A study on clinical profile of neonates with seizures

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Abstract:
Depolarization can result from excessive excitatory amino acid release (e.g., glutamate) or deficient inhibitory neurotransmitter (eg, gamma amino butyric acid [GABA]). Another potential cause is disruption of ATP-dependent resting membrane potentials, which causes a flow of sodium into the neuron and potassium out of the neuron. Hypoxic-ischemic encephalopathy disrupts the ATP- dependent sodium-potassium pump and appears to cause excessive depolarization. It as an important cause of neonatal seizures. Each seizure episode reported by mother and subsequently observed in the NICU was recorded and relevant information was gathered: age at onset of seizure, duration of seizure in minutes, associated autonomic changes (HR, RR, 02 Saturation), medication required to control seizures and response time to medication. Most neonatal seizure occur in the first week of life 99 (90%). 55 (50%), 23 (20.91%), and 8 (7.27%) babies developed seizures on 1st, 2nd and 3rd day of life respectively. 78.18% of neonatal seizures occurred during first three days of life. The mean age of presentation of seizures was 3.79 days. Commonest type of neonatal seizure was subtle seizures (41.8%) followed by multifocal clonic (32.73%), focal clonic (17.27%), tonic (5.45%) and myoclonic seizures (2.73%).

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1. Introduction

The incidence varies from 1.5-3.7/1000 live births in term babies and 6-12% in babies weighing less than 1500 grams.

Seizures occur when a large group of neurons undergo excessive synchronized depolarization. Depolarization can result from excessive excitatory amino acid release (e.g., glutamate) or deficient inhibitory neurotransmitter (e.g., gamma amino butyric acid [GABA]). Another potential cause is disruption of ATP-dependent resting membrane potentials, which causes a flow of sodium into the neuron and potassium out of the neuron. Hypoxic-ischemic encephalopathy disrupts the ATP- dependent sodium-potassium pump and appears to cause excessive depolarization. It as an important cause of neonatal seizures. The biochemical effects of neonatal seizures included derangements of energy metabolisın. Energy-dependent ton pumps are compromised and ADP levels rise. The rise in ADP stimulates glycolysis with the ultimate increase in pyruvate, which accumulates as a result of compromised mitochondrial function [1].

"Brainstem Release Phenomenon characterized by the release of primitive brainstem and spinal motor patterns from tonic inhibition normally exerted by forebrain structures often there is a strong indication of severe cerebral cortical disturbances ("functional decortication") such as in cases where there are a lack of cortical structures caused by a destructive process (hydrocephaly) or developmental failure (atelencephaly) thought to represent the mechanism in subtle and generalized tonic seizures where there is no EEG seizure activity EEG seizure activity may be undetected because the seizure is generated by diencephalic or brainstem structures [2].

The enhanced vulnerability to seizures of the neonatal, compared with the adult brain, and the mechanisms of seizure-induced brain damage are incompletely understood. The main proposed pathophysiologic features are outlined here.

The expression of receptors for excitatory and inhibitory neurotransmitters is age dependent. N-methyl-D-aspartate (NMDA) glutamate receptors peak late in the first week.

Maturation of the inhibitory G-aminobutyric acid (GABA) network particularly the GABAB network, is delayed, with receptors slowly expressing over the first three postnatal works, whereas the excitatory receptors are already functional, creating an imbalance of excitatory over inhibitory receptors in early neurodevelopment [3].

Certain properties of NMDA receptors in the neonatal period enhance excitability, such as a higher postsynaptic receptor density in the hippocampus and the neocortex, a greater proportion of NMDA-receptor subunits NR2B than NR2A prolonging excitatory postsynaptic potentials, a lower efficacy of the magnesium channel-blocking, role, reduced inhibitory polyamine-binding sites, and an increased sensitivity to glycine. GluR2- lacking AMPA receptors are

expressed in the immature brain and are permeable to calcium, in contrast to the mature brain calcium-Impermeable AMPA receptors. In addition to neurons, astrocytes regulate extracellular ionic and glutamate concentrations to modulate surrounding neuronal excitability. In the neonate, astrocytes are immature, which contributes to the propensity to generate seizures. Finally, gap junctions are prevalent and the refractory and hyperpolarization periods are shorter during the postictal phase in the neonatal brain, facilitating the spread of depolarizing discharges and prolonged or recurrent seizures [4].

Methodology:

Methods of Collection of Data:

The present study included 11 neonates presenting with seizures admitted to NICU.

- **Baseline characteristics:** These includes sex, gestational age, intrauterine growth status, maternal education and the socioeconomic status (Kuppuswami scale), weight, head circumference and length.
- **Clinical profile of seizures:** Each seizure episode reported by mother and subsequently observed in the NICU was recorded and relevant information was gathered: age at onset of seizure, duration of seizure in minutes, associated autonomic changes (HR, RR, 02 Saturation), medication required to control seizures and response time to medication.
- **Determination of etiology:** Relevant clinical information, antenatal history of infection including TORCH, drug intake, chorioamnionitis, fetal distress (fetal heart rate abnormalities or meconium stained liquor).
- **Investigations:** Essential investigations including blood glucose, ionized sernm calcium, serum sodium, arterial pH and USG of cranium.Additional investigation as guided by history, physical examination and essential investigations. These include sepsis screen, blood culture, cerebrospinal fluid (CSF) examination, haematoc t, serum bilirubin level, serum urea and creatinine, "TORCH"serology, serum calcium/magnesium, metabolic profile for inborn error of metabolism and CT scan.

Inclusion Criteria:

All neonates presenting with seizures or developing clinically identifiable seizures before 28 days of life were included in the study.

Exclusion criteria:

Neonates with doubtful seizures were excluded. Neonates with jitteriness were excluded by holding the limb to determine whether the movement could be stopped.

Detailed antenatal, natal and post natal history were taken as per the proforma enclosed.

Antenatal History:

History of medical illness like fever with rash, Asthma, Tuberculosis, cardiac diseases, diabetes Mellitus were asked. History of obstetric complications like Pili, Sudden increase in fetal movement were taken. Regarding Antenatal Registration, Inj. TI, Iron and folic acid were also asked.

Perinatal History

History of PROM, Prolonged Jabour, repeated per vaginal examinations, foul smelling liquor, place of delivery, type of delivery and indication for caesarean section, were enquired. Accidental injection of the local anaesthetic into the fetal scalp After delivery whether baby cried immediately or not, cord around the neck, cord prolapse, fetal distress, Mcconium stained liquor, mcconium aspiration and any resuscitation done, were enquired. The neonate was diagnosed with birth asphyxia if baby did not cry for more than three minutes after birth or documented APGAR score was: S 3 at one minute and< 7 at 5 minutes of birth.

Post-natal History:

History of lethargy, poor activity, poor feeding, jaundice, excessive cry, vomiting and seizures were taken.

History of Seizures:

The day of onset of seizures, type of seizures, the duration of seizures, number of seizures and consciousness during and between seizures were taken after appropriate history, detailed examination of neonate was done.

Examination

The vitals of the baby (Heart Rate, Respiratory Rate, Peripheral pulses, Blood pressure, temperature, Capillary filling time) were recorded. General physical examination of neonate was done according to the proforma and any disparity in Head size and Shape, Skin lesions were noted. Anthropometry of the neonate was recorded & gestational age was assessed according to New Ballard scoring. CNS examination was done as per the proforma and HIE was staged according to modified Sarnat staging in to stage I, II and III. Other systems were also examined.

Results:

Table 1: Distribution of neonatal seizures according to birth weight.

Birth Weight (gms)	No. of cases	Percent %
LBW (<2500gms)	46	41.82
Normal (2500-4000gms)	61	55.45
Large Babies (>4000gms)	3	2.73
Total	100	100

Birth weight of 61 neonates (55.45%) was normal (2500gms-4000gms), 46 (41.82%) had low birth weight (<2500gms) and 3(2.73%) were large babies (birth weight > 4000gms).

Table 2: Distribution of Neonatal Seizures according to gestational age.

Gestational age	No. of cases	Percentage (%)
Term- appropriate for gestational age(AGA)	75	68.2
Term- short for gestational age (SGA)	10	9.09
Preterm	19	17.27
Postterm	6	5.45
Total	110	100.0

In the present study, out of 110 babies, 85 were full term. Among these 85 full term neonates 75 (68.2%) were appropriate for gestational age and 10 (9.09%) were small for gestational age There were 19 (17.27%) preterm babies and 6 (5.45 %)post-term babies

Table 3: Sex wise distribution of neonatal seizures.

Sex	No. of cases	Percentage (%)
Male	63	57.3
Female	47	42.72
Total	110	100

In our study, 63 (57.3%) were males babies and 47 (42.72%) were female babies with male to female ratio of 1.34:1

Table 4: Place of Delivery of Neonates with seizures.

Place of delivery	No. of cases	Percentage (%)
Home delivery	67	60.91
Hospital delivery	43	39.09
Total	110	100

Out of 110 cases, 67 (60.91%) were born at home and 43 (39.09%) at hospital.

Table 5: Mode of Delivery of babies with neonatal seizures.

Mode of delivery	No. of cases	Percentage (%)
Spontaneous vaginal delivery	80	72.72
Caesarian section	27	24.55
Outlet forceps delivery	3	2.73
Total	110	100

Majority (72.72%) of the neonates in the present study were born by spontaneous vaginal delivery followed by Caesarean section (24.55%) and by outlet forceps (2.73%).

Table 6: Day of onset of Neonatal Seizures.

Days of onset of neonatal seizures	No. of cases	Percentage (%)
First	55	50
Second	23	20.91
Third	8	7.27
Fourth	5	4.55
Fifth	1	0.91
Sixth	1	0.91
Seventh	6	5.45
Eight to twenty eighth day	11	10
Total	110	100

In our study 55 (50%) of the babies developed seizures on the first day of life, 23 (20.91%) on the second day and 8 (7.27%) on the third day of life. 78.18% of neonatal seizures occurred during first three days of life. The mean age of presentation of seizures was 3.79 days.

Table 7: Type of Neonatal Seizures.

Types of neonatal seizures	No. of cases	Percent (%)
Subtle	46	41.82
Multifocal clonic	36	32.73
Focal clonic	19	17.27
Tonic	6	5.45
Myoclonic	3	2.73
Total	110	100

In our study commonest type of neonatal seizures was subtle seizures (41.8 %) followed by multifocal clonic (32.73%), focal clonic (17.27%), tonic (5.45%) and myoclonic seizures (2.73%).

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Discussion:

In a study of Sheth RD *et al* [5] there was a parabolic relationship between seizure rate and gestational age at seizure onset, such that infants between 30 and 36 weeks had a 4.8% seizures rate compared with rates of 11.9% and 14.1% for infants 30 and 36 weeks.

Neonatal seizures have no sex predilection. However in our study male to female ratio was 1.34:1, ilar with the study by Lakra Mahaveer (2:1) [6] and A.R. Moayedi *et al* (1.39:1). The male sex predominated in both full term and preterm groups in the study of Manoel R.R. Holanda *et al* in Brazil.

In our study 60.91% were born at home. This high rate of home deliveries were probably because of low socioeconomic status, lack of awareness and poor access to the health center. In our study majority of neonates with seizures were born by normal vaginal delivery (72.72%) followed by LSCS (24.55%) and outlet forceps delivery (2.73%). In a study of neonatal seizures by Lakhra Mahaveer *et al* [7] 68.7% were born by normal vaginal delivery, 28.1% by LSCS and 3.1% by forceps delivery and in a study A.R. Moayedi *et al* type of delivery in 65.6% of cases was Normal Vaginal Delivery and in 34.5% was Cesarean Section.

In our study 61 (55.45%) neonates had normal birth weight (2500gms-4000gms), 46 (41.82%) had low birth weight (<2500gms) and 3(2.73%) were large babies (birth weight >4000gms). In a study by A.R. Moayedi *et al* 81(73.6%) neonates had normal birth weight (2500gms-4000gms), 25 (22.7%) had low birth weight (<2500gms) and 4 (3.6%) were large babies (birth weight > 4000gms).

In our study 55(50%), 23 (20.91%), and 8 (7.27%) babies developed seizures on 1st, 2nd 3rd day of life respectively. 78.18% of neonatal seizures occurred during first three days of life. The mean age of presentation of seizures was 3.79 days.

In a study by Ronen Gabriel *et al* 8 onset of seizures on first day of life was 36%, and 83% developed seizure within first week of life, which is ilar to our study. In a study by A.R. Moayedi *et al* 32 (29.1%) [8] neonates had seizures in the first 24hr of their life, 28 (25.5%) on the second and third days of life, 14 (12.7%) between the 4th to 6th days of life and 36 (32.7%) on the 7th day or later. Over half the neonates (54.6%) hence had seizures within the first 72hrs of their life. The average age of patients suffering from seizures was 7.9

days. In a study by Ajay kumar *et al* the median age of onset of first seizure episode was 41.5 hrs in term babies 38 hours, in preterm babies 55 hours), with 75% of seizure episodes occurring before 115 hours of age, 52 babies (57.8%) developed first seizure within first 48 hours of life out of which 20 babies had seizure in less than 12 hours of life. Majority of neonatal seizures within first 3 days of life, after 3 days there is a small second peak at the end of first week and early second week.

In the present study 46 (41.82%) babies had subtle seizures either in the form of oro-buccal movements, eye blinking, cycling movements of limbs or apnea associated with tachycardia (i.e., HR > 160/min) or hypertension. followed by multifocal clonic in 36 (32.73%), focal clonic in 19 (17.27%), Tonic in 6 (5.45%) and myoclonic in 3 (2.73%) [9].

Incomplete Subtle seizure was the most common type of neonatal seizures compared with other authors as shown in table, but in a study of neonatal seizures by Soni Arun *et al* generalized tonic seizure was commonest type of seizure, followed by subtle seizures and In a study of Ajay kumar *et al* Multifocal clonic seizures contributed a major proportion with 42.24% followed by generalized tonic seizures (21.55%). Among mixed seizure episodes Multifocal clonic with subtle seizures were present in 21 seizure episodes followed by generalized tonic with subtle seizures in 18 episodes [10].

In contrary to older children and adults, neonates present with subtle and generalized tonic seizures more commonly because of immaturity of central nervous system and more mature limbic system compared to other parts of CNS in neonates.

Subtle seizures are difficult to recognize and also difficult to interpret, as they may be normal neonatal activity and one should be careful in assigning subtle movements as seizures in neonates.

Conclusion

- Neonatal seizures occur more commonly in male babies 63 (57.3%) with male to female ratio of 1.34: 1
- Majority (72.72%) of the neonates were born by spontaneous vaginal delivery followed by Caesarean section (24.55%) and by outlet forceps (2.73%).
- Most neonatal seizure occur in the first week of life 99 (90%). 55 (50%), 23 (20.91%), and 8 (7.27%) babies developed seizures on 1st ,2nd and 3rd day of life respectively. 78.18% of neonatal seizures occurred during first three days of life. The mean age of presentation of seizures was 3.79 days.
- Commonest type of neonatal seizure was subtle seizures (41.8%) followed by multifocal clonic (32.73%), focal clonic (17.27%), tonic (5.45%) and myoclonic seizures (2.73%).

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