 100% O2 or O2 through non rebreathing mask in this study. O2 through non can be given only when the respiration is regular and adequate only in case of NCSE because all CSE cases and most of the NCSE cases the respiratory muscles also involved in seizure activity resulted in apnea. Apnea is not the contra indication for giving ACDs but is an indication for initiating BVM in them. Most of them were presented with shock also and needed fluid boluses and ionotropes support but nearly 20% of cases the shock left uncorrected in ER needed prolonged inotropic support. In hemo dynamically unstable patients, phenytoin should be used cautiously or it can be substituted with other ACDs. Fos phenytoin is found to be safe in these patients but it was not used as an ACD in this study. Commonest side effect observed after stating phenytoin infusion was shock and hypotension rarely arrhythmias needed ionotropes support. Frequent monitoring of BP and HR/rhythm perfusion status is must. Preferably phenytoin is avoided in young infants of <3 months. 2 cases were found to have hypotension at arrival and subsequently died.

The incidence of RSE is 15% in this study where as 11.3% in **Garzon et al [84]** study, 26/418 in a previous study conducted in ICH by **Santhosh Paulin[96].**

Mortality in this study is 15.7% which is comparable with many international as well as Indian literatures [3, 4, 5]. **Kalra veena et al [97]** showed 30 % mortality and **Garzon E [84]** showed 19.5% and **Hui AC et al [89]** showed 26% mortality, where as 5.6 % mortality was observed by **Simon J et al [93]** and 3-10% mortality was observed in Indian children as per **Singhi S et al [95]** study and 4-6 % in US [2]

Etiology of SE: FSE 15%, remote symptomatic34%, idiopathic epilepsy 17%, acute CNS infection 15%, septic shock 7%, acute metabolic/toxic encephalopathy 7%, others 5% were observed in this study. Etiology [100]: Fever – 36% (non –CNS infection), idiopathic - 24 – 39%, chronic neurological disease- 15%, metabolic /toxic- 8%, medication change -20%, anoxia -5%, CNS Infection -5%, tumor-1%, acute trauma / abuse - 4%, degenerative disease- 2%, vascular disease -3%. Causes of SE [3]: Idiopathic -30%., fever- 25%, acute symptomatic- 35%, remote symptomatic- 15%, progressive- 5%. Most common causes are AED withdrawal or non compliance, metabolic disturbance, drug toxicity, CNS infection, CNS tumor, Refractory epilepsy, head trauma, febrile SE.

CNS infection is more common in our setup but it is low in western countries (5%) due to the implementation of Hib, Pneumococal vaccination and improvement in quality of life style, environmental sanitation and safe water supply. We come across only 2 new neurological sequele during this study. Both were due to acute CNS infection. 18/114 new neurological deficit observed in **Dunn W [91]** study and 17/193 new neurological deficits occurred in **Maytal J et al [98]** study.

V. Summary And Conclusion

Mortality in SE in this study is 15.7%. Most of the cases of SE were young children of <6 years of age and mortality is also high in young children of <3 years who had 85% mortality. There is no significant sex difference. Commonest seizure type is GTCS. Next is NCSE that accounts for 26% of the cases. All were required supplementary oxygen at arrival and most of them were apneic, hypoxic and shocky. 9% of the children had hypoglycaemia and 11% had hyper glycaemia at arrival but all of them received 25% dextrose. Common causes of SE are acute CNS infection; septic shock, idiopathic epilepsy, febrile SE and CNS co morbidity like CP. Febrile SE and idiopathic epilepsy were associated with good prognosis. All the children in FSE group recovered completely without any sequele. CNS infection and septic shock were associated with poor outcome. New neurological sequele occurred in 2 cases both of them had acute CNS infection as the underlying aetiology. Long term outcome in these survivors need to be evaluated further. Acute CNS infection, duration of SE, distance travelled to seek medical advice and respiratory failure requiring IPPV, are independent risk factors that influence the outcome adversely. 109 /127 cases responded to I line ACDs. 18 cases diagnosed as RSE and out of them 10 survived. Refractory SE is associated with poor outcome and prolonged hospital stay. Most of them responded to midazolam and only 2 cases required thiopentone but not controlled with thiopentone also. All cases of RSE were intubated using midazolam IV as the sedative and neuromuscular blockade avoided. Common complication of midazolam infusion is shock and noted only with higher doses >6 mcg/kg/min and managed with ionotropes. Common cause of SE is acute CNS infection and this results in higher mortality, morbidity and later neurological sequel and is one of the independent risk factor for poor outcome in SE. Duration and distance travelled to seek medical advice is also important independent risk factors influencing poor outcome. Many of the complications and consequences like shock, respiratory failure, aspiration pneumonias, hypo/hyperglycemias, dyselectrolytemias can be managed successfully with anticipation and early intervention, protocol based management. Management of vital signs and underlying cause of SE along with specific ACD therapy are the priorities in the management of SE. Midazolam is safe and effective for the treatment of RSE in children.

Referance:

[1]. Treatment of SE, Brien J Smith, MD. PCNA, Neurology clinics: vol. 19 no 2 may 2001 page 347-364.
[2]. Status Epilepticus-2000, Evaluation and Management, Emory Pediatrics Acute Care Symposium- July 12, 2000. Dr. Philip Holt: Division of Pediatric Neurology, Department of Pediatrics. Emory University School of Medicine
[3]. Shinnar, Berg AT, Moshe SL, the risk of seizure recurrence after a first unprovoked afebrile seizure in childhood, an extended follow up. Pediatrics 1996:98:216-225
[4]. Knowng KL, Lee SL, Yung A, status epilepticus in 37 Chinese children: etiology and outcome. J Ped child health.1995:31(5):395-398.
[5]. Longroscino G, Hesdorffer DC, Casino G, Annegers JF, Hauser WA, short term mortality after a first episode of SE.epilepsia.1997:38:1344-1349.
[6]. Nevander G. Ann Neurol 1985; 18(3):281-90.
[7]. Gastaut H. Clinical and electroencephalographical classification of epileptic seizures Epilepsia 1970; 11: 102-13
[8]. Lothman E. The biochemical basis and pathophysiology of status epilepticus Neurology- 1990; 40: 13-23.
[9]. Text book of pediatric intensive care: Status epilepticus. Robert C Tasker, J Michael Dean. Page 747-774.
[10]. Towne AR, Waterhouse EF, Boggs JG, et al: prevalence of NCSE in comatose patients. Neurology:. 54: 1421-1428, 2000.
[11]. Amy Baxter, MD: Acute confusional state in the ED. Paediatric emergency medicine.vol4, no3. sep2003. 215-220
[12]. Krumholz A, Sung GY, Fisher RS, et al. CPSE accompanied by serious morbidity and mortality. Neurology 45: 1499-1504, 1995
[13]. Krumholz A: Epidemiology and evidence for morbidity of NCSE. J of Clin Neuro-physiol.16: 314-322, 1999.
[14]. Bleck TP, RSE, neurology chronicle: 1992: 2,1-4.
[15]. Current concepts, new England journal of medicine. Vol: 338 no: 14. P- 970-975.1998 april2.daniel H Lowenstein MD, Brian K Alledridge: pharm .D
[16]. Appleton R, Choonara I, Martland T, et al. The treatment of convulsive status epilepticus in children The Status Epilepticus Working Party, Members of the Status Epilepticus Working Party Arch Dis Child 2000; 83 (5):415-9
[17]. Lowenstein DH, Bleck T, Macdonald RL. It's time to revise the definition of status epilepticus. Epilepsia 1999;40(1):120-2.
[18]. Greenblatt DJ, Divoll M. Diazepam versus lorazepam: relationship of drug distribution to duration of clinical action. Adv Neurol 1983; 34: 487-91.
[19]. Leppik IE, Derivan AT, Homan RW, et al. Double-blind study of lorazepam and diazepam in status epilepticus. JAMA 1983;249: 1452-4.
[20]. Chamberlain JM, Altieri MA, Futterman C, et al. A prospective, randomized study comparing intramuscular midazolam with intravenous diazepam for the treatment of seizures in children Pediatric Emerg Care 1997;13(2):92-4.
[21]. Towne AR, DeLorenzo RJ. Use of intramuscular midazolam for status epilepticus J Emerg Med 1999; 17 (2):323-8.
[22]. Burneo JG, Anandan JV, Barkley GL. A prospective study of the incidence of the purple glove syndrome. Epilepsia 2001; 42: 1156-9.
[23]. O'Brien TJ, Cascino GD, So EL, et al. Incidence and clinical consequence of the purple glove syndrome in patients receiving intravenous phenytoin. Neurology 1998; 51: 1034-9.
[24]. Kilarski DJ, Buchanan C, Von Behren L. Soft-tissue damage associated with intravenous phenytoin. N Engl J Med 1984; 311:1186-7.
[25]. Rao VK, Feldman PD, Dibbell DG. Extravasation injury to the hand by intravenous phenytoin. Report of three cases. J Neurosurg 1988; 68: 967-9.
[26]. Louis S, Kutt H, McDowell F. The cardio circulatory changes caused by intravenous Dilantin and its solvent. Am Heart J 1967; 74: 523-9.
[27]. Goldschlager AW, Karliner JS. Ventricular standstill after intravenous diphenylhydantoin. Am Heart J 1967; 74: 410-2.
[28]. Earnest MP, Marx JA, Drury LR. Complications of intravenous phenytoin for acute treatment of seizures. Recommendations for usage. JAMA 1983; 249: 762-5.
[29]. Wallis W, Kutt H, McDowell F. Intravenous diphenylhydantoin in treatment of acute repetitive seizures. Neurology 1968;18: 513-25.
[30]. DeToledo JC, Lowe MR, Rabinstein A, et al. Cardiac arrest after fast intravenous infusion of phenytoin mistaken for fosphenytoin.Epilepsia 2001; 42: 288.
[31]. Jamerson BD, Dukes GE, Brouwer KL, et al. Venous irritation related to intravenous administration of phenytoin versus fosphenytoin. Pharmacotherapy 1994; 14: 47-52.
[32]. Ramsay R, Philbrook B, Martinez D, et al. A double-blind, randomized safety comparison of rapidly infused IV loading doses of fosphenytoin vs. phenytoin. Epilepsia 1995; 36 (Suppl 4): S90.
[33]. Eldon M, Loewen G, al Ve. Pharmacokinetics and tolerance of fosphenytoin and phenytoin administration intravenously to healthy subjects. Can J Neurol Sci 1993; 20: 5180.
[34]. Browne TR, Kugler AR, Eldon MA. Pharmacology and pharmacokinetics of fosphenytoin. Neurology 1996; 46: S3-7.
[35]. Walton NY, Uthman BM, El Yafi K, et al. Phenytoin penetration into brain after administration of phenytoin or fosphenytoin. Epilepsia 1999; 40: 153-6.
[36]. Pellock JM. Fosphenytoin use in children. Neurology 1996;46: S14-6.
[37]. Koul R, Deleu D. Sub therapeutic free phenytoin levels following fosphenytoin therapy in status epilepticus. Neurology 2002; 58: 147-8.
[38]. Takeoka M, Krishnamoorthy KS, Soman TB, et al. Fosphenytoin in infants. J Child Neurol 1998; 13: 537-40.
[39]. Smith RD, Brown BS, Maher RW, et al. Pharmacology of ACC-9653 (phenytoin prodrug). Epilepsia 1989; 30: S15-21.
[40]. Leppik IE, Boucher BA, Wilder BJ, et al. Pharmacokinetics and safety of a phenytoin prodrug given IV or IM in patients. Neurology 1990; 40: 456-60.
[41]. Kumar A, Bleck TP. Intravenous midazolam for the treatment of refractory status epilepticus. Crit Care Med 1992; 20: 483-8.
[42]. Parent JM, Lowenstein DH. Treatment of refractory generalized status epilepticus with continuous infusion of midazolam. Neurology 1994; 44: 1837-40.
[43]. Pellock JM. Use of midazolam for refractory status epilepticus in pediatric patients. J Child Neurol 1998; 13: 581-7.
[44]. Singhi S, Murthy A, Singhi P, et al. Continuous midazolam versus diazepam infusion for refractory convulsive status epilepticus. J Child Neurol 2002; 17: 106-10.
[45]. Rivera R, Segnini M, Baltodano A, Perez V. Midazolam in the treatment of status epilepticus in children. Crit Care Med 1993;**21**:991-994.
[46]. Brown LA, Levin GM. Role of propofol in refractory status epilepticus. Ann Pharmacotherapy 1998; 32: 1053-9.

[47]. Stecker MM, Kramer TH, Raps EC, et al. Treatment of refractory status epilepticus with propofol: clinical and pharmacokinetic findings. Epilepsia 1998; 39: 18-26.
[48]. Makela JP, Iivanainen M, Pieninkeroinen IP, et al. Seizures associated with propofol anesthesia. Epia 1993; 34: 832-5.
[49]. Parke TJ, Stevens JE, Rice AS, et al. Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports. BMJ 1992; 305: 613-6.
[50]. Hanna JP, Ramundo ML. Rhabdomyolysis and hypoxia associated with prolonged propofol infusion in children. Neurology 1998; 50: 301-3.
[51]. Goldberg M, McIntyre H. Barbiturates in the treatment of status epilepticus. In: Delgado-Escueta A, Wasterlain C, Treiman D, Porter R. Advances in Neurology, Vol. 34, Status Epilepticus New York: Raven Press, 1983: 499-503.
[52]. Crawford TO, Mitchell WG, Fishman LS, et al. Very-high dose phenobarbital for refractory status epilepticus in children. Neurology 1988; 38: 1035-40.
[53]. Treiman D, Delgado-Escueta A. Status Epilepticus. In: Thompson R, Green J. Critical Care of Neurological and Neurosurgical Emergencies. New York: Raven Press, 1980: 55-99.
[54]. Opitz A, Marschall M, Degen R, et al. General anesthesia in patients with epilepsy and status epilepticus. Adv Neurol 1983;34: 531-5.
[55]. Goitein KJ, Mussaffi H, Melamed E. Treatment of status epilepticus with thiopentone sodium anaesthesia in a child. Eur JPediatr 1983; 140: 133-5.
[56]. Osorio I, Reed RC. Treatment of refractory generalized tonic clonic status epilepticus with pentobarbital anesthesia after high dose phenytoin. Epilepsia 1989; 30: 464-71.
[57]. Rashkin MC, Youngs C, Penovich P. Pentobarbital treatment of refractory status epilepticus. Neurology 1987; 37: 500-3.
[58]. Van Ness PC. Pentobarbital and EEG burst suppression in treatment of status epilepticus refractory to benzodiazepines and phenytoin. Epilepsia 1990; 31: 61-7.
[59]. Tasker RC, Boyd SG, Harden A, et al. EEG monitoring of prolonged thiopentone administration for intractable seizures and status epilepticus in infants and young children. Neuropediatrics 1989; 20: 147-53.
[60]. Honack D, Loscher W. Intravenous valproate: onset and duration of anticonvulsant activity against a series of electro convulsions in comparison with diazepam and phenytoin. Epilepsy Res 1992; 13: 215-21.
[61]. Walton NY, Treiman DM. Valproic acid treatment of experimental status epilepticus. Epilepsy Res 1992; 12: 199-205.
[62]. Giroud M, Grass D, Ecousse A, et al. Use of injectable valproic acid in status epilepticus: a pilot study. Drug Invest 1993; 5: 154-9. SI 10 Epileptic Disorders Vol. 4, Special Issue N0. 2, October 2002 F. Rosenow, et al.
[63]. Price D. Intravenous valproate: experience in neurosurgery. In: Chadwick D. Fourth International Symposium on Sodium Valproate and Epilepsy. London: Royal Society of Medicine Services,1989: 197-203.
[64]. Marlow N, Cooke R. Intravenous sodium valproate in the neonatal intensive care unit. In: Chadwick D. Fourth International Symposium on Sodium Valproate and Epilepsy. London: Royal Society of Medicine Services, 1989: 208-10.
[65]. Czapinski P, Terczynski A. Intravenous valproic acid administration in status epilepticus. Neurol Neurochir Pol 1998; 32: 11-22.
[66]. Uberall MA, Trollmann R, Wunsiedler U, et al. Intravenous valproate in pediatric epilepsy patients with refractory status epilepticus. Neurology 2000; 54: 2188-9.

Dr. N. Kumar, MD. "Clinical Profile, Immediate Outcome and Risk Factors Determining Adverse Outcome of Status Epilepticus in Children–Managed In an Urban Tertiary Level Referral Centre". *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(06), 2022, pp. 25-41.