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Clinical Study on Etiology, Onset and Clinical Manifestations of Neonatal Seizures

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Abstract

Background: Neonatal seizures are clinically significant because very few are idiopathic. Further investigation leading to prompt diagnosis of the underlying condition is important because many of the etiologies have specific treatment. Time of onset of seizures has correlation with etiology. **Objectives:** The objective of the present study is to know the etiology of neonatal seizures, to know the time of onset of neonatal seizures and its relation to etiology and to know the various types of seizures in neonates. **Methodology:** The present study included 127 neonates presenting with Neonatal seizures admitted to NICU (Neonatal Intensive care Unit) of tertiary care hospital from August 2014 to December 2016. Detailed antenatal, natal and post natal history were taken and examination of baby done and HIE staged according to Modified Sarnat's staging. Then relevant investigations were done and etiology of neonatal seizures was diagnosed. **Results:** In the present prospective study, out of 127 neonates studied, 118 were full-term, among these 88 (69.3%) were AGA (Average for gestational age) and 30 (23.6%) were SGA (Small for gestational age). 7 babies (5.5%) were preterm. Male: Female ratio in our study was 1.6:1. In our study onset of seizures within first 3 days of life was seen in 101 neonates (79.5%). After 3 days of life, 26 neonates developed seizures (20.5%). Onset of seizures within first 3 days of life of had statistically significant correlation with birth asphyxia as the etiology with $p<0.001$. Subtle seizures were the commonest type of seizures in our study (49 cases – 38.6%), followed by GTS (Generalized tonic seizures - 42 cases – 33.1%), multifocal clonic (19 cases – 15%) and focal clonic seizures (8 cases - 6.3%). Birth asphyxia was the commonest cause of neonatal seizures in our study (84 cases – 66.1%) followed by hypoglycemia (22 cases – 17.3%) and meningitis (11 cases 8.7%). Out of 84 cases of birth asphyxia 66 (78.6%) mothers had prolonged second stage of labour and 28 (33.3%) had MSAF (Meconium Stained Amniotic Fluid). Hypoglycemic seizures were more common in LBW (Low Birth Weight) babies with statistically significant $p<0.001$. **Conclusion:** The recognition of etiology of neonatal seizures is often helpful with respect to prognosis and treatment. The most common etiology for neonatal seizure is HIE (Hypoxic ischemic encephalopathy) and is frequently associated with perinatal risk factors. Onset of seizures during first 3 days of life has significant correlation with HIE as etiology. Hypoglycemic seizures are more common in LBW babies. Subtle seizures are commonest type of clinical seizures, which is difficult to identify, therefore careful observation of at risk newborns is necessary.

Keywords: Birth Asphyxia, Hypoxic Ischaemic Encephalopathy, Neonatal Convulsions, Neonatal Seizures

1. Introduction

Seizures represent the most distinctive signal of neurological disease in the newborn period. It is caused by sudden, abnormal and excessive electrical activity in the brain[3]. The convulsive phenomenon's are the most frequent of the overt manifestation of neonatal neurological disorders. Neonatal seizures are common and may be the first manifestations of neurological dysfunction after a variety of insults. It is critical to recognize neonatal seizures to determine their etiology and to treat them for 3 major reasons:

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- First, seizures are usually related to significant illness, sometimes requiring specific therapy.
- Second, neonatal seizures may interfere with important supportive measures, such as alimentation and assisted respiration for associated disorders.
- Third, experimental data give reason for concern that the seizures per se may be a cause of brain injury.

Neonatal seizures present with varying manifestations like generalized tonic, multifocal clonic and subtle activity. Newborn babies do not manifest febrile convulsions. Therefore it is important to recognize the seizures and treat it, as delay in recognition and treatment may lead to brain damage. The time of onset of seizure has relationship with the etiology and prognosis. For example, birth asphyxia usually presents in the first three days of life whereas meningitis presents after first week. The incidence rate was 2.6 per 1000 live births, 2.00 for term neonates, 11.1 for preterm neonates, and 13.5 for infants weighing < 2500 at birth[1]. If baby convulse within hours of delivery, it signifies poor prognosis and brain damage. Taking above points into consideration, the study of etiology, onset and clinical manifestations of neonatal seizures has a significant role.

2. Methods

The prospective study included 127 neonates presenting with Neonatal seizures admitted to NICU of tertiary care hospital from August 2014 to December 2016.

2.1 Inclusion Criteria

Neonates (first 28 days of life) presenting with at least one of the following clinical type of seizures:

- Generalized tonic seizures.
- Multifocal clonic seizures
- Focal clonic seizures
- Myoclonic seizures
- With or without accompaniment of subtle motor movements, apneas or autonomic changes or the sole combination of subtle motor and autonomic manifestation were included in the study group.

2.2 Exclusion Criteria

- Neonates with isolated brain release phenomenon, apnea or paroxysmal autonomic changes, i.e., only subtle motor moments or apnea without tachycardia or hypertension were excluded from the study.
- Jitteriness[2] in neonates.
- Tetanic spasms in neonates.

2.3 Antenatal History

Age and parity of mother were noted. History of a regular antenatal checkup was done or not was enquired. History of medical illness like diabetes, fever during first trimester or third trimester was asked. History of obstetric complications like PIH (Pregnancy induced hypertension), Eclampsia, Ante partum hemorrhage, oligo or polyhydramnios was taken.

2.4 Perinatal History

History of PROM (Prolonged Rupture of Membranes), prolonged second stage of labour, Meconium staining of liquor, place of delivery, type of delivery and indication for forceps and caesarean section, were enquired. After delivery whether baby cried immediately or not, was it meconium stained and any resuscitation done, were enquired. If Apgar score was done, it was noted. The neonate was diagnosed with birth asphyxia if baby did not cry for more than three minutes after birth or documented Apgar score was < 3 at one minute and < 7 at 5 minutes of birth.

2.5 Post-Natal History

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

2.6 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.

2.7 Examination:

The vitals of the baby (Heart Rate, Respiratory Rate, Peripheral pulses, Blood pressure, temperature and 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 and gestational age was assessed according to New Ballard scoring. CNS examination was done as per the proforma and HIE staging done according to modified Sarnat's staging as stage I, II and III. Other systems were also examined.

The following investigations were done for neonatal seizures:

- Complete blood count (hemoglobin, Total count, differential count).

- Sepsis screening: Peripheral smear for band cells and toxic granules, CRP and blood culture if necessary.
- Blood glucose: Random blood sugar was done urgently with glucostick and then confirmed by glucose oxidase method. Hypoglycemia was diagnosed if RBS is less than 40 mg /dl.
- Serum electrolytes: Serum electrolytes were done on emergency basis, Serum Calcium, Sodium and Potassium were done by semi auto analyzer (by Colorimetric method). Hypocalcaemia was diagnosed if serum calcium level was less than 7.0 mg/dl. Hyponatremia was diagnosed if serum sodium level is less than 130 mEq/L and Hyponatremia if serum sodium is >150mEq/L.
- CSF analysis: If septicemia or meningitis was suspected, LP was done and CSF analyzed for color, turbidity, protein, sugar, total and differential cell count and culture. Neonatal meningitis was diagnosed if CSF culture showed growth of organisms.
- Other metabolic screening like serum ammonia was done if particular metabolic disease was suspected.
- Chest X-ray: Chest x-ray was done to rule out meconium aspiration syndrome and respiratory distress syndrome.

3. Results

127 babies with neonatal seizures were studied over a period of 3 years. They showed the following results:

Neonatal seizures occur more commonly in male babies with male to female ratio 1.6:1.

Most neonatal seizures occur in the first week of life (91.7%), more so within first 3 days of life (79.5%). Highest number is seen on first day of life (36.2%) Table 1.

Subtle seizures[8] are the commonest type of seizure (38.6%), followed by generalized tonic (33.1%), multifocal clonic (15%), focal clonic type (6.3%) and mixed type of seizures (7%).

Birth asphyxia is the commonest cause of neonatal seizures (61.4%), followed by hypoglycemia (7.3%), neonatal meningitis (8.7%) and hypocalcemia[5] (3.1%).

Table 1. Day of onset of neonatal seizures

Days of onset of Neonatal Seizures	No. of Cases	Percentage
First	46	36.2
Second	34	26.8
Third	21	16.5
Fourth	5	4.0
Fifth[13]	2	1.6
Sixth	2	1.6
Seventh	4	3.2
8to 28 days	13	10.1
Total	**127**	**100.00**

Table 2. Based on etiology of neonatal seizures

Etiology	No. of Cases	Percent
Birth asphyxia	84	66.1
Hypoglycemia	22	17.3
Neonatal meningitis	11	8.7
Hypocalcaemia	4	3.1
Congenital anomaly	2	1.6
Intraventricular hemorrhage	1	0.8
Hyponatremia with meningitis	1	0.8
Hyperammonemia	1	0.8
Unknown	1	0.8
Total	**127**	**100.00**

In neonatal seizures due to birth asphyxia, 44% had subtle seizures, 27.3% had GTS. In hypoglycemic seizures, 41% had subtle seizures and 31.8% had GTS. In neonatal seizures due to meningitis, 27.3% had subtle seizures and 54.6% had GTS. There was no correlation between types of seizures with etiology in our study.

Seizures due to birth asphyxia has onset within first

Table 3. Correlation of etiology with day of onset of neonatal seizures

Day of onset of seizures	Etiology										Total	Percentage
	Birth Asphyxia		Metabolic				Neonatal Meningitis		Others			
			Hypo- glycemia		Hypocalcaemia							
	No.	%	No.	%	No.	%	No.	%	No.	%		
1st	46	100	--	--	--	--	--	--	--	--	46	100.00
2nd	28	82.4	03	8.8	02	5.9	--	--	01	2.9	34	100.00
3rd	9	42.9	11	52.4	--	--	1	4.8	--	--	21	100.00
4th	1	20	4	80	--	--	--	--	--	--	05	100.00
5th	--	--	1	50	--	--	--	--	1	50	02	100.00
6th	--	--	1	50	--	--	1	50	--	--	02	100.00
7th	--	--	1	25	--	--	3	75	--	--	04	100.00
8-28 Days	--	--	1	7.6	2	15.4	6	46.2	4	30.8	13	100.00
Total	**84**		**22**		**04**		**11**		**06**		**127**	**100.00**

four days of life, more so during first 3 days[7] (88%) with statistically significant correlation (p<0.001). Majority of hypoglycemic seizures occur during third and fourth day (68.2%). Seizures due to neonatal meningitis has onset during end of first week and early second week[12]. Hypocalcaemia has 2 peaks, one on second day and the other after first week of life Table 3.

Seizures due to birth asphyxia is seen more commonly in term AGA babies, where as seizures due to hypoglycemia is more common in low birth weight babies i.e., < 2500gm, (14/22-63.6%) with highly significant P value of < 0.001.

Birth asphyxia has many risk factors like prolonged second stage of labour (66 of 84-79.6%), home delivery and commonly seen in term babies.

Neonatal meningitis in our study was the third most common cause of seizures (11/127 – 8.7%). Organisms causing meningitis were mostly Staphylococcus aureus which is community acquired or nosocomial acquired. This can be prevented by proper hand washing technique and hygienic delivery[9] Table 2.

Mortality in our study was 17.3% (22/127) and birth asphyxia is the leading cause seen in 13 cases (59%).

4. Discussion

In our study, out of 127 neonates with seizures 118 were full-term neonates (92.9%), of which 88 were appropriate for gestational age i.e., 2500 gm (69.3%) and 30 were small for gestational age i.e., < 2500 gm (23.6%)[1]. 7 were preterm babies (5.5%) and 2 were post term babies. Birth asphyxia was the commonest cause of seizures in full term babies and is associated with perinatal complications like meconium stained liquor in 28 cases (33.3%), prolonged second stage of labour (>120 minutes) in 66 cases (78.6%) Table 2.

Similar observations was seen in study by Ravneet Sandhu[4] et al where term appropriate for gestational age babies were 81.2% followed by preterm babies in 18.8%.Small for gestational age babies had constituted significantly for neonatal seizure cases. In our study 23.6% were SGA babies, which matches with study of neonatal seizures by Sahiba Rima M et al., where SGA babies were 24 (20%) out of 122 term babies, showing it similar to our study.

In our study, majority of neonates with seizures were born by normal vaginal delivery (75.6%) followed by LSCS (Lower section caesarean section) (19.7%) and forceps outlet delivery (4.7%). In a study of neonatal seizures by Lakhra Mahaveer et al.,[6] 68.7% were born by normal vaginal delivery, 28.1% by LSCS and 3.1% by forceps delivery. Neonatal seizures have no sex predilection. However, in our study, male to female ratio was 1.6:1, showing similarity to the study of neonatal seizures by Lakhra Mahaveer et al.,[6] where male to female ratio was about 2:1.

In the present study, majority of babies with birth asphyxia were a result of prolonged second stage of labour i.e., 66 of 84 (78.6%) and difficult delivery, 28 cases and MSAF (33.3%) and 4 mothers had PIH. Myles TD et al., found slightly higher incidence of birth asphyxia with prolonged second stage of labour compared to normal second stage of labour. In the present study 49 (38.6%) 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[11].

Generalized tonic seizures was observed in 33.1% i.e., 42 cases followed by multifocal clonic in 19 cases (15%), focal clonic seizures in 8 babies (6.3%) and 9 babies had mixed type of seizures. In a study of neonatal seizures by Brunquell Philip J et al.,[15] subtle seizures were the commonest occurring in 51% (27 of 53), followed by focal clonic (42%), multifocal clonic (30%) and GTS (23%).

Lakhra Mahaveer et al.,[16] also reported that subtle seizures were the commonest. But in a study of neonatal seizures by Soni Arun et al., generalized tonic seizure was commonest type of seizure, followed by subtle seizures. 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[10].

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[14]. In our study 101 out of 127 neonates with seizures had onset within first three days of life, among these 63% had onset of seizures within first 2 days life and 36.2% had onset of seizures within first day of life. 26 neonates (20.5%) had onset of seizures after 3 days of life, among these, 8 neonates had onset of seizures on 7th day and 8th day of life Table 1, Table 3.

We did not include non-convulsive seizures in this study. This study was done at tertiary care set up, majority of patients were referred and high risk neonates. Hence, it may not reflect true general population incidence.

This study was conducted to know etiology, types of neonatal seizures in our set up.

5. Conclusion

Neonatal Seizures typically signal underlying significant

neurological disease and represent non-specific response of the immature nervous system to varied insults. The most common etiology for neonatal seizures is hypoxic-ischemic encephalopathy. Most of these are preventable if proper antenatal and perinatal care is given to the mother. The time of onset of neonatal seizures, is significantly associated with the etiology (e.g., onset of seizures within first three days is significantly associated with birth asphyxia). Subtle seizures are commonest type of clinical seizure, which is difficult to identify, therefore careful observation of at risk newborns is necessary for the diagnosis.

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