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Corelation of Various Causes of Neonatal Seizures With Different Patterns of EEG Waveforms

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ABSTRACT

Introduction: *Electroencephalography, or EEG for short, is a non-invasive way to monitor brain activities. It is much helpful in seizures detection and quantification and for assessment of cortical activity.3 In our study we aimed to correlate various causes of neonatal seizures with different patterns of EEG waveforms.* ***Material and methods :*** *the study was conducted in a tertiary care hospital in central India. 120 Full term neonates with clinical seizures were included in the study and an EEG analysis was done for these children.* ***Results:*** *clonic seizures(40%) were the most common type of seizures and birth asphyxia (70%)was the most common aetiology of clinical neonatal seizures. Metabolic causes (hypoglycaemia 71.4%and hypocalcaemia 74%) produced more number of normal , whereas birth asphyxia and meningitis(66.7% each) produced more number of abnormal waveforms on EEG.* ***Conclusion :*** *birth asphyxia and meningitis produce more number of abnormal waveforms on EEG in comparision to metabolic causes of neonatal seizures*

KEYWORDS :

Introduction :

Occurrence of seizure in neonates may be due to very wide range of aetiologies like asphyxia, metabolic disturbances, infection or IVH etc.[1] These seizures may indicate the presence of potentially treatable aetiology and should prompt an immediate evaluation to determine cause and also to institute etiologic specific therapy. In addition, seizure themselves may require emergent therapy since they may affect the infants homeostasis or they can contribute to further brain injury.[2] Electroencephalography, or EEG for short, is a non-invasive way to monitor brain activities. The signal is measured by placing electrodes on the subject's scalp and the potential difference between the electrodes, caused by electrical signals emitted by neurons in the brain, is recorded, and is used to monitor the neurological state of the patient. Although some ictal discharges may have specific significance, a normal interictal EEG indicates good chance of favorable outcome. It is much helpful in seizures detection and quantification and for assessment of cortical activity.[3] In our study we aimed to correlate various causes of neonatal seizures with different patterns of EEG waveforms.

Material and methods :

The study was conducted at a tertiary care hospital in Central India. All the full term appropriate for gestational age neonates less than 28 days of age , who came with history of clinical seizures were included and neonates with congenital defects or low birth weight were excluded from the study. An EEG recording was done during the NICU stay of the neonate and the waveforms were assigned an arbitrary code 0,1,2,3,4,5,6,7,8,9 so that we may have ease in collection, processing and tabulation of the data. The codes were as follows

0 -	Normal
1 –	Focal/ multifocal lateralization
2 –	Positive sharp rolandic waves
3 –	Excessive sharp waves activity
4 –	Periodic low voltage activity
5 –	Multiple poly spike pattern
6 –	Gross asynchronacy/high voltage delta activity
7-	Persistent marked voltage suppression
8-	Burst suppression pattern
9 –	Isoelectric background pattern

Observations and results :

Total 120 neonates were included in the study, out of these 68 (56.66%) cases were male while 52(43.34%) were female, making a male female ratio 1.3:1.

Table : 1 Distribution of cases according to Day of onset of seizures

S.No.	Day of onset of seizures	No. of cases	Percentage	P value/ χ^2 value
1.	< 24 hrs	62	51.67%	p<0.01 and χ^2 =34.32
2.	24-72 hrs	30	25%	
3.	72 hrs -7 days	16	13.33%	
4.	> 7 days	12	10%	
Total		120	100%	

This table clearly shows that the occurrence of seizures during <24 hrs. age is significant (p<0.01 and χ^2=34.32). Ninety two (76.67%) cases had onset of seizure within 72 hrs. of life which is significant for onset in <72 hrs. of life (p<0.01 and χ^2 =76.21).

Table No. 2 Distribution of cases according to type of seizures

S.No.	Type of seizures	No. of cases	Percentage
1.	Clonic	48	40%
2.	Subtle	38	31.67%
3.	Tonic	24	20%
4.	Myoclonic	04	3.33%
5.	Mixed	06	5%
Total		120	100%

Clonic seizures in 48(40%) cases were found most common type of seizures in the present study, followed by subtle 38 (31.67%), Tonic 24 (20%), myoclonic 4(3.33%) and mixed seizures 6(5%). Those cases who had more than 1 type of seizures were considered as having mixed seizures.

Table No. 3 Distribution of etiology of seizures

S.No.	Etiology	No. of Cases	Percentage	P value/ χ^2 value
1.	Birth Asphyxia	84	70%	p< 0.01 and χ^2 = 119.38
2.	Hypocalcemia	14	11.67%	
3.	Hypoglycemia	08	6.67%	
4.	Meningitis	12	10%	
5.	Other	02	1.66%	
	Total	120	100%	

Birth asphyxia 84(70%) was the most common etiology observed in the study followed by metabolic 22(18.34%), CNS infection 12(10%) and then other cases 2(1.66%). The other cases include intraventricular hemorrhage or for which the etiology could not be found.

Birth asphyxia ($p<0.01$, $\chi^2 = 119.38$) was significantly associated as the cause seizures in the present study.

Table No. 4 Distribution of etiology with day of onset of seizures

S. No.	Day of onset	Birth asyphyxia	Hypocalcemia	Hypoglycemia	Meningitis	Others	Total
		No. (%)	No.(%)	No.(%)	No.(%)	No.(%)	No.
1.	< 24 hours	56(66.7%)	04(28.6%)	02(25%)	00(0%)	00(0%)	62
2.	24hours-72hrs	26(30.9%)	04(28.6%)	00(0%)	00(0%)	00(0%)	30
3.	72 hrs-7 days	02(2.4%)	04(28.6%)	06(75%)	04(33.3%)	00(0%)	16
4.	> 7 days	00(0%)	02(14.2%)	00(0%)	08(66.7%)	02(100%)	12
Total		84(100%)	14(100%)	08(100%)	12(100%)	02(100%)	120

Total 66.7% cases of birth asphyxia had seizures within 24 hrs. of age also most of the cases having seizures within 24 hrs. of age were due to birth asphyxia. Most of the seizures due to metabolic disturbances were found to be of onset between > 24 hrs. to < 7 days of age. Total 66.7 % cases of meningitis had seizures after 7 days of age.

Table No. 5 Distribution of pattern of EEG with etiology of seizures

S. No.	EEG pattern	Birth asyphyxia	Hypocalcemia	Hypoglycemia	Meningitis	Others	Total
		No. (%)	No.(%)	No.(%)	No.(%)	No(%)	No.
1.	Normal	28(33.3%)	10(71.4%)	06(75%)	04(33.3%)	00(0%)	48
2.	Focal/ multifocal lateralization	08(9.5%)	2(14.3%)	00(0%)	00(0%)	00(0%)	10
3.	Positive sharp rolandic waves	04(4.7%)	00(0%)	00(0%)	00(0%)	00(0%)	04
4.	Excessive sharp waves activity	00(0%)	00(0%)	02(25%)	02(16.7%)	00(0%)	04
5.	Periodic low voltage activity	04(4.8%)	2(14.3%)	00(0%)	00(0%)	00(0%)	06
6.	Multiple poly spike pattern	20(28.8%)	00(0%)	00(0%)	04(33.3%)	2(100%)	26
7.	Gross asynchronacy/ high voltage delta activity	02(2.38%)	00(0%)	00(0%)	00(0%)	00(0%)	02
8.	Persistent marked voltage suppression	08(9.5%)	00(0%)	00(0%)	00(0%)	00(0%)	08
9.	Burst suppression pattern	08(9.5%)	00(0%)	00(0%)	02(16.7%)	00(0%)	10
10.	Isoelectric background pattern	02(2.38%)	00(0%)	00(0%)	00(0%)	00(0%)	02
		84 (100%)	14(100%)	08(100%)	12(100%)	02(100%)	120

Fourty eight cases who had normal pattern neonatal EEG, out of them 28 cases were of birth asphyxia. Seventy two cases had abnormal pattern EEG and most of the abnormal pattern EEG were found in birth asphyxia. Most of the cases of hypocalcemia and hypoglycemia were having normal pattern EEG.

Discussion :

This study shows that the occurrence of seizures during <24 hours is most common and is highly significant ($p<0.01$ and $\chi^2=34.32$). In our study, ninety two (76.67%) cases had onset of seizure within 72 hours of life which is highly significant for onset in <72 hours of life ($p<0.01$ and $\chi^2 = 76.22$). Similarly in a study of neonatal seizures by **Ronen Gabriel et al** onset of seizures on first day of life was 36%, 64% had onset of seizures within first 48 hours, and 83% within first week of life.

Clonic seizures in 48(40%) cases were found most common type of seizures in the present study, followed by subtle 38 (31.67%), tonic 24 (20%), myoclonic 4(3.33%) and mixed seizures 6(5%). Those cases who had more than 1 type of seizures were considered as having mixed seizures. Similarly **Ajay kumar et al**[5] and **Tekgul et al**[6] also found that the clonic seizure to be the most common type of seizures.

Brunquell et al[7] and **Lakra Mahaveer et al**[8] showed that subtle seizures are the most common type of neonatal seizures but in the present study clonic seizures were found to be most common, it may be due to the fact that Subtle seizures are difficult to recognize and also difficult to interpret, as they may be normal neonatal activity. This study included only the term babies while the subtle seizures are primarily seen in preterms babies.

The diagnosis of seizures in this study was based on clinical description. The variability inherent to the capacity of clinically identifying neonatal seizures has been evaluated previously; showing reliability in recognizing seizures based on the analysis of medical records. It is widely known that the gold standard to recognize neonatal seizures is video-EEG.

A systematic review of literature of previous cohort study by **Nunes ML et al**[9] on neonatal seizures, was performed they found that from the 36 selected studies, 24 (67%) studies were based only on clinical diagnosis of seizures, 7 used confirmed EEG seizures and only 2 of them were based on video-EEG. The interesting finding of this study is that the clinical profile of the newborns, risk factors and outcome were similar, independently of the methodology used to diagnose the seizures. In a study by **Rushda Aftab et al**[10] most common seizures noted were multifocal clonic constituting 50% of all cases, while tonic seizures were present in 25.26% and subtle seizures were present in 12.63% cases.

Birth asphyxia 42(70%) was the most common etiology observed in the study followed by hypocalcemia 14(11.7%), CNS infection 12(10%), hypoglycemia 8 (6.7%) and then other causes 2(1.66%) . The other cases include intraventricular hemorrhage or for which the etiology could not be found. Birth asphyxia ($p<0.01$, $\chi^2 = 119.38$) was significantly associated as the cause of seizures in the study. Birth asphyxia as the commonest cause of neonatal seizures in studies by **Soni Arun et al** seen in 76.9% of cases and **Ronen Gabriel et al** seen in 40% of cases according to most of the studies birth asphyxia is the commonest cause of neonatal seizures followed by metabolic or infectious causes. Intracranial hemorrhage constitutes small percentage of seizures.

In this study the cases having seizures within 24 hours of age were due to birth asphyxia(66.67%). Most of the seizures due to hypocalcemia and hypoglycemia were found to be of onset between > 24 hours to < 7 days of age. Eight (66.67%) cases of meningitis had onset of convulsion at the age >7 days.

In a study of neonatal seizures by **Rose Arthur L et al**[11], majority

of babies with perinatal anoxia convulsed on first day of life (5/10 – 50%), hypoglycemic neonates convulsed on second and third day (5/7 – 71%), majority of neonates with CNS infection convulsed at the end of first week and early second week (9/13 – 69%) and babies with hypocalcemia present with convulsions during first and second day of life (6/28) and again during late first week and second week (19/28).

Birth asphyxia usually presents with seizures within first three days of life, preferably within first 48 hours. Hypoglycemia presents on second and third day, as there is depletion of glycogen stores. Hypocalcemia presents on first and second day if it is early onset hypocalcemia and later i.e., late first week and second week, if it is late onset hypocalcemia. Neonatal meningitis presents with seizures during late first week and second week.

In this study 4 out of 7 cases of hypocalcemia had onset of seizures between >3days to <7 days. This is due to feeding of neonates with phosphate rich milk e.g., formula feeding. Hypocalcemia should be diagnosed early and treated with IV calcium.

In a study by **Cockburn F et al**[12] serum calcium was low in neonates who were top fed, than the babies who were breastfed. **Tushar Parikh B et al**[13], showed that late onset meningitis is more common than early onset meningitis.

One case who was having birth asphyxia was died at the age of 2 months, after discharge from the hospital. While no death was reported from non-asphyxia cases. This shows that the hypocalcemia, hypoglycemia and meningitis if corrected timely are associated with more chances of survival.

Forty eight cases who had normal pattern neonatal EEG, out of them 28 cases were of birth asphyxia. Seventy two cases had abnormal pattern EEG and most of the abnormal pattern EEG were found in birth asphyxia. Early workers usually did not correlate specific abnormalities recorded in standard EEG to the stage of HIE but noted whether it is normal or abnormal. **Rose and Lombroso**[11] reported abnormalities in HIE in 70% cases while **Mizrahi and Kallaway**[14] reported it 46.3%.

In our study 4 (28.56%) cases of hypocalcemia had abnormal EEG. Abnormal records in standard EEG in hypocalcemia has been reported in 34.4% by **Keen and Lee**[15] and in 27.8% by **Rose and Lombroso**[11]. In the present study in case of hypoglycemia only 1 (25%) case had abnormal EEG. Abnormal records in standard EEG in hypoglycemia has been reported in 42.9% cases by **Rose and Lombroso**[11] and in 4.9% cases by **Mizrahi and Kallaway**[14]. In meningitis 33.33% had normal EEG while 66.67% had abnormal EEG.

Conclusion :

In neonatal seizures due to birth asphyxia and meningitis , most of the times EEG pattern is abnormal , whereas in metabolic causes the EEG pattern is normal in more number of cases comparatively.

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