IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 6 Ser. 4 (June. 2019), PP 73-78
www.iosrjournals.org

Outcome of Neonatal Seizure: Experience from a Tertiary Care Hospital

Dr Sibnath Gayen[1], Dr. Ram Prasad Saha[2], Dr. ParthaSarathi Das[3]
[1]*MBBS, MD Paediatrics; Associate Professor, Paediatrics, RGKMCH*
[2]*MBBS, MD Paediatrics,(Ex Resident), RGKMCH*
[3]*MBBS, MD Paediatrics; Clinical Tutor in Neonatology, RGKMCH*
Corresponding Author: Dr.Ram Prasad Saha

Abstract:
Background:
Seizures are more common in the neonatal period than during any other time throughout life. Seizures in the neonatal period are also the most common neurological emergency and are associated with high mortality and morbidity. The severity and timing of the pathologic process continue to be the major determinants for outcome.
Objectives:*To find out short term outcome of the causes of seizures in neonates admitted in a Tertiary care hospital.*
Materials and Methods:*The study was cross sectional, observational & analytical in nature, performed over a period of 1 year. Data were analyzed in microsoft excel using standard statistical techniques.*
Results: *The long term outcome were poor in babies having 1st day seizure (64%) & having HIE as a cause of seizure (38%).*

Date of Submission: 23-05-2019 Date of acceptance: 08-06-2019

I. Review of Literature

A seizure is a transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain. 40 Seizures occur more frequently in the neonatal period than at any other time of life. The incidence of seizures in infants born at term is 0.5-3 per 1000 live births; the incidence is even higher in preterm infants, ranging from 1-13% of very low birthweight infants[1]

The immature brain has many differences from the mature brain that render it more excitable and more likely to develop seizures (i) Clinical seizure patterns in the neonate reflect the ―reduced connectivity in the neonatal brain, with prominence of focal ictal characteristics and rarity of generalized patterns of clinical seizures.41

(ii) The balance of excitatory and inhibitory processes in the immature brain are weighted toward excitation.

Based predominantly on animal studies, these are delay in Na+, K+ ATPase maturation and increased NMDA and α-amino-3- hydroxyl-5-methylisoxazole-4-propionate (AMPA) receptor density, particularly those that are permeable to calcium (GLUR2 AMPA receptors). This contributes to increased excitability and to the long-term consequences associated with seizures, particularly from perinatal hypoxia. In fact, GABA in the immature brain has an excitatory function as the chloride gradient is reversed relative to the mature brain, with higher concentrations of chloride being present intracellularly than extracellularly. Opening of this chloride channels in the immature brain results in depolarizing the cell and not in hyperpolarizing it. Although it is susceptible to develop seizures, the immature brain appears to be more resistant to the deleterious effects of seizures than the mature brain, as a result of:-

a. Increases in binding proteins that buffer injury-related increases in calcium,
b. Increased extracellular space,
c. Decreased levels of the second messenger inositol triphosphate, and,
d. The immature brain‘s ability to tolerate hypoxic conditions by resorting to anaerobic energy metabolism.[2]

Several classifications have been proposed, of which the classifications by Volpe43 (according to clinical features only) and by Mizrahi and Kellaway3,4 (according to pathophysiology: epileptic or non-epileptic origin) are more widely used .

Volpe classification of neonatal seizures[5]		
Type	**Characterisation**	**Ictal EEG abnormalities**
Subtle	Ocular, oral-buccal-lingual, autonomic, apnoea, limb posturing and movements	Variable
Clonic	Repetitive jerking, distinct from jittering. Focal or multifocal	Common
Myoclonic	Rapid isolated jerks. Focal, multifocal or generalised	Common if generalised, uncommon if focal
Tonic	Stiffening. Decerebrate posturing. Focal or generalised	Common if focal, uncommon if generalized

The Volpe classification has the disadvantage of not including silent electrographic seizures.

Classification of Mizrahi and Kellaway [3,4]		
Type	**Characterisation**	**Epileptic origin**
Focal clonic	Rhythmic muscle contractions	Y
Focal tonic	Sustained posturing of limb/trunk	Y
Myoclonic	Random single contractions	Y/N
Spasms	Flexor or extensor, ± in clusters	Y
Electrographic	By definition no clinical correlate	Y
Generalized tonic	Sustained symmetric posturing	N
Motor automatism	Ocular, oral-buccal-lingual or progression movements of limbs	N

The Mizrahi classification has the advantage that it takes the origin of events into account and includes clinically silent electrographic seizures.

Causes of Neonatal Seizures according to common age of presentation [2]
AGES 1-4 DAYS 1. Hypoxic–ischemic encephalopathy 2. Drug withdrawal, maternal drug use of narcotic or barbiturates 3. Drug toxicity: lidocaine, penicillin 4 .Intraventricular hemorrhage 5. Acute metabolic disorders Hypocalcemia, Hypomagnesemia,Hyponatremia or Hypernatremia, SIADH Sepsis Hypoglycemia- Perinatal insults, prematurity, SGA, Maternal diabetes, Hyperinsulinemic hypoglycemia 6. Inborn errors of metabolism Galactosemia, Hyperglycinemia, Urea cycle disorders 7.Pyridoxine deficiency and pyridoxal-5-phosphate deficiency (must be considered at any age)
AGES 4-14 DAYS 1. Infection 2. Meningitis (bacterial) Encephalitis (enteroviral, herpes simplex) 3. Metabolic disorders Hypocalcemia- Diet, milk formula Hypoglycemia, persistent, Anterior pituitary hypoplasia, pancreatic islet cell tumor, Beckwith

syndrome Inherited disorders of metabolism Galactosemia, Fructosemia, Leucine sensitivity, Hyperinsulinemichypoglycemia,hyperinsulinism, hyperammonemia syndrome 4. Drug withdrawal, maternal drug use of narcotics or barbiturates 5. Benign neonatal convulsions, familial and nonfamilial 6. Kernicterus, hyperbilirubinemia 7. Developmental delay, epilepsy, neonatal diabetes syndrome
AGES 2-8 WK 1. Infection Herpes simplex or enteroviralencephalitis,Bacterial meningitis 2. Head injury Subdural hematoma,Child abuse 3. Inherited disorders of metabolism Aminoacidurias, Urea cycle defects, Organic acidurias, Neonatal adrenoleukodystrophy 4. Malformations of cortical development Lissencephaly, Focal cortical dysplasia 5. Tuberous sclerosis 6. Sturge-Weber syndrome

Prognosis:

With advancements in obstetric and intensive neonatal care, prognosis of neonatal seizures has improved. Mortality has decreased from 40% to 20% [2] with few studies showing mortality rate of even <10% in term infants.[6] Morbidity rates have changed less, partly due to increased numbers of survivors among ill premature newborns who have a greater risk of neurologic sequelae. Long-term sequelae like cerebral palsy and intellectual disabilities still occur at a high rate of up to 30% to 35%, with seizures occurring in up to 20% in later life. Useful indicators for poor outcome

a. The underlying etiology of the seizures is the main determinant of outcome. E.g. patients with seizures secondary to HIE have a 50% chance of developing normally, even fewer with a brain malformation, whereas those with seizures caused by primary subarachnoid hemorrhage (90%) or hypocalcemia have a much better prognosis

b. Abnormal background EEG, prolonged electrographic seizures (>10 min/hr), multifocal periodic electrographic discharges, and spread of the electrographic seizures to the contralateral hemisphere correlate with poorer outcome.

c. Gestationalage is also an important factor with increasing mortality and morbidity with increasing immaturity.

Useful clinical indicators for a good outcome include

a. a normal neonatal neurologic exam,

b. normal or mildly abnormal neonatal EEG background activity, and ,

c. normal neuroimaging or abnormalities limited to extraparenchymal injury

II. Material And Methods

The study was cross sectional, observational & analytical in nature, performed over a period of 1 year (May 2016 to April 2017). Data were collected in a predesigned proforma. We organized & analyzed data in Microsoft Excel 2010 using standard statistical techniques.

AIMS & OBJECTIVES:

To find out short term outcome of the causes of seizures in neonates admitted in a Tertiary care hospital.

III. Results And Analysis

Relation Between Day Of Onset Of Seizure And Outcome

To show the relationship between day of onset of seizures and outcome of the babies we have formulated the following table

Table No. 1

		Outcome		
		No neurodeficit (67)	Neurodeficit (23)	Death (10)
Day of Onset of seizure	Day 1	28 (41.8%)	16 (69.6%)	3 (30%)
	Day 2	9 (13.4%)	4 (17.4%)	3 (30%)
	Day 3	12 (17.9%)	-	1 (10%)
	Day 4	9 (13.4%)	2 (8.7%)	2 (20%)
	Day 5	6 (9.0%)	-	-
	Day 6	1 (1.5%)	-	-
	Day 7	-	1 (4.3%)	-
	Day 8 onward	2 (3.0%)	-	1 (10%)

From the above chart we can see that babies presenting with seizures within 24 hrs of life had favourable outcome (NND) of 59.6%, in contrast babies presenting with seizures after 24 hrs of life had favourable outcome (NND) of 73.6%, so babies presenting with seizures after 24 hrs has better outcome than the other group. On the other hand babies with seizures within 24 hrs of life had more chances of neurodeficit (69.6%) in contrast to babies presenting with seizures after 24 hrs who had chances of neurodeficit in only 30.4% cases, so babies presenting with seizures within 24 hrs has poor outcome than the other group. Although percentage of death was more in babies with seizures after 24 hrs of life.

Antenatal Risk Factors

The following abbreviations have been used in the charts for categorizing different antenatal risk factors PIH-preeclampsia, GDM- gestational diabetes mellitus, OLIGOoligohydramnios, IUGR-intrauterine growth retardation, MG- multiple gestation, PD- post dated, FPI- feto-placental insufficiency, BL.IN- blood group incompatibility, IUI- intra uterine infection, NIL- no risk factors present.

Table No. 2:

		Anternatal Risk Factors									
		PIH	GDM	OLIGO	IUGR	MG	PD	FPI	BL.IN	IUI	NIL
ETIOLOGY OF SEIZURES	HIE(55)	12	2	-	-	2	4	-	-	-	36
	EONS(11)	3	1	2	1	-	-	1	-	-	7
	LONS(18)	8	2	-	-	-	-	-	-	-	10
	K(4)	-	-	-	-	-	-	-	2	-	2
	ICH (1)	-	-	-	-	-	-	-	-	-	1
	MAL(2)	-	-	-	-	-	-	-	-	1	1
	MD(4)	-	1	-	-	-	-	-	-	-	3
	MH(3)	-	-	1	2	-	-	-	-	-	1
	MI(1)	-	-	-	-	-	-	-	-	-	1
	MP(1)	-	-	-	-	-	-	-	-	-	1

We can see from the above chart that antenatal risk factors is present in about 34.5% of HIE babies , 36.4% of early onset neonatal sepsis babies, 38.9% of babies with late onset neonatal sepsis and 66.7% of babies with hypoglycemia as a cause of neonatal seizure. On the other hand it is less frequently present in babies with dyselectrolytemia, bilirubin encephalopathy and malformations, absent in babies with intracranial haemorrhage and inborn error of metabolism as a cause of neonatal seizure (confounded by the small number of babies with this risk factors).

We considered NND (No Neurological Disability) as favourable outcome and ND (Neurodisability) & D (Death) together as poor outcome and if we analyze the data obtained for three major cause of neonatal seizure

Table No. 3:

		Outcome of HIE		Row total
		Favourable	Poor	
Antenatal risk factors of HIE	None	27	9	36
	1 or more	7	12	19
Coloumn total		34	21	55 (Grand total)

The chi square statistics is 7.6717. The p value is .005609. The result is significant at $p<0.05$. 38% of this group had a poor outcome.

Table No. 4:

		Outcome of EONS		Row total
		Favourable	Poor	
Antenatal risk factors of EONS	None	6	1	7
	1 OR MORE	3	1	4
Coloumn total		9	2	11 (Grand total)

The chi square statistics is 0.1964. The p value is 0.657619. The result is not significant at $p<0.05$. 18% of this group had a poor outcome.

Table No. 5:

		OUTCOME OF LONS		Row total
		Favourable	Poor	
Antenatal risk factors of LONS	None	9	1	10
	1 or more	6	2	8
Coloumn total		15	3	18 (Grand total)

The chi square statistics is 0.72. The p value is 0.396144. The result is not significant at $p<0.05$. 16% of this group had a poor outcome.

IV. Discussion

Our study reported mortality of 10%.The mortality rate observed by Sabzehiet al was 14.7%, which was higher than that (9%) reported in the study by Ronen et al [7], but similar to the finding reported by moayedi et al. (13.6%) 60. This increased mortality may be due to the severity of the etiological factors in newborns with neonatal seizure. The chart below shows the outcome in our study compared to two other studies showing better outcome both in terms of mortality and morbidity

Table No. 6:

	▫	Sabzehi et al [8]	Alcover et al [9]	Present study
Outcome	Survive	87 (85.3%)	79.2%	90%
	Expire	15 (14.7%)	20.8%	10%
	Abnormal outcome		45.4%	33%

V. Conclusion

The long term outcome were poor in babies having 1st day seizure (64%) & having HIE as a cause of seizure (38%). There is a statistically significant relation between antenatal risk factors and outcome of babies with HIE and presence of antenatal risk factors predicts the poor outcome of HIE babies. No such relation was found between sepsis (both early and late onset) and antenatal risk factors.

AUTHORSHIP INFORMATION:

DrGayen S: Study conceptualization; manuscript editing; DrSaha RP: data collection, analysis, manuscript writing; Dr. Das PS manuscript writing. All authors approved final version of manuscript.

Acknowledgement

We thank all the Doctors& Nurses of SNCU &Paediatrics& SNCU staffs for their kind assistance the administration of RG Kar Medical College and Hospital (RGKMCH) for their kind assistance in permitting us to use patients' data in this study. The contents of this study are solely responsibility of the authors and are in no way representative of the official views of RGKMCH.

References

[1]. BERG A, JALLON P, PREUX P. The epidemiology of seizure disorders in infancy and childhood: definitions and classifications. In: O Dulac et al (Eds), Handbook of Clinical Neurology. Pediatric Neurology, Part 1 (3rd edition), pp 381-398. Elsevier, Amsterdam, Netherlands, 2013

[2]. Mohamad A. Mikati and Abeer J Hani.NeonatalSeizures.In Robert M. Kliegman, Bonita F. Stanton, Joseph W. St gemeIII, Nina F. Schor Richard E. Behrman. Nelson Textbook of paediatrics Elsevier.20th Edition.Philadelphia.p2849-2854.

[3]. Mizrahi EM, Kellaway P. Diagnosis and Management of Neonatal Seizures (1st edition).Philadelphia, Lippincott-Raven, 1998. 45. Vasudevan C, Levene M. Epidemiology and aetiology of neonatal seizures. Semin Fetal Neonatal Med2013; 18(4): 185-19

[4]. Mizrahi EM, Kellaway P. Characterization and classification of neonatal seizures. Neurology 1987; 37:1837-1844.

[5]. Berg A, Jallon P, Preux P. The epidemiology of seizure disorders in infancy and childhood: definitions and classifications. In: O Dulac et al (Eds), Handbook of Clinical Neurology. Pediatric Neurology, Part 1 (3rd edition),pp 381-398. Elsevier, Amsterdam, Netherlands, 2013.

[6]. Arnold J. Sansevere and Ann M. Bergi.Neonatal Seizures. In Eric C. Eichenwald, Anne R. Hansen, Camilia R. Martin and Ann R. Stark. Cloherty and Stark's Manual of Neonatal Care. Wolters Kluwer.8th Edition.p 812-829.

[7]. Gabriel M, Ronen, Sharon Penny, Wayne Andrews. The epidemiology of clinical neonatal seizures in New Found land: A population based study. J Pediatr 1999;134: 71-75

[8]. Sabzehei MK, Basiri B, Bazmamoun H. The Etiology, Clinical Type, and Short Outcome of Seizures in Newborns Hospitalized in Besat Hospital/ Hamadan/ Iran. Iran J Child Neurol. 2014 Spring 8(2):24-28.

[9]. Alcover-Bloch E, Campistol J, Iriondo-Sanz M. Neonatal seizures, our experience. Rev Neurol. 2004; 38:808–812

Dr. Ram Prasad Saha. "Outcome of Neonatal Seizure: Experience from a Tertiary Care Hospital." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 6, 2019, pp 73-78.