

Hypoxic Ischemic Encephalopathy in Neonates with Birth Asphyxia - A Hospital Based Study

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ABSTRACT

Introduction: Each year approximately 4 million babies are born asphyxiated, which results in 1 million deaths and an equal number of serious neurological sequelae. One of the commonest organs involved in birth asphyxia is brain which may lead to a syndrome of clinical manifestation called Hypoxic Ischemic Encephalopathy (HIE). **Aims:** To find out possible maternal and neonatal risk factors for Hypoxic Ischemic Encephalopathy, to analyze clinical presentations and outcome of HIE in asphyxiated newborns. **Methods:** Hospital based observational study was carried out among fifty newborns with Apgar score less than 7 at 1 minute of life admitted in Nepalgunj Medical College Teaching Hospital, Kohalpur, Banke. **Results:** The incidence of birth asphyxia and birth asphyxia with HIE were 37.2 per 1000 live births and 14 per 1000 live births with male: female ratio of 1.27:1. Most of the neonates 22(44%) were in HIE stage II. Meconium stained amniotic fluid 18 (36%) was the most common intrapartum risk factor followed by maternal use of intrapartum medications 14 (28%), Premature Rupture of Membrane (PROM) 8 (16%), prolonged labor 5 (10%) and obstructed labor 6 (12%). Four (8%) asphyxiated neonates with HIE had cord prolapse and 7 (14%) had cord around the neck. The most common resuscitation done was bag and mask ventilation (56%) ($P < 0.05$). Majority of the studied neonates were of normal birth weight (76%) and head circumference (84%) ($P < 0.05$) with clinical presentations of respiratory distress (88%), seizures (44%), apnea (22%), bradycardia (8%), tachycardia (6%) and bulged anterior fontanel (6%). The overall mortality of neonates with HIE was 20% of which most were of HIE stage III. **Conclusion:** Certain measures could be taken to prevent birth asphyxia: early detection and intervention of high risk pregnancy, prompt and effective resuscitation of asphyxiated newborns.

Keywords: Birth asphyxia, Hypoxic ischemic encephalopathy, Neonates

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INTRODUCTION

Birth asphyxia is a serious clinical problem worldwide. Each year approximately 4 million babies are born asphyxiated, which results in 1 million deaths and an equal number of serious neurological sequelae, such as cerebral palsy, mental retardation, and epilepsy.¹ Birth Asphyxia is defined by World Health Organization (WHO) as "the failure to initiate and sustain breathing at birth." The Neonatology forum of India has defined birth asphyxia as "gasping and ineffective breathing or lack of breathing at one minute after birth."² National neonatology forum of India and WHO use an Apgar Score of 0-3 and 4-7, at one minute, to define severe and moderate asphyxia respectively.³ Essential criteria to diagnose perinatal asphyxia in newborns by The American Academy of Pediatrics Committee on newborn

includes prolonged metabolic or mixed acidemia ($pH < 7.0$), Apgar score of 0-3 for > 5 mins, and neurological manifestations (seizure, hypotonia, coma, HIE) and evidence of multiorgan dysfunction in immediate neonatal period.³ However, there is no gold standard test for birth asphyxia. According to Nepal Demographic Health Survey (NDHS) 2011, most of the births (72%) in Nepal occur at home, or during transport on the way to hospital. Also most of the births in Nepal are unattended (64%). This leads to the increased risk of birth asphyxia and neonates are brought to the hospital in moribund stage.⁴ Risk factors for causing birth asphyxia in newborn are antepartum, intrapartum and postpartum in 50%, 40% and 10% of cases respectively.⁵ The evaluation of risk factors for asphyxia can help identify fetuses at risk of birth asphyxia.

METHODS

A hospital based observational study was carried out among fifty newborns with Apgar score less than 7 at 1 minute of life that were admitted to neonatal intensive care unit (NICU) from labor room and obstetric ward of Nepalgunj Medical college Teaching Hospital, Kohalpur, Banke over the period of one year from February 2019 to January 2020. Newborn babies with Apgar score less than 7 at 1 minute of life were included in the study whereas those mothers not willing to participate delivered outside NGMCTH, neonates with congenital anomalies were excluded from the study. Apgar score was taken immediately after birth at one and five minutes of life. The newborns with Apgar score less than 7 in 1 minute of life were enrolled in the study. Informed written consent from the mother or the attendant of each case was taken. Maternal history was taken and information was documented on the predesigned proforma. Grading of asphyxiated newborn babies with HIE was done according to Levene classification for HIE.³ Appropriate data entry and statistical analyses were performed on Microsoft Excel and SPSS version 20.0. Data was summarized using descriptive statistics. Chi Square Test and Fischer Exact Test were used to compare the association among two or more categorical variables. P-value of <0.05 was taken as statistically significant. The study was aimed to find out possible maternal and neonatal risk factors for Hypoxic Ischemic Encephalopathy (HIE) and to analyze clinical presentations, outcome of HIE in asphyxiated newborns.

RESULTS

During the study period there were 3978 live births in Nepalgunj Medical College Teaching Hospital, Kohalpur, Banke. Among them 778 (19.5%) neonates were admitted in NICU. Out of 778 neonates, 148 (19%) neonates had birth asphyxia. Among the asphyxiated newborns 56 (37.83%) developed HIE. The incidence of birth asphyxia and birth asphyxia with HIE were 37.2 per 1000 live births and 14 per 1000 live births respectively. Out of 56 asphyxiated newborns with HIE only 50 were included in the study. Six babies were not included in the study because consent was not given by the parents for 3 babies and 3 babies died shortly after birth. Among 50 newborns with HIE, 28 (56%) were males and 22 (44%) females with Male: Female ratio 1.27:1.

HIE Grading	Frequency (n)	Percent (%)
HIE I	16	32
HIE II	22	44
HIE III	12	24
Total	50	100

Table I: Grading of HIE according to Levene Classification (n=50).

Most of the neonates (44%) in the study were in HIE stage II, followed by HIE stage I (32%) and HIE stage III (24%) respectively.

Risk Factors	Frequency (n)	Percent (%)
General Anesthesia during LSCS	5	10
Spinal Anesthesia during LSCS	11	22
PROM	8	16
Prolonged Labor	5	10
Obstructed Labor	6	12
Cord Prolapse	4	8
Cord around Neck	7	14
MSAF	18	36
Intrapartum Medications	14	28
Intrapartum Fever	6	12
Chorioamnionitis	1	2

*MSAF: Meconium Stained Amniotic Fluid.

Table II: Risk Factors for the Asphyxiated Newborns with HIE (n=50).

The most common intrapartum risk factor in asphyxiated newborns with HIE was meconium stained amniotic fluid which was present in 18 (36%) mothers. Maternal use of intrapartum medications, Premature Rupture of Membrane (PROM), prolonged labor and obstructed labor were present in 14 (28%), 8 (16%), 5 (10%) and 6 (12%) mothers respectively. Four (8%) asphyxiated neonates with HIE had cord prolapse and 7 (14%) studied neonates had cord around the neck.

Mode of Resuscitation	Frequency (n)	Percent (%)
Stimulation	14	28
BMV	28	56
ET-IPPV	4	8
ET-IPPV, CC	2	4
ET-IPPV, CC, Adrenaline	2	4
Total	50	100

*ET-IPPV: Endotracheal Tube- Intermittent Positive Pressure Ventilation, CC: Chest Compression, BMV: Bag Mask Ventilation.

Table III: Mode of Resuscitation in newborns with HIE (n=50).

All the neonates 50 (100%) required one or other form of neonatal resuscitation at birth. In the study, stimulation and BMV were required in 28% and 56% of cases respectively. ET-IPPV, ET-IPPV with chest compression and Et-IPPV with chest compression and adrenaline was required in 4 (8%), 2 (4%) and 2 (4%) neonates respectively.

Mode of Resuscitation	HIE Grading			Total	P Value
	HIE I n(%)	HIE II n(%)	HIE III n(%)		
Stimulation	8 (51.7%)	6 (42.9%)	0 (0%)	14 (100%)	0.012
BMV	7 (25%)	14 (50%)	7 (25%)	28 (100%)	
ET-IPPV	1 (25%)	0 (0%)	3 (75%)	4 (100%)	
ET-IPPV, CC	0 (0%)	1 (50%)	1 (50%)	2 (100%)	
ET-IPPV, CC, Adrenaline	0 (0%)	1 (50%)	1 (50%)	2 (100%)	
Total	16 (32%)	22 (44%)	12 (24%)	50 (100%)	

*ET-IPPV: Endotracheal Tube- Intermittent Positive Pressure Ventilation, CC: Chest Compression.

Table IV : Association of Mode of Resuscitation with Severity of HIE (n=50).

Most neonates who required simpler mode of resuscitation had HIE I and HIE II whereas the neonates who required extensive neonatal resuscitation care had HIE III. Association of mode of resuscitation at the birth with the severity of HIE was statistically significant (p<0.05).

Anthropometry	Frequency (n)	Percent (%)	Mean (± S.D)
Birth Weight			
<1500 gm	0	0	2695.4 (±483.457) gm
1500 gm-2499 gm	12	24	
2500gm-4000gm	38	76	
>4000gm	0	0	
Head Circumference			
<32 cm	7	14	32.94(±1.284) cm
32-35 cm	42	84	
>35 cm	1	1	

Table V: Distribution of Anthropometric Measurements (n=50).

The above data shows twelve (24%) neonates were of Low Birth Weight (LBW) and remaining 38 (76%) were of normal birth weight with mean (±S.D) 2.69(±0.483) Kg. There was no neonate with birth weight less than 1500 gm. Head circumference ranged from 30 to 36 cm with mean (±S.D.) 32.94(±1.284) cm.

Anthropometric Variables	HIE Grading			Total n (%)	P Value
	HIE I n (%)	HIE II n (%)	HIE III n (%)		
Birth Weight					
<2500 gm	0 (0%)	9 (75%)	3 (25%)	12 (100%)	0.008
2500-4000 gm	16 (42.1%)	13 (34.2%)	9 (23.7)	38 (100%)	
Head Circumference					
<32 cm	0 (0%)	6 (85.7%)	1 (14.3%)	7 (100%)	0.05
32-35 cm	16 (38.1%)	15 (35.7%)	11 (26.2%)	42 (100%)	
>35 cm	0 (0%)	1 (100%)	0 (0%)	1 (100%)	

Table VI: Association of Anthropometric Measurements with Severity of HIE (n=50).

In the study, association of birth weight and head circumference of the asphyxiated neonate with the severity of HIE was statistically significant (P<0.05).

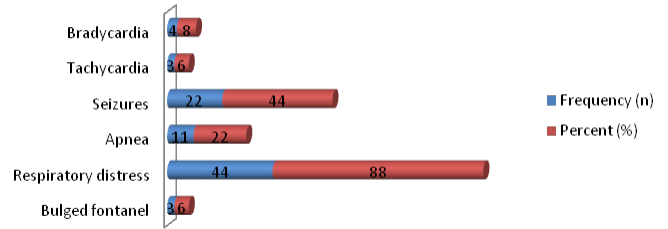


Figure 1. Clinical Profile of Asphyxiated Neonates with HIE (n=50).

In this study, 44 (88%) had respiratory distress, 22 (44%) had seizures, 11 (22%) had apnea and 3 (6%) had bulged anterior fontanel. Tachycardia and bradycardia was present in 3 (6%) and 4 (8%) neonates respectively.

Immediate Outcome	HIE Grading		
	HIE I n (%)	HIE II n (%)	HIE III n (%)
Recovered	16 (100%)	19 (86.4 %)	3 (25%)
Died	0 (0%)	2 (9.1%)	8 (66.7%)
Referred	0 (0%)	1 (4.5%)	0 (0%)
LAMA	0 (0%)	0 (0%)	1 (8.3%)
Total	16 (100%)	22 (100%)	12 (100%)

*LAMA: Leave Against Medical Advice.

Table VII: Immediate Outcome of the Asphyxiated Newborns with HIE (n=50).

The above table shows that all of the asphyxiated neonates with HIE I and most of the neonates with HIE II recovered but majority of the neonates with HIE III died.

DISCUSSION

The incidence of birth asphyxia and HIE in present study was 37.2 and 14 per 1000 live births which was comparable to the studies done by Ramya C et al⁷ and Chandra S et al⁸ respectively. In the present study, male to female ratio was 1.27:1. Many other studies of asphyxiated newborns with HIE also showed the male predominance over female.^{9,10,11} Among different HIE classification systems, Levene classification of HIE was used in this study because of its applicability in resource constraint settings like ours. Most of the neonates (44%) in the study were of HIE stage II followed by HIE stage I (32%) and HIE stage III (24%). Koreti S et al¹² and Shah GS et al¹³ also found that most of the asphyxiated neonates with HIE were of HIE stage II. Meconium Stained Amniotic Fluid (MSAF), the commonest intrapartum risk factor for birth asphyxia in the present study, was present in 36% patients which was similar to other studies.^{6,14} MSAF is an indicator of fetal distress and

its detection warrants immediate delivery by available means to prevent birth asphyxia and thus HIE. In the present study cord around the neck was present in 7 (14%) neonates and cord prolapse in 4 (8%) neonates. Maetinez-Biarze M et al¹¹ and Palsdottir K et al¹⁵ found a significant association of cord around neck at birth with birth asphyxia. Cord prolapse leads to the abrupt cessation of oxygen supply to the fetus and results in birth asphyxia. Premature Rupture of Membrane (PROM) was present in 16% cases in the present study. Many other studies have shown significant association of PROM with birth asphyxia.^{11, 16, 17, 18} Many studies have established prolonged labor as an independent risk factor for birth asphyxia.^{8, 16, 18} Ten percent mothers in this study had prolonged labor. In the present study obstructed labor was present in 12% cases among asphyxiated neonates with HIE which was similar to the study by Mohan K et al.¹⁹ Intrapartum maternal fever was present in 12% which is similar to the study done by Aslam HM et al.¹⁶ Chorioamnionitis was present in only one (2%) mother of the studied neonates. Association of maternal fever and chorioamnionitis with birth asphyxia could be attributed to the inflammatory pathways involving cytokines and chemokines which is common to all these processes.¹⁶ In this study 8% of mother's labor was augmented by oxytocin which was consistent with the finding of Futrakul S et al.¹⁰ Sustained uterine contraction due to the use of oxytocin could interfere with the fetal blood supply increasing the risk of birth asphyxia. All the infants in this study required one or other form of resuscitation at birth. Most of the asphyxiated newborns (56%) were resuscitated by Bag and Mask Ventilation (BMV) whereas only 28% were resuscitated by stimulation, 8% by endotracheal tube positive pressure ventilation, 4% by endotracheal tube positive pressure ventilation and chest compression, and 4% by endotracheal tube positive pressure ventilation, chest compression and adrenaline. BMV was the most common mode of resuscitation in various studies and it could have been so because it is recommended not to waste too much time in providing tactile stimulation to the asphyxiated neonates at birth during resuscitation.^{3,20} The mean weight of the studied neonates in this study was 2.69 (± 0.403) kg. This finding was similar to other studies where most of the asphyxiated neonates had normal weight.^{17, 20} Eighty-eight percent of studied neonates in the present study had respiratory distress which was high compared to other studies.^{17,19} High incidence of respiratory distress in the neonates with HIE in this study could be explained by the fact that meconium stained amniotic fluid was the commonest intrapartum risk factor for birth asphyxia in this study. Seizure was present in 44% of the studied neonates in this study. Similar occurrence rate of seizure in neonates with HIE has been documented in different studies.^{7,19,21} In birth asphyxia seizures occur due to cerebral edema, Na/ K pump failure and metabolic complications like hypoglycemia and hypocalcemia. The incidence of apnea was 22% among the

studied neonates in this study which was similar among the neonates with HIE in various studies.^{19,21} Mohan K et al¹⁹ and Shah GS et al²³ reported full anterior fontanel in 11% and 10% neonates with HIE which were higher compared to the present study (6%). Raised intracranial pressure secondary to cerebral edema in asphyxiated neonates leads to bulging fontanel. The overall mortality of the asphyxiated newborns with HIE in this study was 20% which was similar to the study done by Gupta SK et al²⁰ and Dongol S et al²³ In the present study mortality in HIE stage I (0%), HIE stage II (9.1%) and HIE stage III (66.7%) which was similar with the studies done by various authors.^{20, 24}

LIMITATIONS

Small sample size, single center study, unable to randomize the samples are some of the limitations of this study.

CONCLUSION

Incidence of birth asphyxia and birth asphyxia with HIE in this study were 37.2 per 1000 live births and 14 per 1000 live births respectively with male: female ratio of 1.27:1. Most of the neonates were in HIE stage II 22 (44%).16 (32%) were in HIE stage I whereas 12 (24%) were in HIE stage III Meconium stained amniotic fluid 18 (36%) was the most common intrapartum risk factor. All the neonates with HIE got one or other form of neonatal resuscitation, commonest being bag and mask ventilation (56%) ($P < 0.05$). Majority of the studied neonates were of normal birth weight (76%) and head circumference (84%) ($P < 0.05$) with clinical presentations of respiratory distress (88%), seizures (44%), apnea (22%), bradycardia (8%), tachycardia (6%) and bulged anterior fontanel (6%). The overall mortality of neonates with HIE was 20% of which most were of HIE stage III.

REFERENCES

1. Leviton A, Nelson KB. Problems with Definitions and Classifications of Newborn Encephalopathy. *Pediatr Neurol.* 1992; 8(2):85-90.
2. World Health Organization. Basic Newborn Resuscitation; A Practical Guide. World Health Organization: Geneva 1997 [Online] [Cited 2019 Dec 25]. Available at <http://WWW.who.int/reproductivehealth/publication/MSM98/introduction.en.html>.
3. Agrawal R, Paul VK, Deorari AK. Newborn Infants. In: Paul VK, Bagga A, editors. Ghai Essential of Pediatrics. 8th ed. New Delhi: CBS publisher and distributor; 2013:p.125, 137-8,144,166.
4. Nepal Demographic Survey. In: population PdMoha, editor: New ERA, ORC Macro international INC; 2011. [Online] [Cited 2019 Dec 25].
5. Dilenge ME, Majnemer A, Shevell MI. Long term developmental outcome of asphyxiated term neonates. *J Child Neurol.* 2001;16(11):781-92.

6. Badawi N, Kurinczuk JJ, Keogh JM, Alessandri LM, O'sullivan F, Burton PR. Antepartum risk factors for newborn encephalopathy: the Western Australian case-control study. *BMJ*. 1998;317(7172):1549-53.
7. Ramya C, Shantappa K, Madoori S, Ravali R. Clinico etiological profile of Hypoxic ischemic encephalopathy in preterms and their outcome. *Perspectives in medical research*. 2016;4(1):31-5.
8. Chandra S, Ramji S, Thirupuram S. Perinatal asphyxia. Multivariate analysis of risk factors in hospital births. *Indian Pediatr*.1997;34(3):206-12.
9. Shrestha S, Shrestha GS, Sharma A. Immediate Outcome of Hypoxic Ischaemic Encephalopathy in Hypoxiate Newborns in Nepal Medical College. *J Nepal Health Res Counc*. 2016;14(33):77-80.
10. Futrakul S, Praisawanna P, Thaitumyanon P. Risk factor for Hypoxic-Ischemic Encephalopathy in asphyxiated newborn infant. *J Med Assoc Thai*.2006;89(3):322-8.
11. Martinez-Biarge M, Diez-Sebastian J, Wusthoff CJ, Mercuri E, Cowan FM. Antepartum and Intrapartum Factors Preceding Neonatal Hypoxic-Ischemic Encephalopathy. *Pediatrics*.2013;132(4):e952-9.
12. Koreti S, Gupta A. Simple and feasible blood markers- as predictors of perinatal asphyxia. *International Journal of Contemporary Pediatrics*. 2017;4(3):1041-5.
13. Shah GS, Agrawal J, Mishra OP, Chalise S. Clinico- Biochemical Profile of Neonates with Birth Asphyxia in Eastern Nepal. *J Nepal Paediatr Soc*.2012;32(3):206-9.
14. Dalal EA, Bodar NL. A study on Birth Asphyxia at Tertiary Health Centre. *National Journal of Medical Research*;2013; 3 (4): 374-6.
15. Palsdottir K, Dagbjartsson A, Thorkelsson T, et al. Birth asphyxia and hypoxic ischemic encephalopathy, incidence and obstetric risk factors. *Laeknabladid*.2007;93(9):595–601.
16. Aslam HM, Saleem S, Afzal R, Iqbal U, Saleem SM, Shaikh MW, et al. Risk factors of birth asphyxia. *Ital J Pediatr*.2014;40:94.
17. Tiwari B, Tripathi VN, Kumar S. Perinatal Asphyxia-Clinical Profile in M R A Medical College Ambedkar Nagar Uttar Pradesh. *Journal of Evolution of Medical and Dental Sciences*. 2014; 3(52):12094-9.
18. Babu BVA, Devi SS, Kumar BK. Birth asphyxia – Incidence and immediate outcome in relation to risk factors and complications. *Int J Res Health Sci*.2014;2(4):1064-71.
19. Mohan K, Mishra PC, Singh DK. Clinical Profile of Birth Asphyxia in Newborn. *International Journal of Science & Technology*. 2013;3(1):10-9.
20. Gupta SK, Sarmah BK, Tiwari D, Shakya A, Khatiwada D. Clinical Profile of Neonates with Perinatal Asphyxia in a Tertiary Care Hospital of Central Nepal. *J Nepal Med Assoc*.2014;52(196):1005-9.
21. Perez JMR, Golombek SG, Sola A. Clinical hypoxic-ischemic encephalopathy score of the Iberoamerican Society of Neonatology (Siben): A new proposal for diagnosis and management. *Rev Assoc Med Bras*. 2017; 63(1):64-9.
22. Shah GS, Singh R, Das BK. Outcome of newborn with birth asphyxia. *J Nepal Med Assoc*. 2005; 44(158): 44-6.
23. Dongol S, Singh J, Shrestha S, Shakya A. Clinical Profile of Birth Asphyxia in Dhulikhel Hospital: A Retrospective Study. *J. Nepal Paediatr. Soc*. 2010;30(3):141-6.
24. Panthee K, Sharma K, Kalakheti B, Thapa K. Clinical Profile and Outcome of Asphyxiated Newborn in a Medical College Teaching Hospital. *J. Lumbini. Med.Coll*.2016; 4(1):1-3.