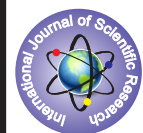


A STUDY OF ETIOLOGY, ONSET AND CLINICAL MANIFESTATIONS OF NEONATAL SEIZURES



Pediatrics

KEYWORDS: Neonatal seizures; Birth asphyxia; HIE; Subtle seizures; Hypoglycemia.

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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 100 neonates presenting with seizures admitted in the NICU of hospitals attached to C.U.Shah Medical colleges, Surendranagar during the period of June 2013 to August 2014. 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 were diagnosed.

Results: In the present study, out of 100 neonates studied, 94 were full-term, among these 73 were AGA and 21 were SGA. 5 were preterm. Male:Female ratio in our study was 1.7:1.

In our study onset of seizures within first three days of life were seen in 84 neonates (84%). After 3 days of life 16 neonates developed seizures (16%). Onset of seizures within first 3 days of life 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 (44 cases – 44%), followed by GTS (29 cases – 29%), multifocal clonic (11 cases – 11%) and focal clonic seizures (8 cases – 8%).

Birth asphyxia was the commonest cause of neonatal seizures in our study (74 cases

– 74%) followed by hypoglycemia (14 cases – 14%) and meningitis (8 cases – 8%). Out of 74 cases of birth asphyxia 35 (48.6%) mothers had prolonged second stage of labour and 18 (24.3%) had MSAF. Hypoglycemic seizures were more common in LBW 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 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.

MATERIALS AND METHODS

Methods of Collection of Data:

The present study included 127 neonates presenting with seizures admitted to NICU of C.U.SHAH MEDICAL COLLEGE, SURENDRANAGAR during the period of June 2013 to August 2014.

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, apnea or autonomic changes or the sole combination of subtle motor and autonomic manifestation were included in the study group.

Exclusion Criteria:

1. Neonates with isolated subtle phenomenon, apnea or paroxysmal autonomic changes, i.e., only subtle motor movements or apnea without tachycardia or hypertension were excluded from the study.
2. Jitteriness in neonates.
3. Tetanic spasms in neonates.

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

RESULTS

Analysis of Cases and Results:

There were 100 neonates admitted to NICU of C.U.Shah Medical college and hospital, Surendranagar during period of June 2013 to August 2014.

Gestational Age:

Table-7: Distribution of Neonatal Seizures according to gestational age

Gestational Age	No. Of cases	Percentage
Term – Appropriate for gestational age (AGA)	73	73
Term – small for gestational age (SGA)	21	21
Preterm	5	5
Post-term	1	1
Total	100	100.00

In the present study, out of 100 babies, 94 were full term. Among these 94 full term neonates 73% were appropriate for gestational age and 21% were small for gestational age. There were 5% preterm babies and 1% post-term babies.

Sex Distribution:

Table-8: Sex wise distribution of neonatal seizures

Sex	No. of Cases	Percentage
Male	64	64
Female	36	36
Total	100	100.00

In our study, 64 were males and 36 were female babies with male to female ratio of 1.7:1.

Place of Delivery:

Table-9: Place of Delivery of babies with neonatal seizures

Place of Delivery	No. of Cases	Percentage
Home delivery	15	15
Hospital delivery	85	85
Total	100	100.00

Out of 100 cases, 15% were born at home and 85% at hospital..

Figure 2- Sex wise distribution of neonatal seizures

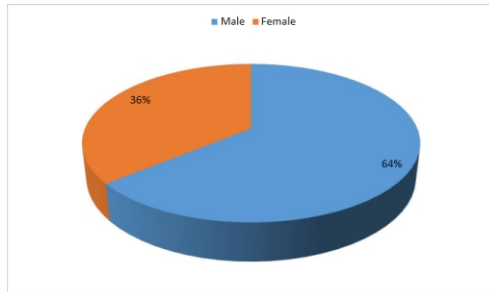
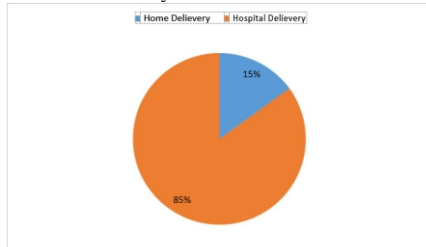


Figure 3- Place of Delivery of babies with neonatal Seizures



Type of Delivery of babies with neonatal seizures:

Table-10: Type of Delivery of babies with neonatal seizures

Type of Delivery	No. of Cases	Percentage
Spontaneous vaginal delivery	82	82
Caesarian section	15	15
Outlet forceps delivery	3	3
Total	100	100.00

Day of onset of Neonatal Seizures:

Table-11: Day of onset of Neonatal Seizures

Days of onset of Neonatal Seizures	No. of Cases	Percent
First	40	40
Second	30	30
Third	14	14
Fourth	3	3
Fifth	0	0
Sixth	2	2
Seventh	3	3
8to 28 days	8	8
Total	100	100.00

In our study onset of seizures on first day of life was seen 40 neonates (40%), on second day of life 30 neonates developed seizures (30%), on third day of life 14 (14%) babies developed convulsions. The first three days of life together constituted 84% of neonatal seizures.

Type of Seizures:

Seizures were classified according to Volpe ams:

- Generalized tonic.
- Subtle
- Multifocal and focal clonic and
- Myoclonic seizures

Figure 4- Day of onset of Neonatal Seizures

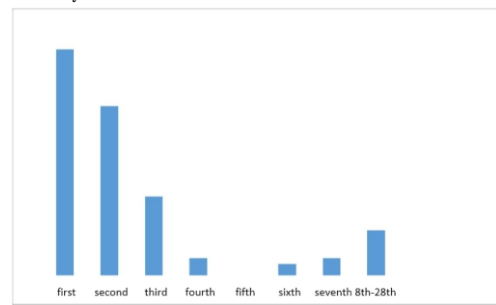
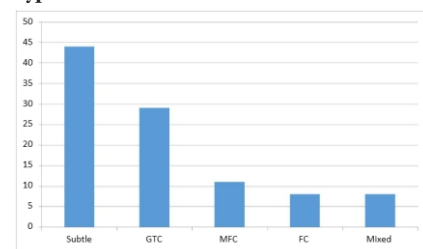


Table-12: Type of Neonatal Seizures

Type of Neonatal Seizures	No. of Cases	Percent
Subtle	44	44
Generalized tonic	29	29
Multifocal clonic	11	11
Focal clonic	8	8
Subtle with GTS	5	5
Subtle with clonic	3	3
Total	100	100.00

In our study out of 100 neonatal seizures, 92 neonates had one of the 4 classically described neonatal seizures. Among these 44 neonates had subtle seizures, 29 neonates had generalized tonic seizures, 11 had multifocal clonic seizures and 8 had focal clonic seizures. 8 neonates had mixed type of seizures, among these 5 had subtle with generalized tonic seizures and 3 had subtle with clonic seizures.

Figure 5- Type of Neonatal Seizures



Etiology of Neonatal Seizures:

Table-13: Etiology of Neonatal Seizures

Etiology	No. of Cases	Percent
Birth asphyxia	74	74
Hypoglycemia	14	14
Neonatal meningitis	8	8
Hypocalcemia	1	1
Congenital anomaly	1	1
Intraventricular hemorrhage	0	0
Hyponatremia with meningitis	1	1
Hyperammonemia	1	1
Unknown	0	0
Total	100	100.00

Correlation of etiology with day of onset of neonatal seizures:

Table-14: Correlation of etiology with day of onset of neonatal seizures:

Day of onset of seizures	Birth Asphyxia		Metabolic Hypo-glycemia		Metabolic Hypo-calcemia		Neonatal Meningitis		Others		Total	Percent
	No.	%	No.	%	No.	%	No.	%	No.	%		
1st	40	100	--	--	--	--	--	--	--	--	40	100.00
2nd	26	86.6	2	6.6	1	3.3	--	--	1	3.3	30	100.00
3rd	7	50	7	50	--	--	--	--	--	--	14	100.00
4th	1	33.3	2	66.6	--	--	--	--	--	--	3	100.00
5th	--	--	--	--	--	--	--	--	--	--	--	100.00
6th	--	--	1	50	--	--	1	50	--	--	02	100.00

7th	--	--	1	33.3	--	--	2	66.6	--	--	03	100.00
8-28	--	--	1	12.5	--	--	5	62.5	2	25	8	100.00
days												
Total	74		14		01		08		03		100	100.00

Chi squared for onset of seizures on first three days and more than three days with etiology – $\chi^2=72.84$ with p value of < 0.001 (statistically highly significant for onset of seizures on first three days of life with birth asphyxia).

- The onset of seizures on first day was seen in 46 neonates and all of them were due to birth asphyxia.
- On 2nd day 30 babies developed seizures and 26 (86.6%) were due to birth asphyxia, two were due to hypoglycemia alone, 1 were due to hypocalcemia and one was due to congenital anomaly.

Figure 6- Etiology of Neonatal Seizures

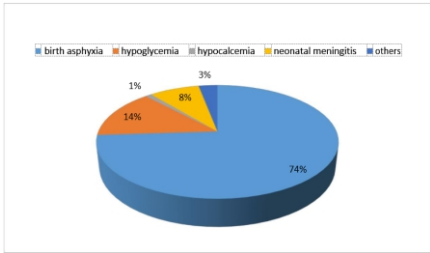
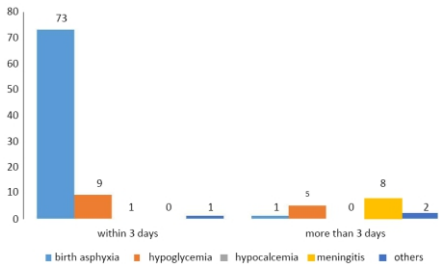


Figure 7- Correlation of etiology with day of onset of neonatal seizures



On third day 14 babies developed seizures and 7 were due to hypoglycemia And 7 were due to birth asphyxia.

From 4th to 7th day again hypoglycemia was the commonest cause, occurring in 4 babies out of 8 babies followed by meningitis seen in 3 babies and one had birth asphyxia.

After first week, 8 babies developed seizures and 5 were due to meningitis.

Seizures during first three days of life has statistically significant correlation with birth asphyxia with P value of < 0.001.

Table-15: Correlation of Etiology with type of neonatal seizures:

Etiology	Type of Seizures										Total	
	Subtle		GTS		MFC		FCS		Mixed			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Birth Asphyxia	35	47.2	19	25.7	8	10.8	7	9.6	5	6.5	74	100.00
Hypoglycemia	7	50	3	21.4	2	14.3	1	7.1	1	7.1	14	100.00
Hypocalcemia	--	--	01	100	--	--	--	--	--	--	01	100.00
Meningitis	2	25	5	62.5	--	--	--	--	1	12.5	08	100.00
Others	--	--	01	33.3	01	33.3	--	--	01	33.3	03	100.00
Total	44		29		11		8		8		100	

Chi squared for neonates with GTS, Subtle seizures and clonic seizures with etiology: $\chi^2=0.27$ – p>0.05 not significant

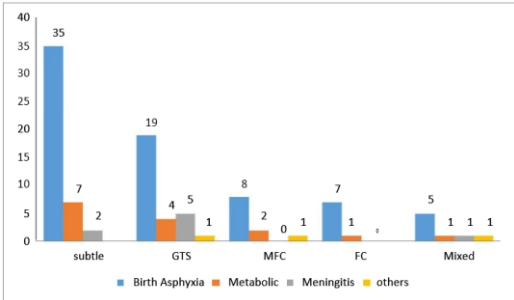
In present study, out of 74 neonates with birth asphyxia, 35 (47.2%) had subtle seizures, followed by GTS in 19 neonates (25.7%) & MFC in 8 (10.8%) neonates.

In neonates with hypoglycemic seizures, 07(50%) babies had subtle seizures followed by GTS in 03 (21.4%) neonates.

In neonates with meningitis (8 neonates), 2 developed subtle seizures (25%) and 5 had GTS (62.5%).

In our study there was no correlation between type of neonatal seizures with the etiology (p>0.05).

Figure-8: Correlation of Etiology with type of neonatal seizures



Correlation of Etiology of Neonatal Seizures to Gestational Age:

Table-16: Correlation of Etiology of Neonatal Seizures to Gestational Age

Gestational Age

Etiology	Term				Preterm		Post-term		Total	
	AGA		SGA							
	No.	%	No.	%	No.	%	No.	%	No.	%
Birth asphyxia	61	82.4	10	13.5	2	2.7	1	1.3	74	100.0
Hypoglycemia	5	35.7	6	42.8	3	21.4	--	--	14	100.0
Hypocalcemia	1	100	--	--	--	--	--	--	01	100.0
Neonatal meningitis	3	37.5	5	62.5	--	--	--	--	8	100.0
IVH	--	--	--	--	0	0	--	--	00	100.0
Others	3	100	--	--	--	--	--	--	03	100.0
Total	73		21		05		01		100	100.0

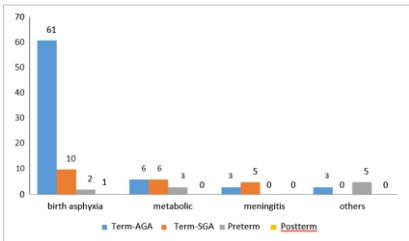
Chi squared for neonates ≥2500 gm & < 2500gm with etiology. $\chi^2=16.99$, P < 0.001.

In the present study, out of 73 term AGA babies, 58 had birth asphyxia, 3 had asphyxia with septicemia, 5 had hypoglycemia, 3 had meningitis, 1 had hypocalcemia, 1 had congenital anomaly and hyperammonemia, hyponatremia with meningitis . Out of 21 IUGR, term babies, 10 had birth asphyxia, 6 had hypoglycemia, one had hypoglycemia with birth asphyxia and 5 had meningitis.

Out of 5 preterm babies, 3 had hypoglycemia, 2 had asphyxia. Out of 1 post-term babies had birth asphyxia.

Low birth weight babies are more prone for seizures due to hypoglycemia with statistically significant P value of < 0.001

Figure-9 Correlation of Etiology of Neonatal Seizures to Gestational Age



Birth Asphyxia

Hypoxic ischemic encephalopathy was found to be the commonest cause of neonatal seizures in our study i.e., in 74 cases (74%). Isolated birth asphyxia was responsible in 70 cases (70%) and in remaining 4 cases, hypoglycemia was also seen (4%).

Type of Delivery:

In our study among the 74 neonates with birth asphyxia 68 were born by normal vaginal delivery, among these in the antenatal history 35 (72%) had prolonged second stage of labour, 26 were (41.9%) unbooked cases, 18 (24.2%) had MSAF and 13 neonates were delivered at home.

15 neonates were delivered by LSCS, and indication was prolonged second stage of labour with fetal distress in 12 cases (80%). 3 neonates were delivered by forceps & all mothers had prolonged second stage of labour.

Day of Onset of Convulsion in Birth Asphyxia:

In our study out of 74 cases of birth asphyxia with neonatal seizures, 40 babies developed convulsion on first day of life (54%), 26 babies (35.1%) developed seizures on second day of life, 7 babies (9.46%) developed seizures on 3rd day and one baby developed seizures on 4th day.

Majority of babies with birth asphyxia developed seizures within first 72 hours of life and more so within first 24 hours of life.

Type of seizures in Birth Asphyxia:

Table-17: Type of seizures in Birth Asphyxia

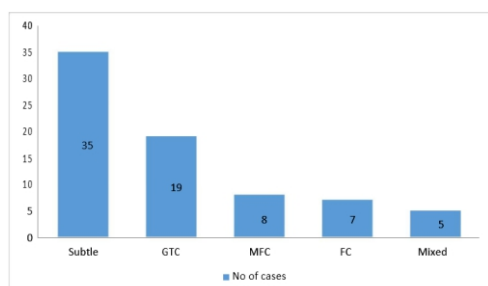
Type of convulsion	No. of Cases	Percent
Subtle	35	47.2
GTS	19	25.7
Multifocal clonic	8	10.8
Focal clonic	7	9.6
Mixed type	5	6.5
Total	74	100.00

In the present study, out of 74 neonates with birth asphyxia, 35 neonates had subtle seizures, 19 babies had GTS, 8 babies had multifocal clonic seizures, 7 babies had focal clonic seizure.

Perinatal and Antenatal factors:

In our study in neonatal seizures with birth asphyxia (74 cases) 35 mothers had prolonged second stage of labour, 18 mothers (24.3%) had meconium stained liquor, 7 mothers had PROM and 4 mothers had PIH.

Figure 10—Type of seizure in Birth Asphyxia



Metabolic Disorders

Hypoglycemia:

Hypoglycemia was the second most common cause of convulsions in neonates in our study. There were 14 babies with hypoglycemia (excluding complicated hypoglycemia associated with birth asphyxia) who presented with seizures.

Two babies with hypoglycemia had onset of seizures on 2nd day, 7 had onset on third day, 2 on fourth day and 1 each on 6th, 7th and 4th week of life. So majority of hypoglycemic convulsions occurred on third day (50%) followed by 4th (6.6%) and 2nd day (6.6%).

Out of 14 babies, 6 were small for gestational age babies (42.8%), 5 were term AGA babies and 3 were preterm babies.

Hypocalcemia:

In present study there was 1 baby with hypocalcemia who presented with seizures on second day of life.

Others:

In our study one baby had hyponatremia with neonatal meningitis, presented during 2nd week of life. One baby had hyperammonemia, presented during 2nd week.

Neonatal Meningitis:

8 babies were diagnosed as neonatal meningitis in our study and was the third most common cause of neonatal seizures. One case had hyponatremia with neonatal meningitis. Three neonates presented between 4th to 7th day and remaining 5 neonates presented between 2nd to 4th week of life.

In babies with meningitis 5 babies had generalized tonic seizures, 2 had subtle seizure, 1 had mixed seizures.

Out of 8 babies with neonatal meningitis, all were born at hospital and 1 mother of a baby had fever before and during delivery. Out of 8 babies with Neonatal meningitis, 5 were IUGR babies.

Congenital anomalies:

- A male baby presented with convulsions (multifocal clonic type) on 2nd day. The baby had prominent frontal and parietal eminence with short unequal limbs, simian crease and microcephaly.

The diagnosis was not known in a patient presenting with seizures (GTS) on 5th day. All the investigations were within normal limits.

Mortality:

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

CONCLUSION

Neonatal Seizures typically signal underlying significant neurological disease and represent non-specific response of the immature nervous system to varied insults. Neonatal seizures are unique & distinctive when compared to seizures in adults because of the immaturity of the nervous system and require separate classification.

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