An electroencephalographic study in birth asphyxia and correlation of electroencephalographic pattern with neurodevelopment outcome at 6-month age

Ashish Jain[1], Jyotsna Shrivastav[2], Jyoti Prajapati[3]

From [1]Associate Professor, Department of Paediatrics, Bundelkhand Medical College, Sagar, [2]Professor and Head, Department of Paediatrics, Gandhi Medical College, Bhopal, [3]Assistant Professor, Department of Pediatrics, MGM Medical College and MY Hospital, Indore, Madhya Pradesh, India

Correspondence to: Dr. Jyoti Prajapati, Department of Pediatrics, MGM Medical College and MY Hospital, Indore, Madhya Pradesh, India. E-mail: drjyotimdpedia108@gmail.com

Received - 29 April 2018 Initial Review - 18 May 2018 Accepted - 19 August 2018

ABSTRACT

Background: Perinatal asphyxia is one of the most common medical emergencies of newborn and important cause of neonatal morbidity and mortality. In India, about 1 million babies suffer from birth asphyxia every year, and it is responsible for nearly 28.8% of the neonatal deaths and the subsequent major sequelae. **Objectives:** The objective of the study was to evaluate the clinico-etiological and electrophysiological profile of neonates with birth asphyxia and its correlation with the neurodevelopment outcome at 6 months of age. **Methods:** In this prospective observational follow-up study, 50 neonates of >35 weeks of gestation with a history of birth asphyxia were included. Electroencephalographic (EEG) was performed within the first 72 h of life or as soon as neonate was stable. Follow-up visits were scheduled as per NNF guidelines at 6, 10, and 14 weeks, 3 and 6 months of age. Detailed neurological examination, neurodevelopment and tone were assessed by Denver II and Amiel–Tison method, respectively, on every visit. **Results:** All neonates were on hypoxic-ischemic encephalopathy (HIE) Stage I had normal EEG recording; 36.7% with HIE Stage II had abnormal EEG recording while 100% the neonates of HIE Stage III showed abnormal EEG. All neonates, who had normal EEG recording, survived, and 96.5% (n=28) of them show normal neurodevelopment outcome. 3.7% (n=1) showed developmental delay. All the neonates who had abnormal background on EEG showed adverse outcome. 50% of them expired and rest 50% had abnormal neurodevelopment outcome on follow-up. **Conclusion:** The severity of encephalopathy in asphyxiated neonates correlates well with the abnormalities on EEG records.

Key words: *Electroencephalographic, Hypoxic ischemic encephalopathy, Neurodevelopment*

Perinatal asphyxia is defined as an insult to fetus or newborn due to lack of oxygen and/or a lack of perfusion to various organs of sufficient magnitude and duration leading to >33 fleeting functional and/or biochemical changes. Hypoxic ischemic encephalopathy (HIE) describes encephalopathy with objective data to support a hypoxic/ischemic mechanism [1]. Perinatal asphyxia is one of the most common medical emergencies of newborn and important cause of neonatal morbidity and mortality [2]. The incidence of birth asphyxia, in developed countries, has declined in past few years; however, in developing countries, perinatal asphyxia still remains a major cause of neonatal morbidity and mortality, and overall incidence varies from 1 to 8.5% [3-5]. The burden of the problem can be estimated by fact that in India, about 1 million babies suffer from birth asphyxia every year and it is the leading cause of neonatal mortality accounting for nearly 28.8% of neonatal deaths and the subsequent major sequelae causing physical and mental handicap [2].

Electroencephalographic (EEG) is accepted as positive diagnostic procedure along with neurological evaluation to detect the brain damage in neonates. It reveals the electrical activity of cerebral cortex and reflects the electrophysiological integrity of the cerebral hemisphere. EEG monitoring has two main indications: (a) To assess the subclinical seizure activity that may require treatment and (b) to evaluate the background EEG to aid in prognosis [4]. The objective of the present study was to evaluate the clinico-etiological and electrophysiological profile of neonates with birth asphyxia and to assess its correlation with the neurodevelopment outcome at 6 months of age.

MATERIALS AND METHODS

The present study was a prospective, observational follow-up study conducted at the neonatal intensive care unit (NICU) of a tertiary care hospital over 1 year period. A total of 50 newborns admitted in NICU, with birth asphyxia were enrolled in this study.

The included patients had gestational age at birth ≥35 weeks with a history of delayed cry and any of the following [1]: Cord blood pH <7.0 or base deficit >12 of cord or first blood gas, persistence of low Agar score <3 for >5 min, signs of neonatal neurological dysfunction, and evidence of multiple organ involvement. All stillborn patients and those with congenital infections, anomalies, suspected metabolic abnormality, and early onset sepsis were excluded from the study. This study was given Ethical Clearance by Ethical Committee, and written consent was taken from the parents of newborn before enrolment.

A detailed antenatal, perinatal history, and sociodemographic characters were recorded on a predesigned pro forma. Complete neurological examination was performed on admission to NICU and was followed up to assess the progress of encephalopathy. The patients were classified into Stages I, II, or III of HIE according to Sarnat and Sarnat clinical staging systems [6]. Antiepileptic drugs were used to control seizures according to the standard guidelines. Conventional EEG was performed within the first 72 h or as soon as neonate was stable. EEGs were performed using full 10–20 montage with a chart speed of 30 mm/s on a 16 channel Medelec profile model machine using a calibration of 50 μv/7 mm and were recorded by the same technician and analyzed by the same physician to avoid inter-observer variation.

During hospitalization and after discharge, stimulation therapy was conducted by parents themselves under supervised education in the pediatric department in various domains of intervention, i.e., motor, visual, auditory, tactile, and environmental. Follow-up visits were scheduled as per NNF guidelines [7] at 6, 10, and 14 weeks, and 3 and 6 months. Detailed neurological examination, neurodevelopment and tone were assessed by Denver II and Amiel–Tison method, respectively, on every visit.

Denver II is World Wide popular simple model to assess child development in four domains gross motor, fine motor-adaptive, language, and personal social. It consists of 125 items in 4 development domains; each item has 25th, 50th, 75th, and 90th mark. Infant age is plotted by age line in the chart in each domain. Test was interpreted normal if child was able to pass 3 items on left side of age line (above 75% mark) and maximum number of 1 cautions (age line falls between 75th and 90th and child fails or refuses that item) and abnormal if child fail an item that falls on left side of age line at 90% mark and has 2 or more cautions [8]. Amiel–Tison method is the screening test for neuromotor assessment. Hypertonia or hypotonia was defined by measuring adductor, popliteal, ankle dorsiflexion, and scarf sign. Hypertonia in upper and lower limb is defined when tested angle is restricted on less than age-specific norms [9] adductor, and popliteal angels are best studied and so were used for assessment of tone in this study.

Age-specific Norms Angles for Amiel–Tison Tone Assessment

Months	3	6	9	12
Adductor angle	40–80	70–110	100–140	130–150
Popliteal angle	80–100	90–120	110–160	150–170

Abnormalities in EEG are classified as mild, moderate, and severe. (1) Mild abnormalities include dysmaturity, excessive sporadic sharp transients, and background disorganization in the absence of marked amplitude suppression or an electroconvulsive discharge. (2) Moderate abnormalities include abnormal or absent sleep-wake cycles, excessive discontinuity, persistent asymmetry, and epileptiform abnormalities including seizures. (3) Severe abnormalities include persistent low voltage, background suppression, and inactive/isoelectric EEG and always reflect a marked disturbance in cerebral function and indicate an unfavorable outcome [4,5,10,11].

Background suppressions are as follows: (1) Isoelectric EEG/electrocerebral silence - indicates severe cerebral dysfunction and (2) persistent low voltage - extremely low voltage, with amplitude <5 μV or with no perceptible cerebral activity. Progressive decline in amplitude is a particularly grave sign and may end in electrocerebral silence. (3) Burst suppression is characterized by periods of excessively suppressed background (≤5 μV) interrupted by bursts of abnormal activity. It is normal in premature (21–32 week) and continues until 34 weeks, beyond this, it is always associated with an unfavorable outcome and has been correlated with severe neuronal necrosis at autopsy.

A repetitive rhythmic activity of >10 s duration identifies an electrographic seizure, with a sharp beginning, middle, and end with clear evolution. Most of the electroconvulsive discharges are focal in onset; some remain focal and others generalized. A constant focus may indicate a local brain disturbance, especially cerebral infarction or hemorrhage in the term newborn [4-6].

Data were recorded and analyzed using software SPSS 23 for windows and variables were analyzed with t-test and Chi-square. Critical levels of significance of the results were considered at 0.05 and $p<0.0001$ was considered highly significant.

RESULTS

A total of 50 neonates were recruited in the study (67.5% male and 32.5% female). Of 50 neonates, preterm (26%), term (62%), and post-term (12%) while low birth weight was 42% and 58% were AGA neonates. The mean birth weight and gestational age for preterm infants were 2.23±0.56 g and 35.82±1.23 weeks, respectively, for full term; it was 2.52±0.98 g and 37.88±1.78 weeks, and for post-term, was 2.89±0.86 g and 42±1.46 weeks. In the present study, 67.5% (n=27) babies were born by vaginal delivery while 32.5% (n=13) were born by LSCS delivery in study group ($p<0.05$).

Details of the HIE staging and outcome of these neonates are given in Table 1. All neonates with HIE Stage I had normal EEG recording, 36.7% with HIE - Stage II had abnormal EEG while 100% the neonates with HIE Stage III showed abnormal EEG. Thus, the severity of encephalopathy in asphyxiated neonates corelated well with abnormalities on the EEG record (Table 2). All neonates who had normal EEG recording survived and 96.5% (n=28) of them show normal neurodevelopment outcome while 3.7% (n=1) showed developmental delay. All the neonates, who had abnormal background on EEG showed adverse outcome.

50% of them died and rest 50% had abnormal neurodevelopment outcome on follow-up (Table 3).

DISCUSSION

In our study, total 50 neonates were included, and there was clear male preponderance in the study group. Similar results were also observed in other studies that male babies are more prone to develop complication in response to various degree of perinatal neurological insults and adversities due to altered intrauterine metabolic environment, different times of postnatal maturation, or differences in epigenetic transmission [12-16].

In the present study, LSCS delivery and incidence of birth asphyxia were statistically significant ($p<0.05$). Other studies [16,17] also reported a higher incidence of asphyxia (38.5%) in cesarean section, and it is attributed to higher number of non-booked cases and high-risk indication for caesarian section. This is in accordance with the present study as the majority of cesarean sections (12 of 13 LSCS) were emergency section with some high-risk factors as primary indications for cesarean sections.

In the present study, the maximum number of cases (62%) had Stage II HIE, 20% were on Stage I, and 18% cases were in Stage III. This observation was similar to the results of other studies [10,17]. In the present study, of 31 cases of HIE-II, 12.9% (n=4) cases had seizures within 6 h of birth, 25.8% (n=8) had seizures within 6–12 h while 54.9% (n=17) cases had seizure after 12 h of life. 6.5% (n=2) cases had no seizures. In HIE Stage III, 2 had seizures, while none of the neonate in HIE Stage-I had seizure. In this study, all of the HIE III babies and 5 HIE II baby were on phenobarbitone therapy to control clinical seizures.

According to various studies, majority of the post asphyxial seizures occur within first 24 h after neurological insult, 50% or more occurring within 12 h of birth [5,6,10,18]. In the present study, among the 31 neonates who had seizures, multifocal clonic seizure was the most common type present in 45.16% (n=14) cases. This was followed by tonic seizures 22.58% (n=7), subtle seizures 19.35% (n=6), myoclonic 9.68% (n=3), and focal clonic seizure in 3.23% (n=1) cases. Although many infants had >1 seizures type, the single most prominent seizure type was assigned to the infant in each case.

Along with neurological dysfunction other systemic manifestations observed were metabolic abnormality in 40% (n=16) of cases, acute renal failure in 17.5% cases (n=7), respiratory distress 15% cases (n=6), liver dysfunction in 12.5% cases (n=5), meconium aspiration syndrome (MAS), necrotizing enterocolitis (NEC), DIC, apnea, and hyperbilirubinemia in 2.5% cases each (n=1). Various studies also reported similar complications as MAS, respiratory distress syndrome, NEC, hyperbilirubinemia, and DIC in cases of birth asphyxia [6,16,17]. The exact contribution of hypoglycemia and hypocalcemia, as a cause of seizure in babies with birth asphyxia, is uncertain. Attempts were made to exclude such episodes of seizure by prior administration of calcium and dextrose before attributing the cerebral asphyxia as the cause of seizures.

On assessing the role of EEG as the predictor of outcome; in mild encephalopathy, EEG was normal in all 10 cases, and there was no mortality or neurodevelopment abnormality. In HIE Stage II, 38.71% (n=12) of 31 EEG showed abnormality while in HIE - Stage III, EEG could be done only in 5 cases and all of them showed severe background abnormality.

EEG was done in total 46 cases (3 expired) and was normal in 63% (n=29). On neurodevelopment follow-up of

Table 1: Neurological outcome in cases of birth asphyxia on follow-up

HIE Stage	Number of cases	Outcome		p
		Normal (%)	Abnormal (%)	
I	10	10 (100)	0 (0)	
II	29	21 (72.4)	8 (27.6)	p<0.05*
III	3	0 (0)	3 (100)	
Total	42	31 (73.8)	11 (26.2)	

HIE: Hypoxic-ischemic encephalopathy

Table 2: EEG abnormality in cases of birth asphyxia

EEG (abnormal/total)	Birth asphyxia		
	HIE-I (0/10)	HIE-II (12/31)	HIE-III (5/5)
Severe background abnormality	0	5	5
Moderate EEG abnormality (electroconvulsive discharge)			
Generalized	0	0	0
Multifocal	0	5	0
Focal	0	2	0
Mild EEG abnormality			
Spikes	0	4	0
Sharp waves	0	2	0
Both	0	1	0

HIE: Hypoxic-ischemic encephalopathy, EEG: Electroencephalographic

Table 3: Various EEG patterns and neurological outcome

EEG pattern	Number of cases	Outcome		p
		Normal (%)	Abnormal (%)	
Normal EEG	29	28 (96.5)	1 (3.5%)	
Abnormal EEG	17	3 (17.7)	14 (82.3)	p<0.05*
Severe background abnormality	10	0 (0)	10 (100)	
Moderate EEG abnormalities	5	2 (40)	3 (60)	
Mild EEG abnormality	2	1 (50)	1 (50)	
Total	46	31	15	

EEG: Electroencephalographic

these infants with normal EEG record, only 3.5% (n=1) had abnormal neurodevelopment. Abnormal EEG was obtained in 17 cases, and 82.3% (n=14) of these showed adverse outcome. Background abnormality was seen in 10 cases; 3 of these expired and 5 showed gross neurodevelopment delay on follow-up. Total 5 cases showed multifocal discharge and 60% (n=3) cases showed neurodevelopment sequele and 50% (n=1) of 2 cases of focal discharge had neurodevelopment sequele.

Various studies found that along with seizure etiology, the outcome is strongly associated with background EEG pattern. While normal/mildly abnormal neonatal EEG had favorable prognosis, moderate/severely abnormal EEG has a worse prognosis [3,10,13,18]. It is clearly demonstrable in the present study that the cases with background abnormality, 50% died and remaining 50% had neurodevelopment sequel. Similar observations were seen in other studies [17,18] where they showed that in infants with asphyxia and with electrographic seizures are more likely to die of neurological causes or have microcephaly or severe cerebral palsy. It is also observed in that severely abnormal EEG background activity at 36 h and 48 h after birth is associated with a severe injury on magnetic resonance imaging and abnormal neurodevelopmental outcome [10,11,16,18]. In a full-term asphyxiated infants, immediate and long-term prognosis is strongly associated with suppression of background and burst suppression pattern. Normal neonatal EEGs are highly correlated with favorable outcome. Burst suppression, low voltage, and flat trace in the EEG of term neonates with HIE most accurately predict long-term neurodevelopment outcome [3-5,11,18].

Earlier studies also demonstrated that asphyxiated infants, whose abnormal EEG fails to revert to normal, either die or were found to have significant neurological impairment [16-18]. In the present study, a mortality rate of 16% was found in asphyxiated newborns. Various studies also observed that asphyxiated newborns have high mortality results comparable with present study [11,16,17].

CONCLUSION

According to our study, abnormal background recording is associated with increased mortality and abnormal neurodevelopment. We also observed that abnormal discharge with normal background activity has a better prognosis as compared to abnormal background recording in EEG. Thus, neonatal EEG is an important tool not only for staging encephalopathy in cases of asphyxia but also a significant prognostic value.

REFERENCES

1. Paul VK, Deorari AK, Agarwal R. AIIMS Protocols in Neonatology. New Delhi: JP Books; 2014.
2. National Neonatology Forum of India. National Neonatal perinatal Database-Report for the Year 2002-3. New Delhi: NNF India; 2005.
3. Biarge MM, Sebastian DJ. Predicting motor outcome and death in term hypoxic ischemic encephalopathy. Neurology 2011;76:2055-61.
4. De Weerd AW, Despland PA, Plouin P. Neonatal EEG. The international federation of clinical neurophysiology. Electroencephalogr Clin Neurophysiol Suppl 1999;52:149-57.
5. Toso PA, Alvaro J. Clinical utility of early amplitude integrated EEG in monitoring term newborns at risk of neurological injury. J Pediatr 2014;90:143-8.
6. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976;33:6967057.
7. Evidence Based Clinical Practice Guidelines; 2010. Available from: http// www.nnfpublication.org. [Last accessed on 2018 Apr 23].
8. Jeong SU, Kim GC. The validity of the Bayley-III and DDST-II in preterm infants with neurodevelopmental impairment: A pilot study. Ann Rehabil Med 2017;41:851-7.
9. Tison A. Neurological evaluateion of maturity of newborn. Arch Dis 43;89:1968.
10. Weeke LC, Boylan GB Eur. Role of EEG background activity, seizure burden and MRI in predicting neurodevelopmental outcome in full term infants with hypoxicischaemic encephalopathy in the era of therapeutic hypothermia. J Paediatr Neurol 2016;20:855-64.
11. Tsuchida TN. EEG background patterns and prognostication of neonatal encephalopathy in the era of hypothermia. J Clin Neurophysiol 2013;30:122-5.
12. Monod N, Pajot N. The neonatal EEG: Statistical studies and prognostic value in full term and preterm babies. EEG Clin Neurophys 1972;32:529-544.
13. Holmes G, Rowe J, Hafford J, Schmidt R, Testa M, Zimmerman A. Prognostic value of the electroencephalogram in neonatal asphyxia. Electroencephalogr Clin Neurophys 1982;53:60-72.
14. Di Pietro JA, Kivlighan KT. Prenatal antecedents of newborn neurological maturation. Child Dev 2010;81:115-30.
15. Di Pietro JA, Voegtline KM. The gestational foundation of sex differences in development and vulnerability. Neuroscience 2015;7:68.
16. Harbert MJ, Brown MK. Factors Associated with mortality in the era of therapeutic hypothermia for neonatal encephalopathy. Ann Neurol 2015;2015:S186.
17. Kumar A. Clinico-etiological and EEG profile of neonatal seizures. Indian J Pediatr 2007;74:33-7.
18. Murray DM, Boylan GB, Ryan CA, Connolly S. Early EEG findings in hypoxicischemic encephalopathy predict outcomes at 2 years. Pediatrics 2009;124:e459-67.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Jain A, Shrivastav J, Prajapati J. An electroencephalographic study in birth asphyxia and correlation of electroencephalographic pattern with neurodevelopment outcome at 6-month age. Indian J Child Health. 2018; 5(8):518-521.