

Etiology, clinical profile, and immediate outcome of neonatal encephalopathy in Northeast India: A hospital-based cross-sectional study



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Submission: 26-07-2022

Revision: 27-09-2022

Publication: 01-11-2022

ABSTRACT

Background: Neonatal encephalopathy (NE) is one of the important causes contributing to neonatal death and disability. Knowledge about associated probable risk factors of NE will be helpful in developing strategies for proper intervention and early management. **Aims and Objectives:** This study aims to describe the etiology, clinical features, and immediate outcomes of NE in the northeastern part of India. **Materials and Methods:** This hospital-based, cross-sectional observational study included cases of NE beyond 35 weeks of gestation from February 2018 to July 2019. Demographic profiles, risk factors, clinical features, laboratory investigations, imaging, and outcome data were collected and analyzed. **Results:** A total of 82 patients comprising males (59.7%) and females (40.2%) were included in the study. The mean age of gestation in weeks is 37.60 ± 3.5 SD. Meconium-stained liquor was the most frequent etiology ($n=30$; 36.5%), followed by dyselectrolytemia ($n=8$; 9.7%), abnormal hydramnios (oligo or poly) ($n=5.6\%$), and twin pregnancy and instrumental delivery ($n=4$; 4.8%). Seizures ($n=37$; 45.1%) were the most common presentation followed by respiratory distress or difficulty ($n=25$; 30.4%). Around 41.4% suffered from dyselectrolytemia followed by positive sepsis screening of 39%. Most of the cases (87.8%) were discharged after receiving appropriate treatment. **Conclusion:** The prevalence of neonates with NE as noted in this hospital-based, cross-sectional study was 2.8%. It was found that in most cases, the probable causative factors occurred during the antenatal and intranatal period. Convulsions were the most common clinical presentation among the affected neonates. Most of the admitted neonates had dyselectrolytemia, suggesting that the renal system was predominantly affected, while the immediate outcome was satisfactory.

Key words: Acute kidney injury; Meconium; Neonates; Risk factors; Seizures

INTRODUCTION

Neonatal encephalopathy (NE) is a clinical syndrome of disturbed neurological function in the earliest days of life in the infant beyond 35 weeks of gestation, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal levels of consciousness, and often seizures.¹

In newborn infants, NE is one of the important causes contributing to neonatal death and disability.²⁻⁵

Risk factors causing brain injury can occur at any time, from antepartum to intrapartum to postpartum period, leading to multiple etiologies of NE. Therefore, identifying the precise etiology of neurologic illness in neonates poses challenges.

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v13i11.46981

E-ISSN: 2091-0576

P-ISSN: 2467-9100

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In NE, infants can have varied presentations that can range from tenuous to hyperalert or hypotonic (mild or extreme) states, unconsciousness, absent reflexes, and comas. For therapeutic decisions, knowledge of the exact etiology has minimal impact. Sarnat and Sarnat staging categorizes post-anoxic encephalopathy.^{6,7}

Early diagnosis and treatment of high-risk infants are crucial for appropriate supportive care and treatment to be introduced to avoid neurological deterioration.

Results from this study will provide baseline data for future studies. In addition, information from this study will give an idea of the burden of NE and assess the associated probable risk factors, which will be useful in developing strategies for proper intervention and early management.

The hilly terrain made timely access to health-care facilities problematic and routine antenatal care and timely intervention where necessary were difficult. Moreover, being the only tertiary care health center in the whole state made the burden particularly high. As such, we compared the frequency of various etiologies, clinical profiles, and immediate outcomes in cases of NE.

The objective of this study was to describe etiologies, clinical features, and immediate outcomes of NE in Northeast India.

Aims and objectives

This study aims to study the etiology, evaluate the clinical profile, and know the immediate outcome of NE.

MATERIALS AND METHODS

This hospital-based, observational, cross-sectional study was conducted in the Department of Pediatrics of a Tertiary Care Medical College, CRH, SMIMS, situated in a semi-urban area from February 2018 to July 2019. The study was pre-approved by the Institutional Ethics Committee (IEC) for the final permission. After obtaining the permission of the IEC study was conducted. Eighty-two neonates with more than 35 weeks of gestation, both inborn and outborn, complying with the definition of NE and fulfilling the inclusion criteria were included in the study.

Inclusion criteria

The following criteria were included in the study:

1. All the neonates with gestation period beyond 35 weeks
2. All the neonates fulfilling the definition of NE.

Definition of NE

NE is a clinical syndrome of disturbed neurological function in the earliest days of life in the infant >35 weeks

of gestation, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness, and often seizures.

Data collection procedure

Data were collected by the primary investigator. Parents or caretakers of neonates fulfilling the inclusion criteria were informed about the study. Those who agreed with written consent were included in the study. Data collection was done manually using a predefined questionnaire. Relevant information was obtained from the mother or caregiver of the study participants, regarding sociodemographic and clinical status, such as maternal age and parity, history of associated maternal conditions such as diabetes mellitus, personal habits, exposure to radiation, and number of clinical visits. Soon after the birth and every day during ward rounds, newborns were examined and assessed systematically for the presence of a predefined set of clinical features. Eighty-two cases of NE were diagnosed as per the definition and were studied in detail with respect to demographic profiles, risk factors, clinical manifestations, and outcomes. Investigations including complete blood count, blood culture, serum electrolytes, liver function test, renal function test, random blood sugar, coagulation profile, and cranial sonography were done.

Statistical analysis

Baseline demographics are presented for a period of 1 year. Risk factors, clinical features, and immediate outcomes were tabulated. Data collected were entered into Microsoft Excel Work Sheet 2017. SPSS (version 22) was used for statistical data analysis. Microsoft Excel was used for tabulation. Percentage, proportions, means, charts, and tables were used for description of the data. Analysis of qualitative data was done using Chi-square test. Level of significance is expressed as $P < 0.05$.

RESULTS

Out of the 2291 live births in CRH in our study, 82 neonates were documented to have NE; the number of inborn cases was $n=64$; (78%) and outborn was $n=18$; (22%). The prevalence of NE was found to be 2.8% in CRH. In our study, males ($n=49$; 59.7%) were found to be more commonly affected than females ($n=33$; 40.2%). The relation between gender and NE was not found to be statistically significant with $P > 0.05$ (0.133), Chi-square (2.261), and df (1), 0.163. The mean age of gestation in weeks was 37.60 ± 3.5 SD (Table 1). The mean birth weight (Kg) was 2.69 ± 0.6 SD. Neonates delivered by normal vaginal delivery were 37.8% followed by elective cesarean section (35.3%). The frequency of NE was highest in mothers aged between 25 and 29 years (36.5%) followed by 30–34 years (31.7%). In more than 40% of cases, mothers had irregular visits to the hospital during

the pregnancy. The majority of neonates with NE were of the first order (56%), that is, delivered through primi mothers. About 6% of mothers had a history of previous abortions.

Among probable etiological factors including antepartum, intrapartum, and postnatal factors, we found meconium-stained liquor (MSL) (n=30; 36.5%) to be the most common probable etiological factor, which belongs to the intrapartum etiological factor category, followed by dyselectrolytemia (n=8; 9.7%) belonging to probable postnatal factors, further followed by abnormal hydramnios (oligo or poly) (n=5.6%) belonging to antepartum factors, and twin pregnancy and instrumental delivery (n=4; 4.8%), presenting as antepartum factors and intrapartum factors, respectively (Table 1).

In the present study, on comparing the probable etiological factors, it was noted that most of the cases occurred due to

the presence of both antenatal and intranatal factors causing asphyxia (n=66; 80.4%), followed by intranatal (n=39; 47.5%), antenatal (n=21; 25.6%), and postnatal (n=22; 26.8%) factors independently being the cause (Figure 1).

Seizures (n=37; 45.1%) were the most common presentation, followed by respiratory distress/difficulty (n=25; 30.4%), lethargy (n=13; 15.8%), and feeding difficulties (n=7; 8.5%), in that order (Table 2).

Most of the cases (n=34; 41.4%) suffered from dyselectrolytemia, followed by positive sepsis screening (n=32; 39%), though only 6% had positive blood culture followed by deranged liver function tests (LFT) (n=12; 14.6%), hypoglycemia (n=10; 12.1%), acute kidney injury (n=5; 6%), and thrombocytopenia (n=4; 4.8%), with each of the anemia and deranged clotting factors being n=2; 2.4%. Normal cranial sonography findings were evident in n=79; 96.3% and only n=3; 3.6% had abnormal cranial sonography findings (Table 3).

Most of the cases (87.8%) were discharged after appropriate treatment, with n=8; 11.11% of neonates being discharged on anticonvulsants. Including both outborn and inborn neonates, a total of n=10; 12.1% neonates expired (five out of 18, i.e., 27.7% of cases in outborn and five out of 64, i.e., 7.8% of cases in inborn).

Table 1: Demographic and probable etiological factors for NE and their percentage distribution as observed in our study population

Demographic profile	Number (n)	Percentage
Total live birth in CRH	2291	
Neonates with NE in CRH	82	
Inborn cases with NE	64	78
Outborn cases with NE	18	22
Gender	Number (n)	Percentage
Male	49	59.7
Female	33	40.2
Gestation		
Term (>37 weeks of gestation)	61	74.3
Late preterm/near term (37–37 weeks of gestation)	21	25.6
Etiological factors		
Antepartum factors		
Gestational hypertension	2	2.4
Gestational diabetes mellitus (GDM)	2	2.4
Pre-eclampsia and GDM	3	3.6
Oligo and polyhydramnios	5	6.0
Twin pregnancy	4	4.8
Placental abnormality	3	3.6
Hypothyroid	1	1.2
Intrauterine growth restriction (IUGR)	1	1.2
Intrapartum factors		
Meconium-stained liquor (MSL)	30	36.5
Instrumental delivery	4	4.8
Placental abnormality	2	2.4
Chorioamnionitis	1	1.2
Postnatal factors		
Dyselectrolytemia	8	9.7
Sepsis	3	3.6
Congenital heart disease (CHD)	3	3.6
Congenital anomaly	3	3.6
Respiratory distress syndrome (RDS)	2	2.4
Hypoglycemia	2	2.4
Neonatal hyperbilirubinemia (NNHB)	1	1.2

DISCUSSION

The present study aimed to determine a baseline for NE in neonates in the northeastern part of India, by defining the etiological factors, clinical presentations, and immediate outcomes among all cases of NE identified at our institute during the study period. The prevalence of NE in our study is 2.8%. According to Kurinczuk et al., “the estimated incidence of NE is 3.0/1000 live births (95% CI 2.7–3.3), while the estimated incidence of HIE (a subset of NE) is 1.5/1000 live births (95% CI 1.3–1.7).”⁸ In a study done by Wyatt et al., “2–3/1000 term live births is the incidence

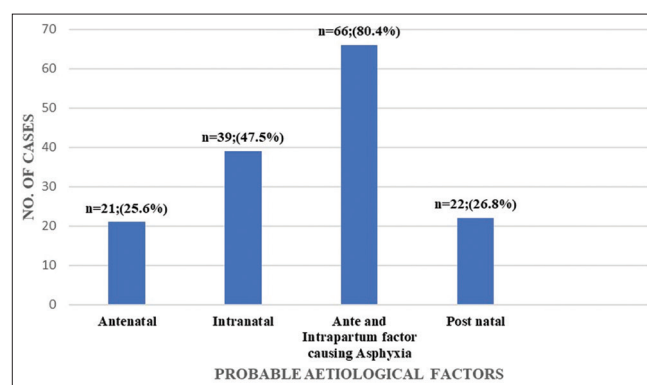


Figure 1: Distribution of probable etiological factors according to natal period

Table 2: Clinical features of NE and their frequency distribution

Clinical features	Frequency	Percentage
Seizures	37	45.1
Respiratory distress or difficulty	25	30.4
Lethargy	13	15.8
Feeding difficulties	7	8.5

Table 3: Frequency and percentage distribution of different laboratory abnormalities in our cases

Investigations	Frequency	Percentage
Anemia	2	2.4
Thrombocytopenia	4	4.8
Deranged clotting factors	2	2.4
Positive sepsis screen	32	39
Positive blood culture	5	6
Dyselectrolytemia	34	41.4
Hypoglycemia	10	12.1
Acute kidney injury (AKI)	5	6
Deranged liver function test (LFT)	12	14.6
Direct Coombs test	1	1.2
Cranial sonography		
Normal	79	96.3
Abnormal	3	3.6

of NE in the USA.”⁹ According to reports from neonatal units in India, the incidence is 14/1000 live births and is 15 times higher than the highly resourced countries.^{4,5}

On comparing the probable etiological factors, it was noted that most of the cases occurred due to the presence of both antenatal and intranatal factors causing asphyxia (n=66; 80.4%), followed by intranatal (n=39; 47.5%), antenatal (n=21; 25.6%), and postnatal (n=22; 26.8%) factor independently being the cause. Our finding was similar to other studies. A study done in the UK by Martinez-Biarge et al.,¹⁰ too found that 70% of cases had both antepartum and intrapartum factors, 20% had only intrapartum factors, 7% of cases had only antepartum factors, and 4% had no identifiable risk factors for the development of NE.

According to a study done by Locatelli et al.,¹¹ in Italy, 26% of cases of NE had only antepartum risk factors, 22% had only intrapartum risk factors, and 44% had a combination of the two, and rest had no risk factors.

However, in a study conducted in West Australia by Badawi et al.,¹² independently antepartum risk factors were present in 69%, 25% had both antepartum and intrapartum risk factors, and 4% had evidence of only intrapartum hypoxia, and 2% had no identified risk factors. And also, according to Pierrat et al.,¹³ distribution of causes of NE cases was, 56% of cases during intrapartum factor, antepartum in 13%, ante-intrapartum in 10%, and postpartum in 2%. In 19% of cases, no underlying cause was identified during the neonatal course.

In our study, it is noted that the most common clinical presentation of NE is seizures (n=37; 45.1%) and this finding is in agreement with the work done by Pierrat et al.,¹³ where 69%; Ellis et al.,¹⁴ 44%; Pfister et al.,¹⁵ 59%; Sudhakar et al.,¹⁶ 66.7% of cases with encephalopathy had seizures as the most common symptoms.

In our study, most of the cases (41.4%) suffered from dyselectrolytemia, followed by positive sepsis screen (39%), deranged LFT (14.6%), hypoglycemia 12.1%, positive blood culture (6%), AKI (6%), and other abnormalities such as thrombocytopenia (4.8%), anemia (2.4%), deranged clotting factors (2.4%), and direct Coombs test (1.2%) were found but were relatively infrequent.

As we know that in cases of encephalopathy, most common organ to be affected is renal, it can be inferred that the most common finding of dyselectrolytemia in our study was because of the renal system getting affected, though deranged renal function test leading to AKI was seen only in 6% of cases.

Most of the cases (87.8%) got discharged after the appropriate treatment. 5/18 (27.7%) cases in outborn and 5/64 (7.8%) cases in inborn expired, showing favorable immediate outcome in cases of NE. A study done by Haque et al.,¹⁷ also showed that 80% of neonates suffering from neonatal convulsion due to NE survived and only 20% died. Finding is also in agreement with study done by Athumani¹⁸ where 78.7% of neonates suffering from HIE got discharged and only 21.3% died. Similarly, a study done by Kumar et al.,¹⁹ showed that 82% of patients with HIE got discharged.

Limitations of the study

The limitation in this study was that as it was a hospital-based study, external validation is limited. Further studies are required to attribute the risk factors of NE. Preterm <35 weeks have been excluded from the study, which are more prone to encephalopathy.

CONCLUSION

The prevalence of neonates with NE as noted in this hospital-based, cross-sectional study was 2.8%. It was found that in the majority of cases, the probable causative factor was MSL. Convulsions were the most frequently noted clinical presentation among the affected neonates. Most of the admitted neonates had dyselectrolytemia, suggesting that the renal system was predominantly affected, though the immediate outcome was satisfactory. The etiologies of NE are diverse, with many cases originating in the antenatal and intranatal period, while better antenatal and intranatal care may also prevent adverse outcomes.

ACKNOWLEDGMENT

The authors would like to acknowledge Department of Pediatrics, CRH, Sikkim Manipal Institute of Medical sciences, Gangtok, Sikkim, India for extending their valuable support in undertaking this study and Department of Pediatrics, MGM Medical College and Lions Seva Kendra Hospital, Kishanganj, Bihar, India for critical revision of the manuscript for important intellectual content.

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Authors Contribution:

AK – Concept and design of the study, acquired the data, analyzed and interpreted the data, statistical analysis, prepared the first draft of manuscript, and revision of the manuscript; **SD** – Concept and design of the study, literature review, and critical revision of the manuscript for important intellectual content; **AP** – supervision of the study, coordination, and critical revision of the manuscript for important intellectual content; **SK** – Drafting of the manuscript, and critical revision of the manuscript for important intellectual content; and **MO** – Acquired the data.

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Source of Funding: None, **Conflicts of Interest:** None.