*Dissertation on*

# CLINICAL PROFILE, IMMEDIATE OUTCOME AND RISK FACTORS DETERMINING ADVERSE OUTCOME OF STATUS EPILEPTICUS IN CHILDREN–MANAGED IN AN URBAN TERTIARY LEVEL REFERRAL CENTRE

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**RESEARCH INSTITUTE, CHENNAI-3.**

# CERTIFICATE

This is to certify that, this dissertation titled, ***Clinical profile, Immediate outcome and Risk factors determining Adverse outcome of Status Epilepticus in Children- managed in an urban tertiary level referral centre***, is a bonafide work done under our supervision by Dr. N. Kumar, at ***Institute of Child Health and Hospital for Children,Chennai.8,*** for MD Degree examinations - September 2006.


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# DECLARATION

I solemnly declare that this dissertation, titled ***Clinical Profile, Immediate Outcome and Risk Factors determining Adverse Outcome of Status Epilepticus in Children –Managed in an urban tertiary level referral centre*** is done by me at, ***Institute of Child Health and Hospital for Children,Chennai.8.Madras Medical College and Research Institute, Chennai-600003.*** during the period from Jan 2005 to Dec2005, under the guidance and supervision of **Prof. R. Duraisami; MD.DCH, Prof. R. Kulanthai Kasthuri; MD.DCH, and Prof. G. Kumaresan MD,DCH,DM(Neuro).** This is submitted for M. D. Degree examinations Sept. 2006 and not done previously or published before in any journals.

**N. Kumar**

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# CONTENTS

# 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]. The approach in generalized convulsive SE is modified by changing concepts regard the definition of SE and studies justifying more aggressive treatment, with earlier intervention started prior to arrival to hospital. 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]. Improvements reflect studies, retrospective data, changing definition of SE (from >60 minutes to > 5 minutes). But most important factor is improved care. 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 as 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].

## IMPORTANT CAUSES

Acute causes:CNS infections, febrile convulsions, trauma, metabolic derangements, toxins, drugs overdose, vascular, hypoxia etc. Static causes: 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: Degenerative cerebral disorders.

## PATHOPHYSIOLOGY

SE is an 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].

### SEIZURE INITIATION AND PROLONGATION

Why seizures start and stop is unknown, although it is likely that seizure initiation is caused by an imbalance between excitatory and inhibitory neurotransmission, leading to the initiation of abnormal neural impulses. Excitatory synapses mature earlier than inhibitory synapses and this, coupled with an increase in the susceptibility of excitatory neurotransmitter receptors, increases the likelihood that an excitation-inhibition imbalance may occur.

The immature cerebral cortex has a high synaptic density at around 2 months of age and this may contribute to the development of hyper synchrony of neural groups. The excitatory amino acid neurotransmitter glutamate increases at the site of the seizure focus at the beginning of seizure activity in adults with temporal lobe epilepsy. It is believed that the same may happen at the onset of generalized seizures. Inhibitory neurotransmitters such as GABA later increase at the seizure focus and redress the balance between excitation

and inhibition. Other mechanisms of inhibitory receptor modulation, such as adenosine receptor agonism, may also contribute to seizure termination. Thus the increased incidence of CSE in childhood is probably caused by a combination of increased seizure susceptibility and decreased ability to mount an adequate inhibitory response. In initiating seizure spread, the synchronization of cerebral neurons is as important as neuronal discharge. The interconnections between the thalamus and cerebral cortex are essential in forming reverberating circuits. The spike and wave discharges occur when cortical neurons are depolarized (spike) or hyper polarized (wave).

## ELECTROPHYSIOLOGY

About 70-80% of cases of CSE throughout all age groups will have a focal onset but be secondarily generalized. A predictable sequence of changes in the EEG has been shown in adult humans and in animal models. 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].

## MOTOR RESPONSE

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.

## ROLE OF EXCITOTOXIC AMINO ACIDS

They 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.

CSE induces the production of heat shock proteins in several brain regions. The presence of heat shock proteins can protect the brain against further stressful stimuli, which are potentially damaging to neurons. 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].

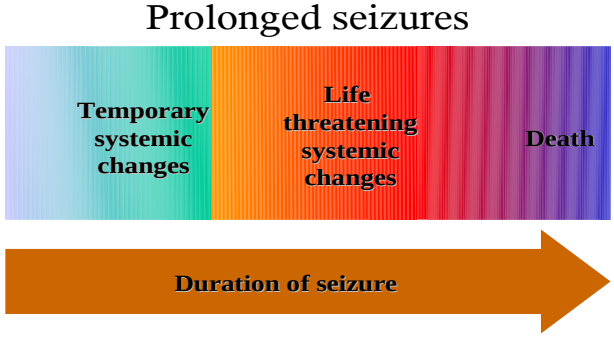
## MECHANISMS BY WHICH GLUTAMATE CAUSES CELL DEATH

Excess extra cellular glutamate may result in cell death by causing necrosis, gene determined cell death, or both. The primary receptor involved in cytotoxicity related to glutamate is the NMDA receptor, although other glutamate receptors may be involved. The NMDA receptor is an inotropic receptor. Influx of calcium through the ionophore occurs due to the binding of glutamate and glycine or D-serine to the appropriate site on the receptor. High intracellular calcium concentrations result in the activation of large number of

calcium dependent processes such as activation of protein kinase C, nitric oxide and free radical formation, activation of phospholipase A2 and activation of protease calpain I.

Glutamate receptor stimulation also results in the formation of immediate early genes, such as c-fos, fos-B, c-jun, and jun-B, c-fos encodes for fos protein, which has a leucine zipper allowing it to bind and form dimers with similar proteins. These dimers bind to a specific DNA region (AP-1 site), which regulates the expression of a number of late effector genes. Some of the genes regulated are harmful and some are potentially neuroprotective. Thus immediate early genes may play a dual role in induction of gene determined cell death and activation of brain repair mechanisms.

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.



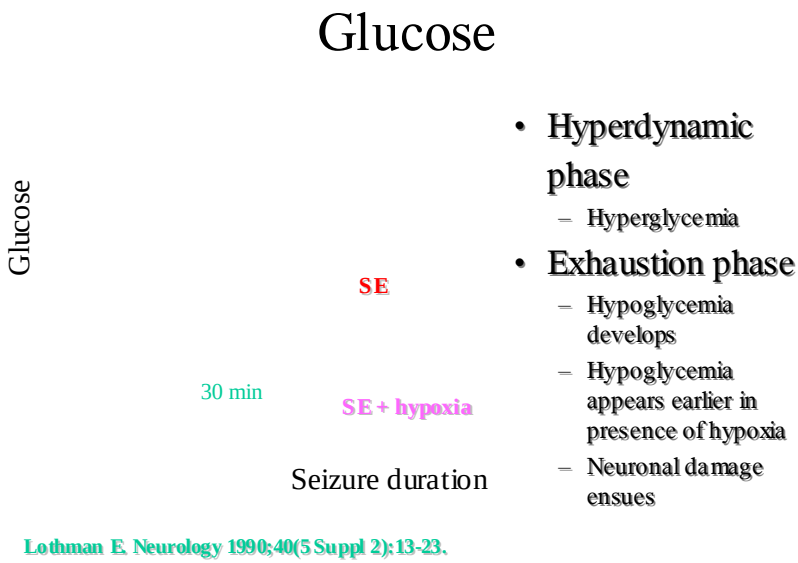
## SYSTEMIC AND CENTRAL PATHOPHYSIOLOGY

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].

## GLUCOSE

Initially hyperglycemia and in phase II become hypoglycemic.

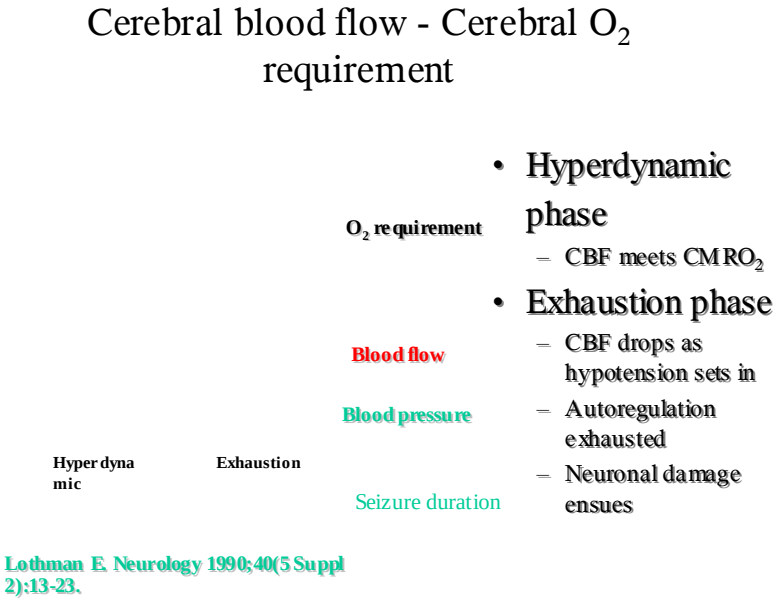


HYPOXIA

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.

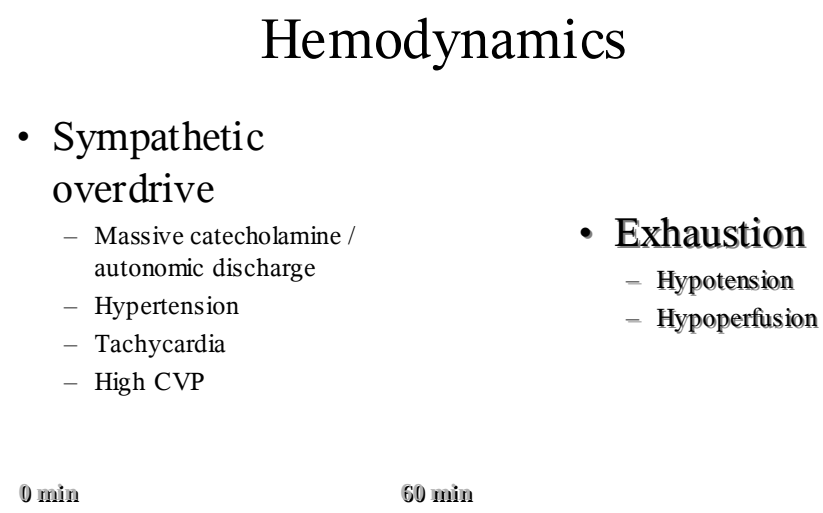
ACIDOSIS

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.



HEMODYAMICS

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.

**ALTERED MENTAL STATUS /NCSE**

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. Further more, 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 etiology rather than seizures. NCSE should be considered in comatose children without signs of seizures activity, an EEG, will help to diagnose this condition[11].

**NCSE**

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 with out 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].

## REFRACTORY STATUS EPILEPTICUS

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 out come 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 OF SE[7]

### Convulsive SE (CSE)

GCSE/ GTCS (primary)
Secondary generalized
Multifocal clonic
Hemi convulsive SE

Tonic SE

Clonic SE

Simple PSE/ Epilepsia partia continualis

**Non convulsive SE (Subtle SE)**

Neurological EMD (Electrical SE)

PCSE

ASE

Myoclonic SE +/- salaam attacks

## INITIAL INVESTIGATIONS

Blood - glucose, calcium, electrolytes

Blood counts

CXR

USG Cranium / CT Brain

CSF analysis

EEG

## OTHER INVESTIGATIONS SUGGESTED

RFT

LFT

Magnesium

ABG

Septic work up (Cultures)

Blood / Urine - AED levels

Toxicological screening

Metabolic screening

X ray skull

MRI

Lactate, NH3

## MEDICAL COMPLICATIONS OF STATUS EPILEPTICUS

STATUS INDUCED

- Epilepsy subsequently (77%)
- Hemi convulsion Hemiplegia (HH)
- Hemi convulsion Hemiplegia Epilepsy (HHE)-rare now

INTER ICTAL COMA

CUMULATIVE ANOXIA

- Cerebral and systemic

## CARDIO VASCULAR COMPLICATIONS

Tachycardia, Bradycardia

Cardiac arrest

- Hypertension, Hypotension
- Cardiac failure,

Cardiogenic shock

RESPIRATORY SYSTEM FAILURE

- Apnea
- Chyne stokes breathing

Bradypnea,

Tachypnea

- Neurogenic pulmonary edema
- Aspiration pneumonia
- Respiratory acidosis
- Cyanosis

RENAL FAILURE

- Oliguria
- Uremia
- ATN
- Rhabdo myo lysis

## AUTONOMIC SYSTEM DISTURBENCE

- Hyperpyrexia
- Excessive sweating, vomiting

Hyper secretions (salivary, tracheo bronchial)

Airway obstruction

## METABOLIC AND BIOCHEMICAL ABNORMALITIES

Acidosis (metabolic, lactate), Anoxemia

Hypernatremia, Hyponatremia

Hyperkalemia

Hypoglycemia

Hepatic failure

Dehydration

Acute Pancreatitis

Leucocytosis

INFECTIONS

Pulmonary

Urinary

Skin

OTHERS

Altered auto regulation of CBF

Increased cerebral metabolic rate of O2 (CMR O2)

DIVC

MODS

Fractures

Thrombo phlebitis

## MANAGEMENT

Longer the duration of seizures, greater the risk of complications, so, every attempt should be made to control epileptic activity (clinically and electrically). Status Epilepticus is a medical emergency that requires an organized and skillful approach to minimize the associated mortality and morbidity. 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.

The longer SE persists, 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]. GCSE is a condition which most likely will not terminate rapidly and / or spontaneously and requires prompt intervention[17]. Primary aim is to control and abort SE as the duration of seizure activity is directionally proportional to immediate mortality and later morbidity. Goal of treatment is the cessation of both clinical and electrical seizures. A time framed protocol is essential in the management of SE in Emergency Room.

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 etiology, 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.

Priority is the management of ABCs along with rapid termination of seizure activity. 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. Intramuscular lorazepam also can be given, but lacks water solubility, thus later onset than midazolam.

Phenytoin is given as 20 mg/kg I.V. over 20 min, then if needed 10 mg / kg IV infusion over 20 min. Its pH is 12, extravasations cause severe tissue injury. Onset is 10-30 min and may cause hypotension, arrhythmias, ventricular standstill [22- 30] but cheap.

Fosphenytoin is a newer pro drug of phenytoin. Given as 20 mg PE/kg IV over 5-7 min, PE = phenytoin equivalent, pH 8.6, extravasations are well tolerated. Onset is 5-10 min, may cause hypotension, but less and it is expensive [31-40]. The main difference between phenytoin and fosphenytoin in children is the pH. Fosphenytoin will not cause the severe tissue damage seen with phenytoin in case of infiltration. If in doubt about serum level free phenytoin is to be measured. Phenytoin is largely protein bound. (> 90%, varies

with serum protein concentration).Free phenytoin = active phenytoin (anticonvulsant and toxic effects). Toxicity is more likely with hypo albuminemia (usually if < 2 g/dl). Therapeutic levels: Total phenytoin: 10 - 20 mcg/ml, Free phenytoin: 0.8 - 1.6 mcg/ml

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 infusion may be used [60-78].

**EEG**

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]. Among children with persistent altered mental status after a seizure an emergent EEG is helpful to identify subtle or NCSE [82].

**NEURO-IMAGING:** CT Brain may be necessary to evaluate safety of LP and to rule out hemorrhage or large mass lesions. MRI will almost always be performed later, even if CT is normal.

**LP** : LP should be done if SE presented in febrile children. And it should be done only after stabilizing the child not at arrival.

**OUTCOME**

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.

| Etiology | Risk of Epilepsy | Risk of Recurrence | Chronic AED Rx |
|---|---|---|---|
| Idiopathic | 0% | 3% | No! |
| Remote symptomatic | ++ | 50% | Yes! |
| Febrile | + | + | No? |
| Acute Symptomatic | 15-30% | + | Yes? |
| Progressive | ++ | 50% | Yes! |

Normal children and children with febrile status have a favorable prognosis. Improved outcome is a result of timely and approximate evaluation and treatment. Most favorable 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. Out come 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, results in recurrence. AED should be continued particularly if a structural lesion resulted in S.E.

**Kwong RL et al [83]:** Features predicting adverse outcome of SE in children. OBJECTIVE**:** To examine variables that might predict abnormal outcome of SE among children. DESIGN: Retrospective study. SETTING**:** Regional Hospital, Hong Kong. INCLUSION : < 15 Years admitted in PICU 1997 – 2002. MAIN OUTCOME**:** Neuro developmental out come. OBSERVATION: 2/25 died (8 %). No patient with febrile seizure or idiopathic SE developed neurological deterioration. 6/23(25%) symptomatic (acute & remote), refractory SE associated with poor outcome. Young age <12 months and duration >60 minutes associated with adverse outcome. Rectal diazepam only in 4 as pre hospital theraphy. CONCLUSION: Pediatric patients who had normal neuro developmental status before SE and who did not sustain an acute insult to the CNS or have progressive encephalopathy had favorable out come. Pre hospital treatment with BZD reduces adverse outcome.

**Garzon E [84]:** Analysis of clinical characteristics and risk factors for mortality in human status epilepticus. OBJECTIVE: To analyze clinical data including etiology, age, antecedents, classification and mortality in human status epilepticus, and to assess prognostic factors for mortality. A prospective study was performed, including detailed analysis of clinical and laboratorial data of SE in individuals of any age, except neonates. SETTING: Department of Neurology and Neurosurgery, Federal University of Sao Paulo. OBSERVATION: 111 SE were included with patient's age ranging from 3 months to 98 years. SE incidence peaked in the first years of life, and 59.4% of the individuals had pervious epilepsy while 40.6% had not. The main underlying causes were noncompliance to treatment in the first group and CNS infection, stroke and metabolic disturbances in the second group. Overall

mortality was 19.8% and deaths were correlated to etiology and patient's age. Refractory SE affected 11.7% of the cases. CONCLUSION: Epileptic patients are at greater risk to develop SE, however, individuals with no prior history of epilepsy and acute neurological problems can also present with SE. Etiology varies with patient's age, and mortality is high and related to age and underlying causes. Clinical and clinico-electrographic classifications are usually convergent, but in some cases the diagnosis of SE would not be established without the EEG.

**Towne AR et al [85]:** Determinates of mortality in status epilepticus. Using univariate and multivariate regression analysis, seizure duration, seizure type, age, etiologies, other clinical features and mortality were studied among 253 adults with SE admitted to the Medical College of Virginia. SETTING: Department of Neurology, Medical College of Virginia, Virginia. OBSERVATION: CVA and discontinuation of AED were the most prominent causes of SE each accounting for approximately 22 % of all patients in the series. The other principle etiologies were alcohol withdrawal, idiopathic, anoxia, metabolic disorders, hemorrhage, infection, tumor, drug overdose and trauma. When the patients were divided into two groups, the group with SE lasting <1hr had a lower mortality as compared with seizure duration > or = 1 h. Low mortality rates were noted in alcohol and AED discontinuation etiologies. Anoxia and increasing age were significantly correlated with higher mortality. The mortality rates of partial and generalized SE were not significantly different. Race and sex did not affect mortality significantly. CONCLUSION: These findings represent the first multivariate analysis of

predictive indicators of mortality in SE and demonstrate that specific factors influence mortality rate in SE.

**Veryty CM et al [86]:** Outcome of SE & lengthy FSE: Findings of National Cohort Study. OBJCTIVE: To study out come after a lengthy FSE & SE in children. DESIGN: Population based birth cohort study. SETTING: Child health and education study. (16004 neonatal survivors born in April 1970),USA. 14676 – Information available. OBSERVATION: Clinical information and tests of intellectual performance at 5 years and 10 years after birth.19 had lengthy FSE, 18 had SE. 2SE died, but not due to it. 4/19 FSE (21%) developed seizures. Intellectual performance: 23 normal, 10 abnormal (8 preceding developmental delay, neurologic abnormality).CONCLUSION: Outcome is better that reported from studies, seems determined more by the underlying cause than by seizures themselves.

**Sahin et al [87]:** Mortality in RSE was related to etiology age and EEG findings. Higher is younger children and with multi focal or generalized abnormalities on the initial EEG.

**Hui AC, et al [88]:** Factors of poor outcome, defined as death or morbidity as measured by deterioration in functional status using the Glasgow outcome score were analyzed in a multivariate logistic regression model. There most common causes were CVA, metabolic derangements and anticonvulsant withdrawal in adult population. 26% had worst functional ability, and mortality rate was 26%. 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).

**Mah JK, Mah MW [89]:** King Khalid national guard hospital, Jeddah, kingdom of SA. Pediatric SE: Perspective from Saudi Arabia. Objective: To assess risk factors and management of SE and non SE seizures. DESIGN: prevalence study of a convenience sample of pediatric seizure admitted from 1992 to 1997. RESULT: Mean age 2year 4month. 43% no prior seizures. 28% (59) of 212 seizures were SE. SE more than non SE in cases with h/o seizure, AED, acute etiology. CONCLUSION: Management of SE in this referral population can be improved by more rapid access to appropriate medical care.

**Dunn DW [90]:** SE in children: etiology, clinical features and outcome. Indiana university school of medicine.Indianapolis-46202.Aug 1984 to sep 1986 prospective case series data- 114 episodes of SE. RESULTS: Symptomatic 72% (chronic59%,acute 13%) . Idiopathic or Febrile - 28%. 63% -precipitating factors present. Most common factor – inadequate blood levels of ACD (32/60 with h/o prior fits). Febrile illnesses excluding CNS infections (38/114). 8 died, 3 with pre existing brain damage,2 with meningitis,2 with poorly defined encephalopathy. 18 developed new neurological deficit (5 in idiopathic or febrile SE group. 13 in symptomatic SE group). Outcome related to etiology, duration, and age is a minor factor.

**Allredge BK, Wall DB, Ferriero DM [91]:** Effect of pre hospital treatment on the outcome of SE in children. University of California, Sanfrancisco. USA. Review of cases. Clinical course of 45 episodes of GCSE evaluated. OBJECTIVE: To determine the effect of pre hospital Diazepam therapy (IV/PR), given by paramedics in many EMS systems throughout USA, on the clinical course of SE and subsequent patient management. OBSERVATIONS: 19 cases had pre hospital therapy.9 PR. Mean dose 0.6

mg/kg.10 IV. Mean dose: 0.2mg/kg. 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. CONCLUSION: Pre hospital administration of diazepam shorter the duration of SE and simplify the subsequent management of these patients.

**Simon J. Parsons, Katarina Tomas, Peter Cox [92]:** Out come of Pediatric Status Epilepticus Admitted to Intensive Care: The authors determine the relationship between seizure duration, etiology, and outcome in a modern intensive care setting and assess the usefulness of computed tomography (CT) and the empiric use of antimicrobial therapy. The design was a retrospective chart review. The setting was a tertiary pediatric critical care unit. Patients included 161 consecutive admissions to the critical care unit at the Hospital for Sick Children, Toronto, with status epilepticus over a 3-year period. There were no interventions. The overall mortality was 5.6%. A further 11% experienced an adverse neurological outcome as determined on hospital discharge. 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 ($P < 0.05$). The CT scan was abnormal in 41% of cases. New findings that directly affected immediate management decisions were found in 20% of CT scans. Both the duration and etiology of status epilepticus affect the outcome. CT scanning should be done without delay, once the patient is stable. Antiviral therapy should be started empirically now that encephalitis is far more common than bacterial meningitis in this group of patients. Studies are lacking that

compare the efficacy of drugs available to treat status epilepticus. These studies need to be done, as the findings could affect the duration of status.

**Murthy JM, Yangala R [93]**. Nizam's institute of medical sciences, Hyderabad. Acute symptomatic seizures incidence and etiological spectrum. A hospital based study done in Nizam's Institute of Medical Sciences considered that etiological spectrum of acute symptomatic seizures in this part of the world is different from that described from developed countries and CNS infection account for a significant number of cases.

**Singhi S, Singhi P, Dass R [94].** Advanced pediatric center PGIMER. Chandigarh. SE: emergency management. SE is a medical emergency and need prompt and aggressive management. In children mortality from SE ranges from 3-10% and morbidity is twice. Morbidity and mortality are highest with SE that associated with CNS infections which is the most important cause of SE in our country. The outcome depends on the underlying etiology, age, rapidity of SE and adequacy of care. Adherence to a time framed protocol in the ED helps in improving the final outcome.

**Santhosh Paulin [95].** ICH and HC,Chennai. Clinical profile of convulsive RSE in children. OBJECTIVE: To assess the incidence, common causes, complications, outcome of RSE in children and efficacy of IV midazolam infusion in controlling RSE.A descriptive study conducted in PICU of ICH from April2002 to Mar2003.RESULTS: 26 cases of RSE among 418 SE cases. male=female. mean age of 3 years with range from 1 month to 12 years.65% needed midazolam of <6 mcg/kg/min. Mean duration for control of seizure 3hr56min.recurrence on tapering noted only in two cases. mean dose

12.5 mcg/kg/min.8/26 had shock recurrence after midazolam infusion.53% on midazolam needed ionotropes, mean duration of midazolam was 2days and 7 hours. Death 35% and 19% had neurological sequele, 46% recovered. Acute CNS infection commonest cause. CONCLUSION: Midazolam infusion is safe and effective in controlling RSE and can be used in the management of RSE. High mortality in that study was due to CNS co morbid conditions.

**Eelco F.M, Wijdicks [96]**: Medical online review and data base on SE, Neurological ICU. Saint Mary's hospital. SE categorized into 5 classes. Convulsive SE (tonic clonic SE),non convulsive SE, myoclonic SE, focal SE, psychogenic SE. Therapy must be aggressive because neuronal excitability can be reversed only early in the course and only quick intervention may decrease the risk of seizure generated neuronal damage. Seizures commonly ceases within 5 minutes.

**Kalra Veena et al [97]:** OBJECTIVE: To study the clinical profile immediate outcome and possible risk factors of SE in Children admitted in PICU. DESIGN: Retrospective, study of case records. SETTING: AIIMS; PERIOD: 451 Neuro emergencies between Jan 1993 to April 2000.in children in a tertiary care center. –30 had SE. INCLUSION: 30 SE Cases. RESULTS: Age: 1- 120 months. Mean 56.6 ± 46.5 months. 17 patients were < 60 months.16 patients (53.3%) had SE I episode with out prior H/o fits.9 (30%) died during hospital course. Seizure duration >45 min (p.0.001) and presence of septic shock (p-0.001) were associated with significantly more mortality. CONCLUSION: There is a need to abort seizure activities at the earliest to improve immediate outcome.

**Maytal J et al [98]:** In an ongoing study of SE, 193 children with SE of varying causes have been followed up for a mean period of 13.2 months. Of those 97 were recruited prospectively. The patient's ages range from 1 month to 18 years. Mean - 5 years. The cause of SE was classified as idiopathic in 46 cases, remote symptomatic in 45, febrile in 46, acute symptomatic in 45, and progressive neurologic in 11. 7 died and new neurologic deficits were found in 17 (9.1%) off the 186 survivors. All of the deaths and 15/17 sequele occurred in acute and progressive neurologic insults group. Only 2/137 other causes sustained any new deficits ($p<0.001$). Duration of SE affects outcome only with in the acute symptomatic group. Sequele occurred mostly in infants (29%) and 11% in 1-3 years group, 6% in > 3 years. 61 had prior unprovoked seizures (32%).

**Sahin M et al [99]:** out come of severe RSE in children. Epilepsia 2001 Nov: 42(11)1461-7. OBJECTIVE: out come of RSE in children. Retrospective review of case records between 1992-2000.children's hospital, Boston, Massachusettes,USA. Factors evaluated age, etiology and initial EEG findings including mortality or return to baseline. RESULTS: 22 patients 4.5 months to 18 years treated for < or = to 146 days .Mortality 7/22(31.8%) related to age, etiology and initial EEG findings. None return to base line. No death in remote symptomatic group.3/4 younger than 3 years died.4/18 older than 3 years died. Focal abnormalities in EEG are associated with less mortality than multifocal or generalized abnormalities. CONCLUSION: High mortality and morbidity for childhood RSE is demonstrated.

**Horn drop:** Study observed that symptomatic SE and refractory SE and associated with poor outcome than idiopathic or febrile SE and young age < 12 months duration of seizure > 60 minutes are associated with adverse outcome.

**Etiology Of Status (Children)**[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.

**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?

**WHY 30 MINUTES? :** 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 influenzing poor out come 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.

# AIM OF THE SYUDY

Aim of this study is to determine clinical profile, and immediate outcome of SE in children, managed in our hospital.

Secondary aim is to identify risk factors influenzing adverse outcome.

| | | |
|---|---|---|
| STUDY DESIGN | : | Descriptive study. |
| STUDY PEROID: | : | Jan 2005 -to –Dec 2005. |
| STUDY POPULATION | : | Children from 1 month to 12 years of age, who have been managed as SE were studied. |
| STUDY PLACE | : | Institute of Child Health and Hospital for Children, Chennai.8 |
| INCLUSION CRITERIA | : | All children presented with SE (including non convulsive SE and secondary generalized), managed with anti convulsant 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.<br>Simple partial SE: and other NCSE like myo clonic SE with normal vital signs and without loss of consciousness).<br>Seizures occurred during hospital stay, not at arrival |
| SAMPLE SIZE | : | Sample size was calculated based on a pilot study of 49 patients. Here the mortality was 20%. From review of MRD records in ICH, 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.

**DEFINITIONS**

**SE**: Defined as > or = 5 minutes of a (a) Continuous seizure or (b) Two or more discrete seizures between which there is incomplete recovery of consciousness.

**CSE**: Refers to GTCS either primary or secondary to focal onset, in which whole or part of the body muscles having visible convulsions (clonic movements)

**NCSE**: Refers to persistent seizure activity (proved by intra ictal EEG), but no visible convulsions. Here they may have subtle signs of seizure activity such as unresponsiveness/ALOC or acute confusional state, apnea, defective DEM, conjugate deviation of eyes, nystagmus, twitching of eye lids, lipsmaking movements, dilated pupils, tachycardia, excessive secretions, hypertension.

**NEURO EMD** (**ELECTRICAL SEIZURES**): No visible sign of seizure activity, but EEG shows ongoing seizure activity. Example: SE in patients paralyzed with neuro muscular blockade.

**INITIAL SEIZURE CONTROL**: Seizure control by drugs at the time of first contact with the ER.

**CLINICAL CONTROL**: No evidence of seizures activity such as convulsions, apnea, unresponsiveness, defective DEM, conjugate deviation of

eyes, nystagmus, twitching of eye lids, lipsmaking movements, dilated pupils, tachycardia, excessive secretions, hypertension and

a stable airway with intact protective reflexes, stable respirations, DEM+, with or without regaining of consciousness.

**GOOD RESPONSE**: Was defined as seizure activity controlled with AED within 60 minutes of contact with hospital and initiation of therapy. That is controlled with first line drugs (BZD, phenytoin, phenobarbitone).

**REFRACTORY SE**: Defined as if the duration of control of seizure activity was more than 1 hour or not controlled with first line drugs (Lorazepam/Diazepam, Phenytoin, Phenobarbitone)

**MORTALITY**: Defined as death occurring in hospital during the course of treatment of SE irrespective of whether it was controlled or not

**AMA**: Means, discharged against medical advice during the treatment of SE without improvement and regaining baseline consciousness.

**DURATION**: Means, time starting from onset of that episode prior to arrival to hospital or starting from the onset of I episode of seizure, in case of more than one episode but with impaired consciousness in between the series of seizures.

**HISTORY OF EPILEPSY**: Defined as two or more unprovoked seizures in the past whether on treatment or not.

**FEBRILE CSE**: Status epilepticus associated with fever in a neurologically normal child between the ages of 6 months and 5 years is considered to have a good prognosis.

**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 out come 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.

FOLLOWING RISK FACTORS ANALYZED FOR PREDICTING POOR OUTCOME:

**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**

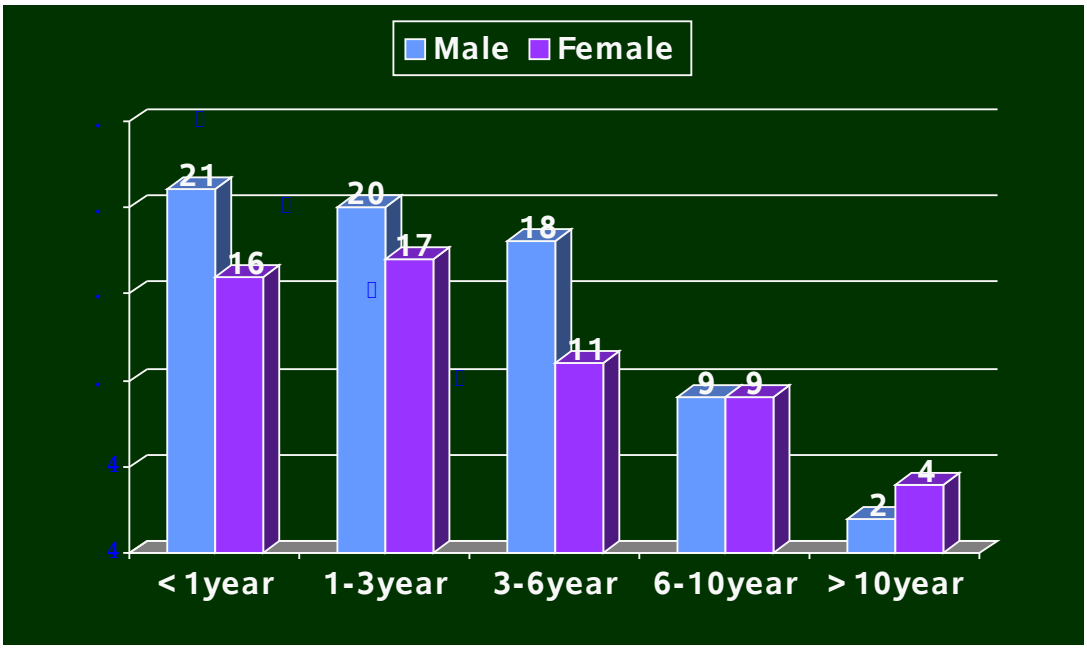
Hypoglycemia at arrival

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.

**AGE AND SEX DISTRIBUTION**:

Out of 127, male children were 70 and female children were 57. M: F ratio was 1.22:1. In this 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. 30% deaths were observed in children of <1 year of age. Females were more than male children in >10 years of age (4 vs. 2) and in other age groups M>F. Mean age was 3 years and 5 months. Range was from 32 days to 12 years.

| | **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:**

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 27$^{th}$ 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.

**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 | |

**ONSET OF SEIZURES:**

Fits started in their home for 116/127 cases (91.3%). Fits started in ICH-OPD for 9 children (7%) and for 2 children had fits while traveling 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 with out 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 constrainments, 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 from ICH, coming from varies parts of Tamil Nadu and Andra Pradesh. 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.

| Distance | frequency | % | Cum.% |
|---|---|---|---|
| <1km | 15 | 11.8% | 11.8% |
| 1-10 | 10 | 7.9% | 19.7% |
| 10-19 | 41 | 32.3% | 52% |
| 20-49 | 27 | 21.3% | 73.2% |
| 50-99 | 9 | 7.1% | 80.3% |
| >99 | 25 | 19.7% | 100% |
| TOTAL | 127 | 100% | |

**DURATION**:

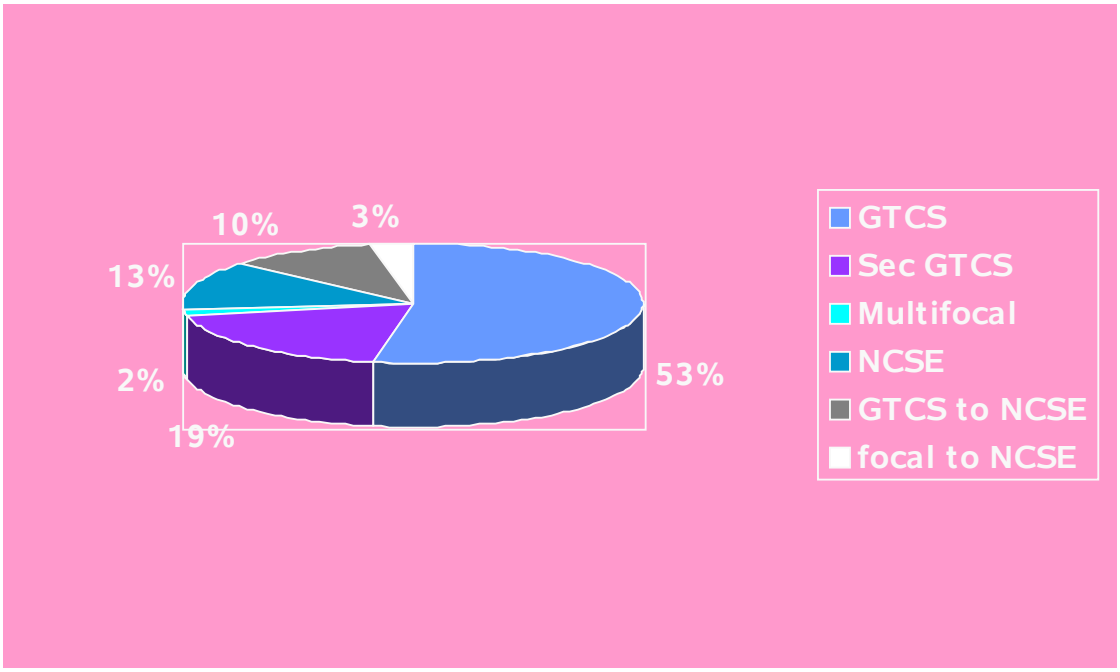
Mean duration was 16 hours and 44 minutes. Maximum duration of 10 days observed. 26 cases (20.5%) attended ER within 30 minutes of onset of fits. 46 cases (31.5%) had seizure of < 60 minutes duration before arrival. 65 children had seizure duration <2 hours before arrival. 40 children had seizure of > 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 ICH. 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 are new sequele observed in FSE (19 cases), though 9 FSE had seizure duration of more than 30 minutes.

**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).

| Type of SE | Frequency | % | Cumm% |
|---|---|---|---|
| **GTCS (Primary)** | **67** | **52.8%** | **52.8%** |
| **NCSE** | **17** | **13.4%** | **66.1%** |
| **Focal to Secondary Generalization** | **24** | **18.9%** | **85%** |
| **Multi focal** | **2** | **1.6%** | **86.6%** |
| **GTCS to NCSE** | **13** | **10.2%** | **96.9%** |
| **Focal to NCSE** | **4** | **3.1%** | **100%** |
| **Total** | **127** | **100%** | |



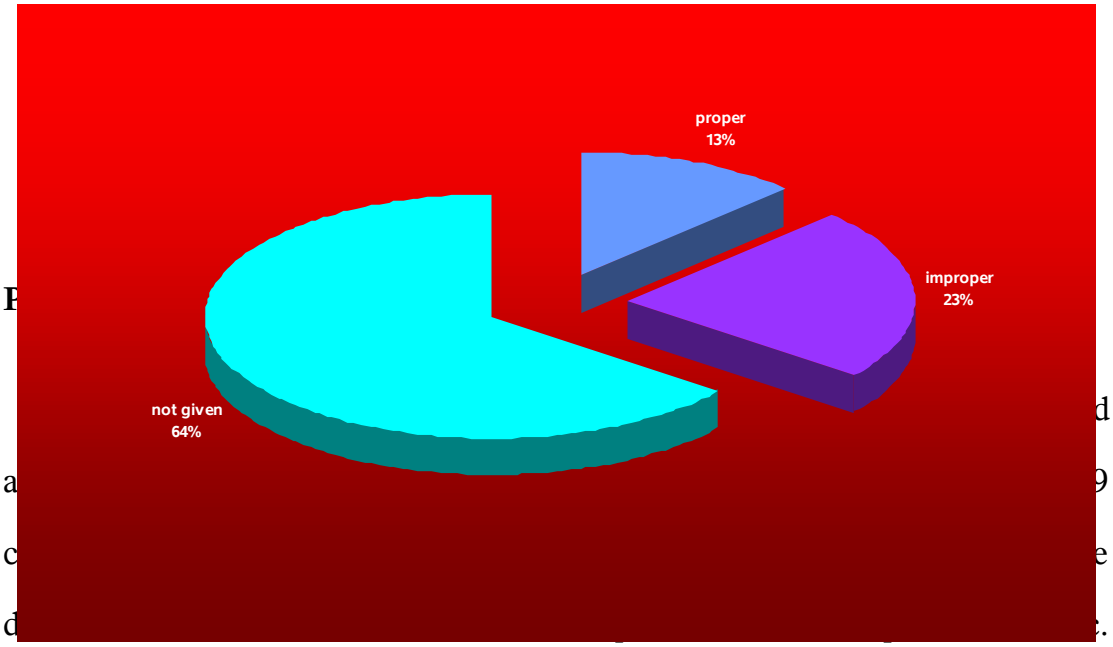

**NUMBER OF FITS:**

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.




**F**

a

c

d

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

**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 ICH 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.

**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 with in 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.

## 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

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**

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 ventilatory 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 I month , one had hydrocephalus and other had hemi paresis which were not present already.

- The incidence of SE was more in male than female in this study (1.22:1) but it is not statistically significant.

- Age range from 32 days to 12 years; mean 3 years and 5 months. 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.

- 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

- Fits started in their home for 91% cases. Fits started in ICH-OPD for 9 children (7%) and for 2 children had fits while traveling towards hospital. Out of 7 cases in which fits started at OPD, 6 have survived and one child died due to prolonged respiratory failure and refractory septic shock

- Nearly 60% children were coming directly with out any referral or treatment before arrival to ICH. 24% children were referred by near by practicing private practioners.11 cases referred by private hospitals for varies reasons (financial constrainments, for further management, AMA discharge etc). Out of 11, 9 children have survived. Only 8% of the children were referred from government set up (GH, PHC).

- 78% of children were taken by Auto and Train and only 7 children (5.6%) were transported by Ambulance with O2.

- Nearly 50 % of the children had seizure duration of < 2 hours prior to arrival to ICH. 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 is 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).Out of 20 deaths 13 cases (65%) were from >100 km distance. 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 were the cause for death in these children.

- ❖ No deaths observed in FSE (19 cases), though 9 FSE had seizure duration of more than 30 minutes.

- ❖ GTCS was the commonest seizure type (74%). NCSE accounts for 26% of the cases.

- ❖ 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. This includes IV/PR Diazepam, IV Lorazepam, IM /IV /PR Midazolam, IV Phenytoin infusion, IV Phenobarbitone infusion. Here 14 children received IV diazepam with (9 cases) or without (5 cases) phenytoin infusion 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. Two cases received rectal ACDs (one was clobazam and other was phenobarbitone). None of the children received rectal diazepam.

- ❖ 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 precipitated seizures in known seizure disorder of 27 children.

- Seizures were controlled with first line drugs in 86.8% and refractory SE in 18 cases(14.2%).

- RSE corrected with midazolam: 16 cases, 2 uncorrected and needed thiopentone. Midazolam dose: 1-25 mcg, mean 6.22 mcg, <6 mcg in 10 cases, mean duration 61 hours. Max 500 h but not controlled.

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

- History of seizures was present in 55% cases. 45% were presented as SE in their first episode of fits itself. In children who had h/o fits, 39 had idiopathic epilepsy and 16 had structural neurological disorder that is CP, MR, PMS, PES, CVA, neuronal migration disorder, neuro cutaneous syndromes etc. 22 had previous SE. Totally 33/127 had CNS co morbidity. 36/127 had delayed miles stones. H/o poor drug compliance was present in 14 cases and that could be the cause of SE in them and in other cases SE is mostly precipitated by fever.

- 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, O2 through non rebreathing mask was given. So, all children received supplementary O2 at arrival. Mean duration of BVM was 29.5 minutes and maximum was 75 minutes. 69 cases (54.3%) had SaO2 <92% at arrival.

- 44 Children needed IPPV. Duration: from 2 hrs to- 560 hrs (23 days). Ventilatory support was given either by manual or by

mechanical ventilator. Mean duration was 64 hrs. 25 had poor outcome and 19 had good outcome in this group. So, all children under poor out come were on IPPV.

- 92 cases (72.4%) had shock at arrival. 2 were hypotensive, both died, corrected in 66 cases. In 21% cases persistent shock was present even with ionotropes at ER, Subsequent shock in nearly 37%.

- Pupil was normal (nearly 64% cases) or dilated and reacting to light (28% cases) in most of the children with SE. 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.**

- 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 89% of cases fits controlled with I line drugs and 18/127 cases needed midazolam infusion. These 18 children were considered to have RSE and out of them 10 survived (55.6%),

- RSE: All children were started on midazolam infusion. Fits controlled with midazolam in 16 cases. Mean duration to control fits in those children was 4 hours 35 minutes. In 8 children fits controlled within 8 hours of starting midazolam infusion. 2 children needed thiopentone infusion to correct refractory SE. But for both of

them fits not controlled with thiopentone also and subsequently died. Maximum duration of midazolam infusion was 500 hours but that child did not respond. Mean duration was 61 hour. No cases observed recurrence of seizures on tapering midazolam. Those who responded to midazolam fits controlled in < 6 mcg/kg/min in 10 cases and others required more for seizure control. In 2 cases those who did not respond to either midazolam or thiopentone, 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. Shock was noticed in 11 cases. 8 cases had shock after starting midazolam infusion and 6 needed inotropes and 2 cases corrected with fluid boluses.

- Seizure recurrence was observed in 28% cases.16.5% had single recurrence and remaining had multiple recurrences. 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 in 10 children those who died.

- Respiratory failure needs prolonged ventilation (35%) and persistent/ recurrent shock (38%) were the commonest complications noted in this study. Pneumonia, DIVC, raised ICP, acute renal failure, phenytoin toxicity even with the therapeutic doses were some of the complications encountered.

- 2 children had pneumo thorax with normal lung before and it could be due to manual IPPV. No cases of hyperthermia or rhabdomyolysis or diabetes insipedus were encountered.

- Hypoglycemia at arrival was noted in 13 children and hyperglycemia in 11 cases. Hypoglycemia may be the cause of SE or consequence. None of the children responded to 25% dextrose alone so the cause of hypoglycemia in this study was due to the consequence of prolonged SE. Low HCO3 was seen in 19 cases and all were found to have metabolic acidosis by ABG. 3 hypo natremias, 14 cases of hypokalemias, 1 case of hyper kalemia, 11 cases of hypocalcemia No case of hyper calcemia or hyper natremia was seen..

- 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 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 it was abnormal in 25 cases (89.2%)

- 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: Most common causes of SE were remote symptomatic ( structural lesions) – 34%, idiopathic epilepsy- 17%, Acute CNS infections- 15%, Febrile SE-15%, septic shock-7%. Others were toxin, drug over dose, acute encephalopathy,

progressive degenerative disorders, metabolic seizures. Deaths mostly occurred in acute CNS infection 7/20, septic shock-5/20, structural brain lesions-5/20. None of the death occurred in febrile SE and idiopathic epilepsy.

**FINAL OUTCOME:**

- 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. 2 children had new neurological sequele at the end of I month , one had hydrocephalus and other had hemi paresis which were not present already both were occurred in acute CNS infection. So totally 19.7% (25/127) of the cases were included in poor outcome group.

**RISK FACTORS DETERMINING POOR OUTCOME:**

Out of varies risk factors analyzed for predicting poor out come, 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 out come 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.

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 ICH, duration of seizures, need for IPPV, acute CNS infection as the etiology are statistically significant risk factors. They are independent risk factors influenzing poor outcome.

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 the 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 with out 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.

- Mortality in SE in this study is 15.7% . Higher mortality in this study is mainly due to the underlying cause than SE itself. 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. But there is no clear cut definition of SE is formulated in this age group till now.

- There is no significant sex difference.

- Commonest seizure type is GTCS. But NCSE also 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 hypoglycemia and 11% had hyper glycemia 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 etiology. 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.

1. Common cause of SE in our part of the country is acute CNS infection and this results in higher mortality, morbidity and later neurological sequele. Acute CNS infection is one of the independent risk factor for poor outcome in SE. Vaccinating with Hib, Pneumococcal vaccines and prompt use of antimicrobial therapy in suspected cases to be undertaken to prevent acute CNS infection.

2. Duration and distance travelled to seek medical advice are also important risk factors influenzing poor outcome. So, early institution of proper time framed therapy even by the nearest hospital will improve the outcome. At least, proper pre hospital therapy like the use of IM/PR/IV Midazolam or IV/PR diazepam and taking care of airway and breathing with supplementary O2 while transporting the child from the peripheries could result in better outcome in SE children.

3. Many of the complications and consequences can be managed successfully with anticipation and early intervention like shock, respiratory failure, aspiration pneumonias, hypo/hyper glycemias, dyselectrolytemias.

4. A bed side EEG will be useful in managing NCSE as the electrical SE or neuro EMD are also associated with same neuronal damage and mortality as CSE. Even if EEG is not available a high index of clinical suspicion of NCSE should be there to identify ongoing seizures in partially treated comatose children. The clinical signs such as persistent apnea, unresponsiveness, defective DEM, nystagmus, conjugate

deviation, excessive secretions and disproportionate tachycardia are some of the very important clues in identifying NCSE.

5. Management of vital signs and underlying cause of SE along with specific ACD therapy are the priorities in the management of SE.

6. Midazolam is safe and effective for the treatment of RSE in children in our country.

## **ANNEXURE**: **PROFORMA**

Serial No:

Hospital No:

Ward admitted:

Name:

Age; years: *.months:*

Sex: *M/F*

Addresses

Phone no:

DOA:

DOD:

No of days in hospital:

Time of arrival to ER:

Fits started at;

1. Home

2. OPD

3. While traveling

4. Pvt hospital

5. GH

6. Others

Referred from:

1.No (self)

2. PHC

3. GH

4. PVT clinic

5. Pvt. Hospital

6. OPD

Distance from onset to ICH:

I. <1

II. 1-9

III. 10-49

IV. 50-99

V. >100

Mode of transport:

1. hand
2. auto
3. car
4. two wheeler
5. ambulance
6. others

Duration of seizure prior to reaching ICH; in minutes:

Type of seizure:

1, GTCS:

2. Non convulsive:

3. Secondary generalization:

4. Others:

Number of attacks:

Each lasted for: in minutes: ---/---/---

Risk factors: /sleep deprivation/stress/trauma/toxin/drugs/unprovoked/medical illness (specify----------)

Level of sensorium between attacks: ALOC/normal

H/o fever: Yes/No; Duration:

H/o ALOC before fits Yes/No

H/o head trauma Yes/No

H/o Toxins/Drugs ingestion Yes/No

Pre hospital therapy: Yes/No

What drug: Route:

1. Diazepam
2. Lorazepam
3. Others.
4. Not known

PAST HISTORY:

Past H/o seizure: Present/absent

Febrile/ Afebrile

Date of last episode;

H/o SE: Yes/No

If yes, date of occurrence:

Duration:

Treatment given:

On AED: Regularly or not

Which drug

Dose and duration

Compliance: good/poor

Last dose:

Developmental history: Normal/delayed

Neurological status before SE: Normal/abnormal.

If abnormal specify:

Co morbid conditions:

1.

2.

3.

4.

CLINICAL EXAMINATION:

Appearance: A/V/P/U

Breathing: required BVM Yes /No, how long: (min):

Required intubation Yes/No: how long (min):

Sa02 at arrival:

Circulation: Shock: Yes/No

If yes: compensated/ decompensated

BP at arrival: mm/hg

Requiring fluids/ requiring ionotropes /Uncorrected

Pupils:

Glucose:

Calcium:

Na+:

K+:

HCO3-:

MANAGEMENT OF SEIZURES:

25% Dextrose/ Lorazepam/ BZD+ Phenytoin/Required PB

Refractory seizure:

IMCU:

Ward:

Midazolam / Thiopentone/ Others: yes/no

Maximum rate:

How long

Subsequently developed shock: yes/no:

Time taken for full recovery of consciousness: hours

Complications:

1. Acidosis
2. Pneumonia
3. Respiratory failure
4. ICP
5. Shock
6. Hyper thermia
7. Rhabdo myo lysis
8. Neuro logical deficit;

Neurological examination:

| | First | at discharge | 1 month |
|---|---|---|---|
| GCS:<br>HF:<br>Cranial nerve<br>Pupil<br>Fundus:<br>Motor:<br>Involuntary Movements<br>sensory:<br>others:<br>developmental: | | | |

INVESTIGATIONS:

Hb:

TC:

DC:

PCV:

Platelets:

PSS:

Urea:

Creatinine:

Urine screening:

NEC:

CXR:

LFT:

CSF analysis:

USG Cranium:

CT Brain:

EEG:

Final diagnosis:

Outcome:

1. Death:

2. New neurological sequele:

MR:

FND:

Extra pyramidal:

3. AMA

4. No New Neurological Sequele

5. Recovered.

SE: STATUS EPILEPTICUS

CSE: CONVULSIVE STATUS EPILEPTICUS

RSE: REFRACTORY STATUS EPILEPTICUS

NCSE: NON CONVULSIVE STATUS EPILEPTICUS

ASE: ABFENT STATUS EPILEPTICUS

PCSE: PARTIAL COMPLEX STATUS EPILEPTICUS

IPPV: INTERMITTENT POSITIVE PRESSURE VENTILATION.

CNS: CENTRAL NERVOUS SYSTEM

AED: ANTI EPILEPTIC DRUGS

ACD: ANTI CONVULSANT DRUGS

GABA: GAMMA AMINO BUTERIC ACID

EEG: ELECTRO ENCEPHALOGRAM

NMDA: N - METHYL D - ASPARTATE

GTCS: GENERALIZED TONIC CLONIC SEIZURES

CVA: CEREBRO VASCULAR ACCIDENTS

GCSE: GENERALIZED CONVULSIVE SE

BZD: BENZODIAZEPENES

LP: LUMBAR PUNCTURE

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