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Study Clinical Profile of Neonatal Seizures at a Tertiary Care Centre

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ABSTRACT
Neonatal seizure is a commonly seen neurologic condition in neonates. They can be defined as paroxysmal alteration in motor activity, behavior, or autonomic function which results due to abnormal activity of brain during the neonatal period. Methodology: The study was conducted at Tertiary care hospital, from June 2007 to June 2009. In this study, a total of 110 neonatal cases were studied. Cases were selected based on the inclusion and exclusion criteria. All the necessary permissions were taken before starting the study. Also a written informed consent was taken from the parents of the neonates. Necessary investigations were made and the information was recorded. Seizure rate was more in out-born babies (5.66%) than in inborn babies (5.0%). It was seen to be slightly more in male babies (5.72%) than in female (4.47%). Highest seizure rate was found in extremely low birth weight babies (8.97%). Intracranial hemorrhage (26.19%), infections (21.42%) and metabolic disturbances (28.56%) were the commonest causes of seizures in preterm babies, while Hypoxic Ischemic Encephalopathy, (48.52%) was predominant etiology in term babies. Incidence of Neonatal Seizures is higher in preterm babies than term babies. Seizure rate is least found in babies between 30-37 weeks of gestation. Maximum babies with seizures are associated with complicated pregnancy and delivery. Subtle seizures are commonest seizure type seen in preterm babies and Multi-focal Clonic type of seizures in term babies. Maximum number of babies had onset of seizure within first 3 days.

INTRODUCTION

Neonatal period is defined as the first 28 days of life after birth. The most prominent feature of neurological dysfunction in neonatal period is seizure. Seizure may be the only sign of central nervous system dysfunction in neonate hence its recognition is important[1]. Neonatal seizures can be defined as paroxysmal alteration in motor activity, behaviour or autonomic function that results from the abnormal electrical activity of brain in neonatal period[1]. There is peak incidence of seizures in the first month of life of the neonates since the neonatal brain is immature. Also, there is an imbalance between inhibitory and excitatory processes as, the development of inhibitory neuronal circuit lags behind the excitatory network. Neonatal seizures represent an age specific seizure disorder, which is usually considered to be a separate category from epilepsy as neonatal seizures differ from convulsions in older children and adults in many ways. Hence, it is important to diagnose and treat the neonatal seizures because neonatal seizures are almost always due to some systemic illness which requires specific treatment. If seizures continue for considerable period of time, they can lead to morbidity and mortality[1].

The above study was conducted in a tertiary care hospital neonatal intensive care unit (NICU). It was conducted find out seizure incidence, various etiologies of neonatal seizures in neonatal intensive care unit and response to anticonvulsant.

MATERIALS AND METHODS

Study place: The study was conducted at tertiary care hospital over 1 year.

Study design: Prospective cohort study design.

Aims and objectives:

- To study incidence of Neonatal seizures in this institution
- To study clinical profile of neonatal seizures
- To evaluate probable aetiology of neonatal seizures

Inclusion criteria: All Neonates admitted in Neonatal Intensive Care Unit with seizure, neonates born both in hospital (inborn) and outside hospital (out-born-referred from other hospitals) and those whose parents were willing to give written consent were included in the study.

Exclusion criteria: Neonates weighting less than 800 grams, i.e., extremely low birth weight babies.

Sample size: 110 neonatal cases were enrolled into the study.

Data analysis: Neonates were grouped in two groups as per birth weight:

- < 2500 g (low birth weight)
- ≥2500 g

Neonates were also grouped according to gestational age as follows:

- **Preterm:** <37 weeks
- **Term:** ≥37 weeks

Ethical considerations: Ethical committee approval has been obtained before the initiation of the study.

Demographic details, perinatal history, birth weight, gestational age, semiology of seizures, number of seizures, probable aetiologies etc were entered in predesigned proforma Mortality was determined in each group, with respect to gestational age, birth weight and etiology wise in preterm and term babies. Data was interpreted, analyzed and entered into Microsoft using SPSS 21 version.

RESULTS

Total of 110 neonates were included in the study, out of which 77 were Inborn (born in our institute and 33 were outborns (referred from other hospital), 3with male to female ratio being 1.7:1 (Table 1).

Table 2 shows the seizure rate at the institution, as there were 9372 live births, in the hospital during study period, out of which 77 babies developed seizures, thus seizure rate for hospital was 8.22 per 1000 live births. Seizure rates in preterm babies and term babies were 22.98 and 6.18 per 1000 live birth, respectively (p<0.001).

Table 1: Distribution of cases in NICU

	Total no of admission in NICU	Total no. of seizure cases	Percentage	p-value
Inborn	1540	77	5.00	>0.05
Outborn	583	33	5.66	

Table 2: Seizure rate at hospital

	Live births	No. of babies with seizures	Rate/1000 live birth
Preterm	1131	26	22.98
Term	8241	51	6.18
Total	9372	77	8.22

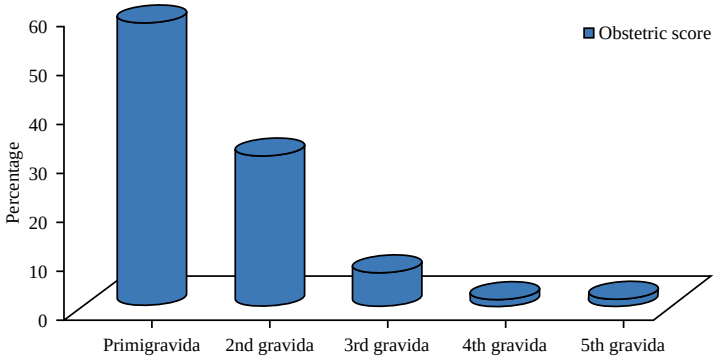

Fig. 1: Obstetrics score

Table 3: Seizure rate in NICU

	Total no. of admission in NICU	Total on. Babies with seizure	Percentage
Preterm	744	42	5.65
Term	1379	68	4.90
Total	2123	110	5.18

Table 4: Sex wise Distribution of seizure cases in NICU

	Total no. admission in NICU	Total no. of seizure cases	Percentage
Male	1206	69	5.72
Female	917	41	4.47
Total	2123	110	5.18

Table 5: Weight-wise distribution of case in NICU

Weight group	Total no. of NICU admission	Total no. of Seizure cases	Percentage
<1000 g	78	7	8.97
1000-1499 g	278	20	7.46
1500-2499 g	766	30	3.91
>2500 g	1011	53	5.24

Table 6: Gestational age wise distribution of cases

Gestational age	Total no of NICU admission	Total no. of seizure cases	Percentage
< 30 weeks	330	20	6.06
30-36 weeks	494	22	4.45
>36 weeks	1299	68	5.23
Total	2123	110	5.18

Table 3 shows that out of 2123 babies admitted in NICU during study period, 110 babies developed seizures during the stay in NICU hence seizure rate was 5.18%.

Table 4 shows that out of 1206 male babies admitted in NICU, 69 developed seizure and out of 917 female babies admitted in NICU, 41 developed seizures during hospital stay. Hence seizure rate was 5.72% in male & 4.47% in female and male: female ratio is being 1.7: 1.

Table 5 shows that seizure rate was maximum in neonate with birth weight < 1000 g i.e., 8.97% and minimum with birth weight 1500-2499 g i.e., 3.91% but it is found that seizure rate was slightly increased in birth weight 2500-3999 g, i.e., 5.24%.

Table 6 shows that seizure rate was 6.06% in babies <30 weeks of gestational age, 4.45% in babies between 30-36 weeks and again increased to 5.23% in babies >36 weeks.

Figure 1 shows that maximum number of babies i.e., 64 (58.18%) were born to primi-gravida and had seizures. Whereas was seen least in babies born to 4th and 5th gravida.

Figure 2 shows antepartum and Intra-partum complications such as Meconium stain liquor, fetal distress, prolong 2nd stage and premature rupture of membrane were most frequent complication observed. Complications were seen more frequent with term babies than preterm babies.

Table 7 shows that subtle seizures were the most common seizure type found in 53 i.e., 48.18% neonates followed by multifocal clonic seizure type found in 45 neonates i.e. 40.91%. In preterm babies, subtle seizure was common type of seizure (61.90%) and in term babies Multi-Focal Clonic was common type of seizure (51.48%). Six (all term babies) out of 110 (5%) had more than one seizure type.

Figure 3 shows that in majority of baby's onset of seizure was 1st day of life i.e., 38.18%, while in 87.28% babies seizure was started within 7 days. Seizure percentage decreases as day of onset increased.

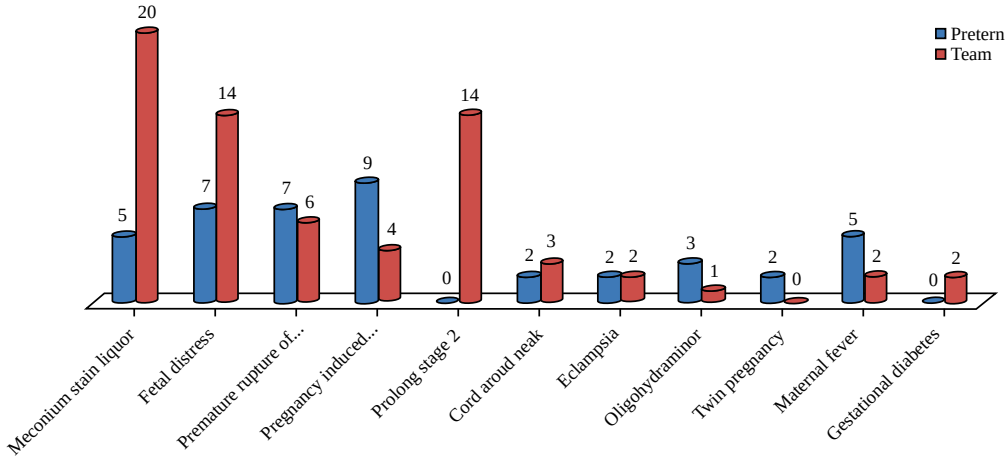

Fig. 2: Antepartum and Intrapartum complications

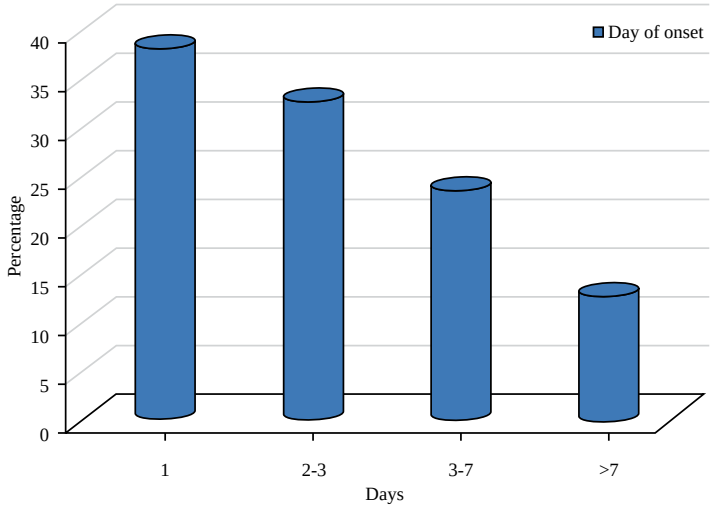

Fig. 3: Day of onset of seizures

Table 7: Types of seizures

Seizure type	Preterm	Term	Total
Subtle	26 (61.90%)	27 (39.70%)	53 (48.18%)
Multifocal clonic	10 (23.80%)	35 (51.48%)	45 (40.90%)
Focal clonic	02 (4.76%)	02 (2.98%)	04 (3.63%)
Tonic	04 (9.52%)	09 (13.23%)	13 (11.81%)
Myoclonic	00 (%)	01 (1.47%)	01 (0.9%)

Table 8: Etiology of Seizures

Etiology	Preterm	Term	Total
Hypoxic ischemic encephalopathy	07 (16.67%)	33 (48.53%)	40 (36.37%)
Infection	09 (21.43%)	16 (23.53%)	25(22.73%)
Hypoglycaemia	10 (23.81%)	10 (14.71%)	20 (18.19%)
Intracranial haemorrhage	11 (26.19%)	05 (7.35%)	16(14.55%)
Hypocalcaemia	02 (4.76%)	03 (4.41%)	05 (4.55%)
Undetermined	03 (7.14%)	01 (1.47%)	04 (3.64%)
Total	42	68	110

Table 9: USG finding in neonatal seizures

USG findings	Preterm	Term
Cerebral edema	10 (23.8%)	30 (44.1%)
Intracranial hemorrhage	11(26.2%)	5 (7.3%)
IATBG	3 (7.1%)	1 (1.5%)
MFIPL	0	6 (8.8%)
Ventriculitis	2 (4.8%)	4 (5.9%)
Normal	16 (38.1%)	22 (32.4%)
Total	42	68

MFIPL: Multi focal ischemic parenchymal lesion, IATBG: Ischemic areas of thalamus and basal ganglia

Table 8 Show that Hypoxic Ischemic Encephalopathy was prominent cause of seizures found in 36.37% babies. In preterm babies intracranial haemorrhages and acute metabolic disturbances were major cause of seizures found in 26.19% and 28.57% respectively followed by infections in 21.43% and hypoxic ischemic encephalopathy in 16.67%. 48.53% seizures in term babies were attributed to hypoxic ischemic encephalopathy followed by infection in 23.53%. Table 9 shows that cerebral edema is maximal finding on USG skull of both preterm as well as term babies.

Table 10 shows that out of 42 preterm babies, CT Brain was done for 12 babies and all 12 preterm babies showed abnormal findings. Out of 68 term babies, CT Brain was done for 39 babies and 34 out of 39 showed abnormal findings.

Table 11 shows that overall mortality rate of NICU was 22.13% while, that in cases of neonatal seizure was 26.36%.

Table 10: CT scan Reports

CT finding	Preterm	Term
Cerebral edema	03	01
Features s/o meningitis	02	10
Feature s/o cerebritis	1	2
IVH	4	1
Hypodensity	2	20
Normal	0	05

Table 11: Case fatality rate

	Admission	Death	Percentage
Total babies in NICU	2123	470	22.13
Babies with Seizure	110	29	26.36

DISCUSSIONS

The present study of neonatal seizures is done at tertiary care hospital over 1 year. In this study total 110 neonatal cases taken and clinical profile was studied.

Total 9372 babies were delivered live born in the hospital during study period, out of which 77 babies developed seizures, thus overall seizure rate for the hospital was 8.22 per 1000 live births. Seizure rate in preterm babies was 22.98 per 1000 live births and in term babies were 6.18 per 1000 live births. Mayes *et al*.[2] found that the incidence of seizures was 27.6 per 1000 live births in preterm and 2.7 per 1000 live births in full term babies. Ajay *et al.*[3] reported that over-all incidences recorded was 1.17% (0.69% in term and 6.14% in preterm).

Total of NICU admissions during study period was 2123 babies out of which 110 neonate developed seizures. Thus seizure rate in NICU was 5.18. Sheth *et al*.[4] found that seizures occurred in 8.6% of infants admitted in NICU. Fischer K l *et al.*, Reported that seizures occurred in 5.9 % of neonates admitted in NICU[5]. Seizure rate in NICU of current study correlates with these studies.

Out of 1540 inborn babies admitted in NICU 77 babies developed seizures thus seizure rate was 5% in inborn babies. Out of 583 out-born babies admitted in NICU 33 babies developed seizures, thus seizure rate was 5.66% in out-born babies. Scher *et al*.[6] reported that that incidence of seizures in NICU was 2.3%, with out-born babies more likely to have seizures than inborn babies.

Omene *et al*.[7] reported that preponderance of male infants in the seizure population, among whom; preterm infants were significantly more common.

In the above study conducted, it shows, neonate with birth weight < 1000 gms carries the maximum risk of 8.97%. The neonates with birth weight 1500-2499 g were at minimum risk of 3.91%. But it is found that seizure rate was slightly high in birth weight 2500-3999 g, i.e., 5.24%. The slightly higher seizure rate in babies with birth weight of 2500-3999 g in our study may be explained on the basis of more number of cases (48.53%) of hypoxic Ischemic encephalopathy. Lanska MJ *et al.*, in his study of neonatal seizures reported that seizures occurred in 3.5 per 1000 live births. The seizure risk varied inversely with birth weight: 57.5 per 1000 live births among very low birth weight infants (less than 1500 g), compared with 4.4 per 1000 live births for infants with moderately low birth weight (1500-2499 g), 2.8 per 1000 live births for those with normal birth weight (2500-3999 g) and 2.0 per 1000 live births for those with high birth weight (4,000 g or more)[8].

In our study, seizure rate was 6.06% in babies <30 weeks of gestational age, which was reduced to 4.45% in babies between 30-36 weeks and again rate increased to 5.23% in babies >36 weeks. Sheth *et al*.[4] found that seizures occurred in 8.6% of infants admitted in NICU. The seizures rate was parabolically related to gestational age such that infants at 30-36 weeks gestation had 4.8% seizure rate, compared with 11.9% in less than 30 weeks and 14.1% in more than 36 weeks gestation.

Maximum number of babies i.e. 64 (58.18%), were born to primigravida and had seizures. The seizure development was seen least in babies of 4th and 5th gravida i.e., 1.81% both respectively. In the study by Curtis *et al*.[9], it was found that these seizures were significantly associated with primiparity. Saliba *et al*.[10] in their population based study found that primiparity was marginally significant for term infants.

Our study showed that babies with seizure had complications during pregnancy or delivery.

Fetal distress (21), premature rupture of membranes (13) and prolonged 2nd stage (14) were the most frequent complication observed. Out of 110 babies 25 babies had meconium-stained liquor. Amongst them 5 babies were preterm and 20 babies were term. Complications were seen more frequently in term babies than preterm babies. Arpino *et al*.[11] reported that neonatal seizures were associated with maternal disease 2 year before pregnancy, mother's weight gain more than 14 kg during pregnancy, placental pathology, pre-eclampsia, low birth weight, low gestational age and jaundice in the first 3 days of life. They concluded that the causal pathways for neonatal seizures often begin before birth and some of the factors identified may be preventable[11]. Minchom *et al*.[12] found that null parity, hydramnios, post-term pregnancy, oxytocin augmentation of labour, abnormalities of fetal heart rate and/or meconium stained amniotic fluid, prolonged second stage of labour, emergency caesarian section, assisted vaginal delivery, low Apgar score, resuscitation at delivery and subsequent ventilator support were all statistically, significantly more common among cases of neonatal seizures.

Current study showed that the maximum i.e. 48.18% of babies suffered from subtle seizures. Multifocal clonic seizure was found in 45 neonates i.e. 40.91%. In preterm babies too, subtle seizure was the

commonest type of seizure (61.90%). But in term babies multi-Focal Clonic seizure was more common (51.48%). Six babies out of 110 babies i.e., 5% had more than one seizure types which included only term babies. Doménech-Martínez *et al*.[13] concluded that 42% babies presented with subtle seizures, 33.9% with tonic, 64.3% with multifocal clonic, 10.7% with focal clonic and 16.1% with multifocal myoclonic seizures. 55.4% of infants had 2 or more types of clinical convulsions. Calciolari *et al*.[14] found that subtle seizures (65% of total) and multifocal clonic seizures (54% of total) were the most common seizure types. Subtle seizures usually occurred in combination with other seizure types. Only one seizure type was related to gestational age i.e., focal clonic seizures in the term infant.

In majority of babies (70.91%), the onset of seizure was within first 3 days of birth while in 87.28% of babies, seizures started within 7 days of birth. Seizure percentage decreases as day of onset increased. Calciolari *et al*.[14] found that 80% of all seizures in first 2 days of life were related to HIE.

In the study conducted above, Hypoxic Ischemic Encephalopathy was predominant cause of seizures in 36.37% babies. In preterm babies, intracranial hemorrhages and acute metabolic disturbances were major causes of seizures found in 26.19 and 28.57% respectively, followed by infections in 21.43% and hypoxic ischemic encephalopathy in 16.66% of babies. 48.52% seizures in term babies were attributed to hypoxic ischemic encephalopathy followed by infection in 23.53 %. Eriksson *et al*.[15] reported that in 48% of infant, hypoxia was considered to be the probable main etiology, while infection and metabolic diseases including hypoglycemia and hypocalcaemia were next commonest causes, 12% for each condition.

Lien *et al*.[16] studied term early onset neonatal seizures. These seizures were attributed to hypoxic events in 37.5%, cerebral malformations in 17.5%, cerebral infarcts in 17.5%, intracranial hemorrhages in 12.5% infections in 7.5% and unknown etiology in 7.5%.

Out of 42 preterm babies CT scan was done in 12 babies. In the scan, cerebral oedema was demonstrated in 3 cases. The findings of meningitis were suggested in 2 cases, that of cerebritis in 1 case, IVH in 4 cases and hypodensity in 2 cases. Out of 68 term babies CT brain of 39 babies was done in which intracranial hemorrhage was found in 1 baby, findings of meningitis were suggested in 10 babies, that of cerebritis in 2 babies and hypodensity in 20 babies.

Overall mortality rate of NICU was 22.13% while in cases of neonatal seizure was 26.36%. The proportional mortality rate in NICU was 6.17%. Cloherty *et al*.[1] found that overall mortality in term and preterm neonates 15 %. Singh[17] has quoted that about one fourth neonates with convulsion die.

CONCLUSION

Incidence of Neonatal Seizures is higher in preterm babies than term babies. (χ^2 = 34.11, p<0.001). Incidence of Neonatal Seizures in between out-born babies and inborn babies is almost similar. (χ^2 = 0.373, p>0.05). There is preponderance of male infants in the seizure population.

Seizure rate is least found in babies between 30-37 weeks of gestation. Maximum seizure rate is seen in babies born to primigravida mother. Maximum babies with seizures are associated with complicated pregnancy and delivery. Subtle seizures are commonest seizure type seen in preterm babies and Multi-focal Clonic type of seizures in term babies. Maximum number of babies had onset of seizure within first 3 days. Hypoxic Ischemic Encephalopathy is prominent etiology of seizure in term babies whereas intracranial hemorrhage, infections and metabolic disturbances are commonest causes of seizures in preterm babies. Case fatality rate of neonatal seizures is more than that of overall mortality in NICU.

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