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Original Article

Paediatrics Section

Early Electroencephalogram as Predictor of Neuromotor Outcome in a Term Newborn with Hypoxic Ischaemia Encephalopathy- A Prospective Cohort Study

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ABSTRACT

Introduction: Birth asphyxia is the leading cause of neonatal morbidity and mortality globally. Early prediction of neuromotor problems in babies with Hypoxic Ischaemic Encephalopathy (HIE) allows parental counseling regarding treatment continuation, better utilisation of limited resources and prompt referral for early intervention services to so that the best possible outcomes can be achieved.

Aim: To investigate the role of early Electroencephalogram (EEG) background activity in prediction of cerebral palsy, epilepsy and developmental delay in term newborn with HIE and also to check the association of EEG background activity with Hammersmith Neonatal Neurological Examination (HNNE), Hammersmith Infant Neurological Examination (HINE) score and various short-term and long-term outcome.

Materials and Methods: This prospective clinical study was conducted in Neonatal Intensive Care Unit (NICU) of Department of Paediatrics, Shyam Shah Medical college and associated Gandhi Memorial Hospital, Rewa (MP) during April 2019 to June 2020. Total 81 term neonates with HIE underwent conventional EEG within six hours of birth using International 10-20 system, (modified for neonate) for electrode placement. At the time of discharge HNNE was performed. On follow-up (6 to 12 months), cerebral palsy was evaluated using HINE and modified Ashworth score, Developmental delay by Development Assessment Scale for Indian Infant (DASII) scale and for epilepsy by clinical history and EEG background activity. Association between EEG background activity, HNNE, HINE score and various short-term and long-term outcome was calculated using Chi-square test and Fisher's-exact test.

Results: In present study, out of 81 cases, 58 (71.6%) cases were male and 23 (28.4%) cases were female with mean Gestational Age (GA) of 39 weeks. A total of 57 neonates were discharged successfully after stay of mean duration 13.8 days in NICU. All neonates with normal/mildly abnormal EEG background activity had 100% survival rates whereas only 68.2% (15) and 37% (10) could be discharged from moderately abnormal and severely abnormal EEG background activity group. Out of discharged patients none with severely abnormal background had optimal HNNE whereas 75% (24) of mildly abnormal EEG had optimal HNNE score. Mean HNNE and HINE score was significantly lower in newborns with severely abnormal EEG (mean score 20.8) as compared to normal EEG group (mean score 30.3). Severely abnormal EEG at birth had significant association with cerebral palsy (p-value<0.0001), epilepsy (p-value= 0.003) and developmental delay (p-value<0.001) as compared to moderately and mildly abnormal EEG background activity in newborns with HIE.

Conclusion: EEG within six hours of birth in term neonate with HIE has very high sensitivity and Negative Predictive Value (NPV) in predicting short-term outcome as death, poor neurological outcome and long-terms outcome as cerebral palsy, epilepsy and developmental delay.

Keywords: Cerebral Palsy, Developmental delay, Epilepsy, Neurological disorder

INTRODUCTION

Birth asphyxia is a leading cause of neonatal mortality and morbidity globally. It accounts for 1-8 and 26 out of every 1000 live births in developed and developing country respectively [1]. In India, estimated incidence of birth asphyxia is 12-16% [2]. Despite of several advancements in perinatal care it is still a major health issue of newborns even in developed countries.

The term HIE is used for neonatal encephalopathy which includes altered level of consciousness and other signs of brainstem and/or motor dysfunction where aetiology is hypoxic injury to the brain [3]. At birth it can lead to seizures, apnoea, bradycardia, feeding difficulties and multiorgan failure whereas on long-term it can lead to motor e.g., cerebral palsy, sensory such as hearing loss and visual impairment, cognitive, behavioural and neurodevelopmental abnormalities [4]. There are high incidence of cerebral palsy, intellectual disability and epilepsy among survivors of HIE. Prediction of the long- term outcome of asphyxiated term infants shortly after birth is challenging. Approximately, 20-30% neonates with HIE dies in neonatal period and 33-50% of survivor develops neurodevelopmental abnormality [1].

EEG abnormalities can be used to aid outcome prediction for infants with HIE [5]. Many characteristics of EEG recordings have been examined for their ability to predict outcomes, and several different grading systems exist [6,7]. Most studies concluded that mild abnormalities predict a normal neurologic outcome in 90% of cases and severe abnormalities predict a poor neurologic outcome (death or severe disability) in almost all cases [6-8]. The prognosis of those with moderate EEG abnormalities is uncertain. The incidence of poor outcomes for these infants ranges from 30% to 60%, depending on the grading system used and the timing of EEG recording [8].

There are several new technologies like cranial ultrasound, CT scan, Magnetic Resonance Imaging (MRI) available to know extent of cerebral injury during neonatal period and predict long-term

neuromotor outcome, but these modalities are not useful until 24 hours of birth or more [9], also in developing countries like India, besides it is not always feasible to perform these studies in clinically unstable babies in early neonatal period [10,11]. De Wispelaere LA et al., concluded that EEG has higher predictive value as compared to MRI for neuromotor outcome in HIE [12].

EEG has been widely used in the diagnosis of seizures in newborn and monitoring of neonates who are already on antiepileptic drugs but only few studies have been carried out during the first few hours following asphyxia and all have been performed in specialist units [13,14]. Also, we couldn't find studies associating early neonatal EEGs with HNNE and HINE scores.

Hence, the present study was done to investigate the role of early EEG background activity in prediction of cerebral palsy, epilepsy and developmental delay in term newborn with HIE and also to check the association of EEG background activity with HNNE, HINE score and various short-term and long-term outcome.

MATERIALS AND METHODS

The present prospective clinical study was conducted in NICU of Department of Paediatrics, Shyam Shah Medical College Rewa, Madhya Pradesh, India. Study was conducted during April 2019 to June 2021 after ethical committee approval number (s.no.9396/SS/PG/MC/2019). The parents of infants fulfilling the inclusion criteria were approached and written informed consent was obtained.

Inclusion criteria: Neonates with Gestational Age (GA) of 37-42 weeks, postnatal age <6 hours. Any one of the following: fetal distress at delivery, need for resuscitation at birth or APGAR score <6 at 5 min, metabolic acidosis pH <7.1 or base deficit >10.8 [15,16] were included.

Exclusion criteria: Babies with congenital heart disease and other major congenital anomaly, inborn errors of metabolism and genetic syndromes were excluded from study.

Sample size calculation: It was calculated using the following formula based on the prevalence of birth asphyxia in India [2].

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} * p^*q}{d^2} = \frac{(1.96)^2 * 12 * 88}{(7.5)^2} = 72 \simeq 81$$

$Z^2_{1-\frac{\alpha}{2}}$= Critical value at 95% confidence level (standard value =1.96)

p= Prevalence of birth asphyxia in India accident (12%) [2]

q = 100-p

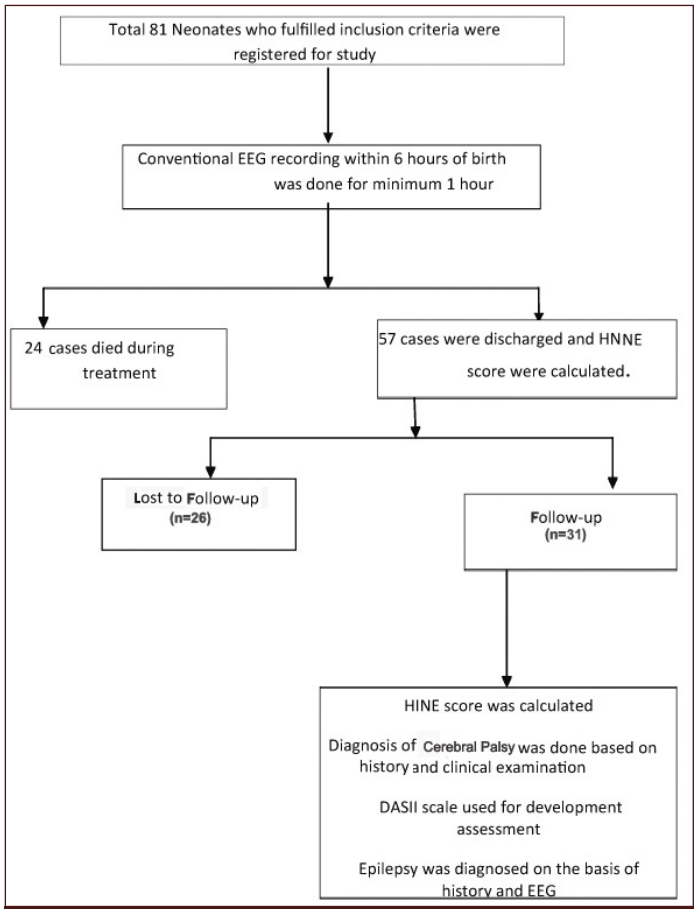
d= Margin of error (7.5%)

β= 80%

Procedure

EEG recording of all enrolled babies was done within six hours of birth using, Root Mean Square (RMS) electronic EEG recorders (Medicare Systems Pvt Ltd) for minimum of one hour duration using International 10-20 system, for electrode placement, modified for neonate [17]. The EEG background activity was graded into 4 groups according to previously defined criteria with some adaptation to the new American Clinical Neurophysiology Society Guideline (ACNS) guidelines by trained paediatric neurologist experienced in neonatal EEGs [17,18]. normal/mildly abnormal (Continuous background activity with slightly abnormal activity, e.g., mild asymmetries, mild voltage depression, poorly defined sleep-wake cycling), moderately abnormal: (Discontinuous activity with interburst interval 10 seconds, no clear sleep-wake cycling, clear asymmetry, or asynchrony,)

- Severely abnormal (Discontinuous activity with interburst interval 10-60 seconds, severe attenuation of background activity, no sleep-wake cycles), and an isoelectric EEG (background activity 60 seconds) flow diagram of study is shown in [Table/Fig-1].



[Table/Fig-1]: Flow diagram of study.

Short-term outcome: At the time of discharge short-term outcome was assessed and poor outcome was defined as death or suboptimal score of HNNE. HNNE was performed and optimality scores were calculated for each component i.e., tone and posture, tone patterns, reflexes, movements, abnormal signs, and behaviour, separately and composite score by combining scores of all components. Composite score of >30.5 was considered optimal [19]. Suboptimal scores for individual items were also assessed as per cut-off scores given by scale developers.

Long-term outcome: Follow-up at preferably between 6 to 12 month of age was done. HINE was performed and age specific cut-off value i.e., for age group 24 to 28 week, 28 to 32 week, >32 week was 73, 76 and 73, respectively, was used to categorise optimal and suboptimal specific for age [20].

Developmental Assessment Scale for Indian infants (DASII) scale: (Indian modification of Bayley's scale for infant development) was used for developmental assessment and Motor Development Quotient (MoDQ) and Mental Development Quotient (MeDQ) was calculated [21]. A Development Quotient (DQ) <70 was considered as delayed. Average of MeDQ and MoDQ <70% was considered abnormal [22].

Epilepsy and cerebral palsy were diagnosed on the basis of clinical history and EEG on follow-up. The diagnosis of cerebral palsy was typically based on observations or parent reports of attained motor milestones, such as sitting, pulling to stand, and evaluation of posture, deep tendon reflexes, and muscle tone and also on the nature of the movement disorder [23-26]. Tone assessment was done using modified Ashworth score [27]. An abnormal long-

term outcome was defined as abnormal HINE score presence of cerebral palsy or epilepsy or developmental delay. Association of EEG background activity (Normal/Mildly abnormal, moderately abnormal and severely abnormal) with mortality, HNNE score (optimal/suboptimal), HINE score (optimal/suboptimal), cerebral palsy, epilepsy and developmental delay was determined.

STATISTICAL ANALYSIS

The data was collected systematically, tabulated in master chart using windows 10 and analysed using Statistical Package of Social Sciences version 19.0. Categorical variables were evaluated using Chi-square test and continuous variable were analysed using Analysis of Variance (ANOVA) test. Predictive ability of the early neonatal EEG was assessed using Positive Predictive Value (PPV), NPV, specificity, sensitivity of binary values. A p-value of <0.05 was considered significant.

RESULTS

The present study included total of 81 neonates with HIE out of which 58 were males and 23 were females with mean GA of 39 weeks. Majority of them were from rural area, first by birth order, born by vaginal delivery, appropriate for GA, belonged to joint family and were from lower socio-economic class [Table/Fig-2] [28].

Characteristics	No. of patient (%)
Residence	
Rural	64 (68.1)
Urban	17 (31.9)
Gender	
Male	58 (71.6)
Female	23 (28.4)
Birth weight	
Appropriate for gestational age	64 (79)
Small for gestational age	17 (20.9)
Mean birth weight	2.64 (0.49)
Mode of delivery	
Vaginal	66 (81.4)
Cesarean	15 (18.6)
Birth order	
First	55 (67.9)
More than one	26 (32.09)
Type of family	
Joint family	67 (82.7)
Nuclear	14 (17.3)
Socio-economic status (Modified kuppuswamy scale 2020) [28]	
Upper	5 (6.2)
Middle	24 (29.6)
Lower	52 (64.2)
Antenatal complications	
Present	18 (22.2)
Absent	63 (77.8)

[Table/Fig-2]: General characteristics of the patients.

Out of 81 neonates, 32 (39.5%), 22 (27.1 %) and 27 (33.3%) had normal/mildly abnormal, moderately abnormal and severely abnormal EEG background activity respectively within six hours of birth. All the patients having normal/mildly abnormal EEG were successfully discharged from NICU whereas only 15 (68.2%) and 10 (37%) could be discharged from moderately abnormal and severely abnormal group. Mean HNNE calculated at time of discharge from NICU was higher in mildly abnormal EEG group as compared to other groups. Out of discharged patients none with severely abnormal EEG had optimal HNNE score although, 24 (75%) of mildly abnormal EEG had optimal HNNE score [Table/Fig-3].

Characteristics	Normal or mildly abnormal (n=32)	Moderately abnormal (n=22)	Severely abnormal (n=27)	p-value
Discharge*	32 (100%)	15 (68.2%)	10 (37%)	<0.001
Mean HNNE score (SD)	30.39 (3.45)	26.5 (3.38)	20.8 (2.663)	<0.001
Death*	0	7 (32%)	17 (63%)	<0.001
Optimal HNNE composite score#	24 (75%)	3 (20%)	0	<0.001
Suboptimal HNNE composite score#	8 (25%)	12 (80%)	10 (100%)	<0.001

[Table/Fig-3]: EEG background activity with short-term outcome of babies with HIE.
*Chi-square test/#One-way ANOVA; A p-value of <0.05 was considered significant

In each component of HNNE score, majority of newborns in normal/mildly abnormal EEG group had significantly optimal score as compared to moderately abnormal and severely abnormal group [Table/Fig-4].

Total 31 patient came for follow-up among these 15 (46.8%) had normal/mildly abnormal EEG, 11 (73.3%) had moderately abnormal EEG and 5 (50%) had severely abnormal EEG. An 86.7% cases of mildly abnormal EEG at birth had optimal HINE score whereas it was optimal in 45% and 0% cases in moderately abnormal and severely abnormal group (p-value<0.001). No patient having mildly abnormal EEG at birth developed cerebral palsy, epilepsy or developmental delay at follow-up, whereas percentage of these neuromotor abnormalities were highest among severely abnormal group (p-value <0.001) [Table/Fig-5].

EEG within six hours of birth has very high sensitivity and NPV in predicting neurodevelopmental outcome. Early EEG in present study had very high sensitivity (100%) and NPV (100%) in predicting cerebral palsy, epilepsy and developmental delay [Table/Fig-6].

DISCUSSION

We have shown that multichannel EEG recordings can be used to predict outcomes after perinatal asphyxia, within 6 hours after birth. Early EEG in birth asphyxia in predicting neurodevelopmental outcome was found strongly significant in our study. A similar study by Murray DM et al., concluded that 100% patients having normal/mildly abnormal EEG at birth had normal outcome [8]. Normal/mildly abnormal early EEG results had 100% PPV for normal outcomes and NPV s of 67%. In our study, abnormal EEG had 100% sensitivity and NPV in predicting outcome of HIE babies which is comparable to above study.

A study by Hamelin S et al., concluded that worse EEG background categories associated with unfavorable neurologic outcome similarly in our study severely abnormal EEG within six hours of birth had significant association with abnormal neurological examination [29].

Spitzmiller RE et al., studied the usefulness of amplitude-integrated EEGl for early outcome prediction after birth asphyxia found that,

S. no	Component of HNNE score	Mean score (SD)	Optimal/suboptimal cutoff	Normal/Mildly abnormal EEG (n=32)	Moderately abnormal EEG (n=15)	Severely abnormal EEG (n=10)	p-value*
1	Posture	8.2 (1.43)	Optimal (≥9)	25 (78.1%)	6 (40%)	0	<0.001
			Suboptimal (<9)	7 (21.9%)	9 (60%)	10 (100%)	
2	Tone Pattern	4.3 (0.82)	Optimal (≥5)	22 (68.8%)	6 (40%)	0	<0.001
			Suboptimal (<5)	10 (31.2%)	9 (60%)	10 (100%)	
3	Reflexes	4.9 (1.12)	Optimal (≥5)	25 (78.1%)	7 (46.6%)	2 (20%)	<0.001
			Suboptimal (<5)	7 (21.9%)	8 (53.3%)	8 (80%)	
4	Movements	2.2 (0.82)	Optimal (≥3)	23 (71.9%)	4 (26.7%)	0	<0.001
			Suboptimal (<3)	9 (28.1%)	11 (73.3%)	10 (100%)	
5	Abnormal signs and pattern	2.4 (0.66)	Optimal (≥3)	21 (65.6%)	4 (26.7%)	0	<0.001
			Suboptimal (<3)	11 (34.4%)	11 (73.3%)	10 (100%)	
6	Orientation and behaviour	5.7 (0.99)	Optimal (≥6)	25 (78.1%)	8 (53.3%)	0	<0.001
			Suboptimal (<6)	7 (21.9%)	7 (46.6%)	10 (100%)	

[Table/Fig-4]: Association of EEG background activity and Component of HNNE Score at the time of discharge from NICU.
*One-way ANOVA

Characteristics	Normal or mildly abnormal n (%)	Moderately abnormal n (%)	Severely abnormal n (%)	p-value
Total follow-up (% of discharged)*	15 (46.8%)	11 (73.3%)	5 (50 %)	0.23
Mean age at follow-up (months)#	10.2 (1.39)	8.68 (1.14)	6.2(1.02)	0.23
Normal modified Ashworth score n (%)*	15 (100%)	6 (54.4%)	1 (20%)	<0.001
Mean HINE composite score M (SEM)#	73.5 (0.74)	68.4 (2.5)	58.6 (2.9)	<0.001
Optimal HINE scores	13 (86.7%)	5 (45.5%)	0	<0.001
Suboptimal HINE composite score n (%)*	2 (13.3%)	6 (54.5%)	5 (100%)	<0.001
DASII scores				
MeDQ (Mean SEM)#	94.3 (1.1)	79.5 (4.9)	54.5 (8.6)	<0.001
MoDQ (Mean SEM)#	93.2 (1.4)	78.5 (4.8)	52.4 (9.1)	<0.001
Total DQ (Mean SEM)#	93.7 (1.1)	79.0 (4.8)	53.5 (8.7)	<0.001
Developmental delay*	0	3 (27.3%)	5 (100%)	<0.001
Epilepsy n (% follow-up)	0	3 (20%)	3 (30%)	0.02
Cerebral palsy n (% follow-up)	0	5 (33.3%)	4 (40%)	0.003

[Table/Fig-5]: EEG background activity with long-term outcome of babies.
*Chi-square test/#ANOVA test; A p-value of <0.05 was considered significant

Neuromotor outcome	Sensitivity	Specificity	PPV	NPV
Cerebral palsy	100%	71.4%	62.5%	100%
Epilepsy	100%	60%	37.5%	100%
Developmental delay	100%	62.5%	43.7%	100%

[Table/Fig-6]: Sensitivity, Specificity and PPV, NPV of EEG in predicting neurodevelopmental outcome.

the sensitivity of an abnormal aEEG tracing for prediction of a poor outcome was 91% , the specificity was 88% which is 100% and 60-70%, respectively in the present study [30].

A study by Anand V and Nair PMC concluded that 80% neonates with normal/mildly abnormal EEG findings had favorable outcome whereas 51% neonates with severely abnormal EEG had unfavorable outcome which was statistically significant (p-value <0.001) and Azzopardi D et al., found that 10 out of 14 infants who had a normal neurodevelopmental outcome had a normal EEG at four hour of age [31,32]. Both infants who developed neurodevelopmental abnormalities on follow-up had an abnormal EEG at four hour of age. Results of both studies are similar to our study where 100% neonate with normal/mildly abnormal EEG had favorable outcome and severe EEG at birth was also associated with poor HINE score, DASII scores on follow-up.

Study conducted by De Wispelaere LA et al., included 89 infants with HIE retrospectively, out of which 37 did not receive therapeutic hypothermia and 48 hours' EEG background pattern had a PPV of 100% and NPV of 58% in these neonates for bad outcome which is comparable to our study [12].

Weeke LC et al., found that EEG background activity was significantly associated with neurodevelopmental outcome at 36 hours (p-value=0.009) and 48 hours after birth (p-value=0.029) and with severity of brain injury on MRI at 36 hours (p-value=0.002) and 48 hours (p-value=0.018) [17]. The PPV of EEG for abnormal outcome was 100% at 36 hours and 48 hours and the NPV was 75% at 36 hours and 69% at 48 hours whereas our study recorded EEG background activity within six hours of birth had PPV of 62.5%, 37.5% and 43.7% for cerebral palsy, epilepsy and developmental delay respectively and NPV of 100% for all above long-term neurological outcome.

It was found that early EEG could predict cerebral palsy and developmental delay which is in consonant with previous studies [12-14,33].

Limitation(s)

Major limitation was lack of continuous EEG monitoring and poor follow-up rate of patients which might attribute to COVID-19 pandemic during period of study.

CONCLUSION(S)

The present study concluded early EEG is very useful tool in predicting neuromotor outcome of neonates with HIE. EEG background activity recorded within six hours of birth in term neonates with HIE has very high sensitivity in predicting short-term i.e., discharge from NICU and long-term outcome such as cerebral palsy, epilepsy, developmental delay. Cases with normally or mildly

abnormal EEG activity had statistically significant better outcome as compared to moderately or severely abnormal EEG background activity. Henceforth, in order to predict outcome of an asphyxiated newborn for early intervention and better utilisation of resources in developing countries like India a bed side EEG is very useful tool. We recommend that in our country every NICU should have a bed side EEG facility to predict outcome within six hours of birth.

REFERENCES

[1] Kurinczuk JJ, White-Koning M, Badawi N. Epidemiology of neonatal encephalopathy and hypoxic-ischaemic encephalopathy. Early Hum Dev. 2010;86(6):329-38.

[2] Paul VK, Singh M, Sundaram KR, Deorari AK. Correlates of mortality among hospital-born neonates with birth asphyxia. Natl Med J India. 1997;10(2):54-57.

[3] Eichenwald EC, Hansen, Martin, Stark cloherty and stark's manual of neonatal care. 8th edition, South Asian Edition, Wolters Kluwer: 2017:790-811

[4] Ahearne CE, Boylan GB, Murray DM. Short and long-term prognosis in perinatal asphyxia: An update. World J Clin Pediatr. 2016;5(1):67-74.

[5] Van Lieshout HBM, Jacobs JWFM, Rotteveel JJ, Geven W, v't Hof M. The prognostic value of the EEG in asphyxiated newborns. Acta Neurol Scand. 1995;91(3):203-07.

[6] Pressler RM, Boylan GB, Morton M, Binnnie CD, Rennie JM. Early serial EEG in hypoxic ischaemic encephalopathy. Clin Neurophysiol. 2001;112(1):31-37

[7] Wertheim D, Mercuri E, Faundez JC, Rutherford M, Acolet D, Dubowitz L. Prognostic value of continuous electroencephalographic recording in full term infants with hypoxic ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed. 1994;71(2):F97-F102.

[8] Murray DM, Boylan GB, Ryan CA, Connolly S. Early EEG findings in hypoxic-ischemic encephalopathy predict outcomes at 2 years. Pediatrics. 2009;124(3):e459-67.

[9] Rutherford MA, Pennock JM, Dubowitz LMS. Cranial ultra-sound and magnetic resonance imaging in hypoxic ischaemic encephalopathy: A comparison with outcome. Dev Med Child Neurol. 1994;36(9):813-25.

[10] Wang Z, Zhang P, Zhou W, Xia S, Zhou W, Zhou X, et al. Neonatal hypoxic-ischemic encephalopathy diagnosis and treatment: a National Survey in China. BMC Pediatr. 2021;21(1):261.

[11] Dalal EA, Bodar NL. A study on birth asphyxia at tertiary health centre. Natl J Med Res. 2013;3(4):374-76.

[12] De Wispelaere LA, Ouwehand S, Olsthoorn M, Govaert P, Smit LS, de Jonge RC, et al. Electroencephalography and brain magnetic resonance imaging in asphyxia comparing cooled and non-cooled infants. Eur J Paediatr Neurol. 2019;23(1):181-90.

[13] Hellstrom Westas L, Rosen I, Svenningsen NW. Predictive value of early continuous amplitude integrated EEG recordings on outcome after severe birth asphyxia in full term infants. Arch Dis Child Fetal Neonatal Ed. 1995;72(1):F34-38.

[14] Eken P, Toet MC, Groenendaal F, de Vries LS. Predictive value of early neuroimaging, pulsed Doppler and neurophysiology in full term infants with hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed. 1995;73(2):F75-80.

[15] Glass HC, Hong KJ, Rogers EE, Jeremy RJ, Bonifacio SL, Sullivan JE, et al. Risk Factors For Epilepsy In Children With Neonatal Encephalopathy. Pediatr Res. 2011;70(5):535-40.

[16] Miller SP, Weiss J, Barnwell A, Ferriero DM, Latal-Hajnal B, Ferrer-Rogers A, et al. Seizure-associated brain injury in term newborns with perinatal asphyxia. Neurology. 2002;58(4):542-48.

[17] Weeke LC, Boylan GB, Pressler RM, Hallberg B, Blennow M, Toet MC, et al; Neonatal seizure treatment with Medication Off -patent (NEMO) consortium. Role of EEG background activity, seizure burden and MRI in predicting neurodevelopmental outcome in full-term infants with hypoxic-ischaemic encephalopathy in the era of therapeutic hypothermia. Eur J Paediatr Neurol. 2016;20(6):855-64.

[18] Dwivedi D, Lin N, Venkatesan C, Kline-Fath B, Holland K, Schapiro M. Clinical, Neuroimaging, and Electrographic predictors of phenobarbital failure in newborns with hypoxic ischemic encephalopathy and seizures. J Child Neurol. 2019;2019:883073819838171.

[19] Dubowitz L, Ricciw D, Mercuri E. The Dubowitz neurological examination of the full-term newborn. Ment Retard Dev Disabil Res Rev. 2005;11(1):52-60.

[20] Haataja L, Mercuri E, Guzzetta A, Rutherford M, Counsell S, Flavia Frisone M, et al. Neurologic examination in infants with hypoxic-ischemic encephalopathy at age 9 to 14 months: use of optimality scores and correlation with magnetic resonance imaging findings. J Pediatr. 2001;138(3):332-37.

[21] Patni B. Developmental assessment scales for Indian infants (DASII). Indian Journal of Practical Pediatrics. 2012;14(4):409-12.

[22] Dwivedi D, Singh S, Singh J, Bajaj N, Singh HP. Neurodevelopmental Status of Children aged 6-30 months with Severe Acute Malnutrition. Indian Pediatr. 2018;55(2):131-33.

[23] O'Shea TM. Diagnosis, treatment, and prevention of cerebral palsy. Clin Obstet Gynecol. 2008;51(4):816-28.

[24] Centers for Disease Control and Prevention. Cerebral palsy. Accessed May 22, 2019. https://www.cdc.gov/ncbddd/cp/facts.html

[25] Novak I, Morgan C, Adde L, Blackman J, Boyd RN, Brunstrom-Hernandez J, et al. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. [published correction appears in JAMA Pediatr. 2017;171(9):919]. JAMA Pediatr. 2017;171(9):897-907.

[26] Smithers-Sheedy H, Badawi N, Blair E, Cans C, Himmelmann K, Krägeloh-Mann I, et al. What constitutes cerebral palsy in the twenty-first century?. Dev Med Child Neurol. 2014;56(4):323-28.

[27] Harb A, Kishner S. Modified Ashworth Scale. 2022 May 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. PMID: 32119459.

[28] Saleem SM. Modified Kuppuswamy socioeconomic scale updated for the year 2020. Indian Journal of Forensic and Community Medicine. 2020;7(1):01-03. Doi: https://doi.org/10.18231/j.ijfcm.2020.00

[29] Hamelin S, Delnard N, Cneude F, Debillon T, Vercueil L. Influence of hypothermia on the prognostic value of early EEG in full-term neonates with hypoxic ischemic encephalopathy. Neurophysiol Clin ClinNeurophysiol. 2011;41(1):19-27.

[30] Hellström-Westas L. Amplitude-integrated EEG--useful for early outcome prediction after birth asphyxia? Nat Clin Pract Neurol. 2008;4(2):74-75.

[31] Anand V, Nair PMC. Neonatal seizures: Predictors of adverse outcome. J Pediatr Neurosci. 2014;9(2):97-99.

[32] Azzopardi D, Guarino I, Brayshaw C, Cowan F, Price-Williams D, David Edwards A, et al. Prediction of neurological outcome after birth asphyxia from early continuous two-channel electroencephalography. Early Human Development. 1999;55(2):113-23.

[33] Allemand F, Reale F, Sposato M, Allemand A. Perinatal Hypoxic-Ischemic Encephalopathy: epileptic and paretic outcome at one year of age. Ital J Pediatr. 2009;35(1):14.

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