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Original Research Article

Profile of hypoxic ischemic encephalopathy in newborns in a tertiary care centre of Bhilai, Chhattisgarh, India

C. Sudhakar, Pallavi Jindal*

Department of Paediatrics, CM Medical College and Hospital, Durg, Chhattisgarh, India

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***Correspondence:**
Dr. Pallavi Jindal,
E-mail: pallavijindal2010@gmail.com

ABSTRACT

Background: Birth asphyxia is an important cause of static development and neurological handicap in both term and preterm infants. Birth asphyxia is found to be responsible for 28.7% deaths in hospital settings and 20% deaths in rural/tribal areas. Approximately the same number develops serious sequelae which cripples these children both physically and mentally. Children who have suffered moderate encephalopathy had varying rates of infant death and morbidity. Precise determination of the prognosis in the term new born, who sustains a hypoxic ischemic insult is hindered by difficulty in determining the severity of insult.
Methods: This was a prospective longitudinal, observational study was conducted in the Department of Paediatrics, CMC Bhilai with close association with the Department of Obstetrics and Gynecology, Department of Radio diagnosis and Department of Neurology. All deliveries taking place in the Department of Obstetrics and Gynecology of CMC Bhilai were enrolled for the study. Each enrolled infant underwent a detailed neurologic examination within the first 12 hours after birth. During the period of data collection 180 babies with birth asphyxia were admitted to NICU. Out of which 126 babies had fulfilled the inclusion criteria and completed one year follow up, hence as cases. Babies who lost follow up were not included in study. The neurological examination was performed 14 days after discharge, then at 1 month, 3-month, 6-month, 9 month and 12 months. Long term outcome in this study is defined as outcome at one year of age in terms of morbidity and mortality.
Results: The female and male ratio is 0.4:1. Most of the asphyxiated newborn, 81 (64%) were in 2500-3000gm. Among the study population, maximum number of cases 76 (60%) were suffering from HIE-I. Majority of study population, 87 (69%) were born by LSCS. Normal CUS in 93 babies and abnormal in 33 babies; with normal CUS, there were no death in study population and out of 33 abnormal CUS, 12 deaths occurred. Out of the different complications enlisted in the table convulsions (66.7%) is most common followed by Apnea (65.08%). Recurrent infections (45.24%) is the most common complication followed by seizure disorders (22.63%) and failure to thrive (20.63%).
Conclusions: Hypoxic ischemic encephalopathy is one of the major consequences of perinatal asphyxia. Despite of best care, some babies are likely to develop it.

Keywords: Cranial ultrasound, Hypoxic ischemic encephalopathy, Perinatal asphyxia

INTRODUCTION

Birth asphyxia is an important cause of static development & neurological handicap in both term and preterm infants. In simple words it is the most important cause of morbidity and mortality in new-borns in developing countries like India. The incidence of perinatal asphyxia is 1-1.5 %in most centres. Estimates of

the incidence of PA vary from 1 to 8 per 1,000 live births.[1] Neonatal encephalopathy (NE) occurs in 1-6/1000 live full-term births and carries a high risk for subsequent neurodevelopmental disabilities.[2] This is usually related inversely to gestational age and birth weight. It occurs in 9% infants in <36 weeks of gestation and 0.5% infants >36 weeks gestation.[3] Birth asphyxia is found to be responsible for 28.7% deaths in hospital settings and 20% deaths in rural/tribal areas. (may be because more high-risk pregnancies are referred to hospital). The 'State of India's newborns published by Save the Children and the National Neonatology Forum (2004), says 1.2 million out of the 26 million newborn children a year die within four weeks of birth. This is the highest share of any single country, i.e., 30 per cent of 3.9 million neonatal deaths worldwide.[4,5] Estimated deaths due to this substantially preventable and treatable cause is 3, 00,000/year and ranks as the second most important cause of neonatal deaths after infections.[6,7] Approximately the same number develops serious sequelae which cripples these children both physically and mentally.[4,8]

Children who have suffered moderate encephalopathy had varying rates of infant death and morbidity.[9] Many cases of neonatal encephalopathy were not associated with perinatal asphyxia.[9-11] Etiology of HIE is multifactorial. Clinical signs and symptoms depend upon severity, timing and duration of insult. It can lead to severe long-term neurological deficit like cerebral palsy Hankins GD et al, mental retardation, epilepsy, deafness and visual impairment.[12] Precise determination of the prognosis in the term new born, who sustains a hypoxic ischemic insult is hindered by difficulty in determining the severity of insult. Lot of studies had been done to assess the prognosis of asphyxiated newborn infants by using clinical staging, presence or absence of seizure, blood investigations and neuroimaging studies.

There are scarcities of studies on the current topic. Keeping the above facts in mind the present work has been designed to delineate the profile of asphyxiated newborns admitted to the Paediatrics Department of a tertiary care centre of Bhilai, Chhattisgarh, India.

METHODS

This was a prospective longitudinal, observational study was designed and planned in the Department of Paediatrics, CMC Bhilai, with close association with the Department of Obstetrics and Gynecology, Department of Radio Diagnosis and Department of Neurology. All deliveries taking place in the Department of Obstetrics and Gynecology of CMC Bhilai, Chhattisgarh were enrolled for the study. The study was conducted from (April 2016 to March 2018).

Sample size calculation[13]

- P = the incidence of mortality in new born with hypoxic ischemic encephalopathy = 5.9% = 0.059.
- 1.96 = z value for 5% confidence level
- e = precision = 5%

Cochran formula for descriptive analysis

Minimum Sample Size = $N = [(1.96)^2 \times p \times (1-p)] / e^2 = (3.8416 \times 0.059 \times 0.941) / (0.05)^2 = 86$

Minimum sample size = 86. To increase reliability and power of the study and to avoid loss of data, we have taken 126 samples

Inclusion criteria

- In borns.
- Asphyxiated babies received from the labour room and obstetric operation theatre, with an Apgar score of 7 or less at 5 min.
- Babies needed immediate neonatal resuscitation including bag or mask ventilation or intubation for >5 min.
- Abnormal neurological examination including the presence of any two or more of the following.
  a) Alterations of muscle tone either hypotonia/hypertonia.
  b) Abnormal neonatal reflexes including Moro's/rooting/sucking.
  c) Failure to arouse the infant even after vigorous stimulation.
  d) Presence of convulsions.
- Term neonates (≥37 weeks of gestational age by modified Ballard's scoring) or ≥2500 gm of birth weight.
- Parents of babies given consent for follow up.

Exclusion criteria

- Neonates born outside CMC Bhilai.
- Preterm babies (<37 weeks of gestation)
- Presence of congenital malformation, metabolic disorders or CNS anomalies.

Each enrolled infant underwent a detailed neurologic examination within the first 12 hours after birth. The examination evaluated 6 components: level of consciousness (hyper alert, lethargy, stupor, or coma); activity (normal, decreased or absent); posture (normal, complete extension, or decerebrate); tone (normal, hypotonic, or flaccid); primitive reflexes (normal, decreased, or absent): and autonomic dysfunction of the pupils (constricted, skew deviation, or nonreactive) heart rate (bradycardia or variability) and respirations (periodic breathing or apnea).

The clinical examination was used to characterize infants into Sarnat stages as follows:

- Stage 1 (S1): hyper alert, normal tone and activity, exaggerated Moro, absence of autonomic dysfunction,

- Stage 2 (S2): lethargy, decreased activity, hypotonia, weak primitive reflexes, constricted pupils, bradycardia or periodic breathing,
- Stage 3 (S3): stupor, coma, decerebrate posture, absent spontaneous activity, flaccid, absent reflexes and nonreactive pupils or apnea.[14]

Abnormalities of 3 of the 6 components of the examination were required to categorize an infant within a specific Sarnat stage. The Sarnat stages S1, S2 and S3 correspond to mild, moderate and severe encephalopathy. For this study, S1, S2 and S3 was considered to represent an abnormal neurologic examination. During the period of data collection 180 babies with birth asphyxia were admitted to NICU from Department of Obstetrics and Gynecology. out of which 126 babies had fulfilled the inclusion criteria and completed one year follow up, hence as cases. Babies who lost follow up were not included in study.

All the patients enrolled in the study were clinically examined on admission and repeated at 6hr, 12hr, 24hr then everyday till 1 week or till the date of discharge. Infants with an initial abnormal neurological examination were evaluated daily in the first week of life and enrolled accordingly in to Sarnat staging; all infants had a neurological examination at the time of hospital discharge.

All patients will undergo EEG examination and CUS scan within 3 days of asphyxia episode. Short term outcome is defined as outcome at 7th day and it is considered poor when there is persistence of encephalopathy in terms of abnormal neurological examination at 7th day (or beyond) or death within 7days. Abnormal neurological examination at Day 7 was considered when child had inability to take breast-feeding plus one or more of following.

- Irritability, lethargy, Impaired consciousness or coma
- Abnormal tone either hypertonia or hypotonia
- Exaggerated or depressed reflexes or clonus
- Convulsion within last 24 hours
- Signs suggestive of raised intracranial tension.

Follow-up examinations

The neurological examination was performed 14 days after discharge, then at 1 month, 3-month, 6-month, 9 month and 12 months. Long term outcome in this study is defined as outcome at one year of age in terms of morbidity and mortality. Data was compiled in MS Excel and checked for its completeness and correctness. Then it was analyzed using online statistical calculator.

RESULTS

Out of the total 126 study population, 40 (32%) are females and 86 (68%) are male. The female and male ratio is 0.4:1 (Table 1).

Table 1: Sex distribution of study group.

Sex	Asphyxiated newborn (study group)
Female	40 (32%)
Male	86 (68%)
Total	126 (100%)

Most of the asphyxiated newborn, 81 (64%) were in 2500-3000gm. The association was found non-significant (Table 2).

Table 2: Distribution of study group according to the birth weight.

Male	Birth weight (gms)			P value
	2500-3000	3000-3500	>3500	
Male	52 (64%)	26 (72%)	8 (89%)	0.26 NS
Female	29 (36%)	10 (28%)	1 (11%)	
Total	81 (100%)	36 (100%)	9 (100%)	

Maximum number of study population, 48(38%) were in the gestational age group of 39-40weeks. The association was found non-significant (Table 3).

Table 3: Distribution of study population according to gestational age.

Gender	GA (weeks)					P value
	37-38	38-39	39-40	40-41	41-42	
Male	23 (77%)	23 (68%)	33 (69%)	6 (60%)	1 (25%)	0.31 NS
Female	7 (23%)	11 (32%)	15 (31%)	4 (40%)	3 (75%)	
Total	30 (100%)	34 (100%)	48 (100%)	10 (100%)	4 (100%)	

Among the study population, maximum number of cases 76 (60%) were suffering from HIE-I. The association was found non-significant (Table 4). Majority of study population, 87 (69%) were born by LSCS. The association was found non-significant (Table 5).

Normal CUS in 93 babies and abnormal in 33 babies; with normal CUS, there were no death in study population and out of 33 abnormal CUS, 12 deaths occurred. There was signification association found between CUS and short-term outcome (Table 6).

Table 4: Distribution of study population according to the grading of hypoxic ischemic encephalopathy.

Gender	HIE grade			P value
	I	II	III	
Male	53 (70%)	24 (63%)	9 (75%)	0.67
Female	23 (30%)	14 (37%)	3 (25%)	NS
Total	76 (100%)	38 (100%)	12 (100%)	

Table 5: Distribution of study population according to the mode of delivery.

Gender	HIE grade			P value
	LSCS	NVD	F/V	
Male	61 (70%)	24 (65%)	1 (50%)	0.72
Female	26 (30%)	13 (35%)	1 (50%)	NS
Total	87 (100%)	37 (100%)	2 (100%)	

Table 6: Neurosonographic abnormality and short-term outcome.

	Outcome		Outcome
CUS (cranial ultrasound)	Death	Discharged	
Abnormal	12 (100%)	21 (18%)	<0.0001
Normal	0 (0%)	93 (82%)	
Total	12 (100%)	114 (100%)	

Table 7: Outcome at one year of age in this study population.

Outcome in 1 year	N	%
Good	81	64
Poor	31	25
NA	14	11
Total	126	100

1 year follow up out of 126 babies 81 had good outcome and 31 had bad outcome (death and morbidity). 14 babies died within 7 days of birth. NA (non-available) for babies died within 7 days of birth (Table 7).

Table 8: Distribution of short-term complications.

Co morbidity	No	%
Convulsion	84	66.67
Respiratory distress	42	33.33
Apnea	82	65.08
NEC	11	8.73
Jaundice	77	61.11
Cardiac arrest	12	9.52
Feeding intolerance	80	63.49
Septicemia	44	34.92
DIC and pulmonary haemorrhage	11	8.73
Hypoglycemia	47	37.3
Electrolyte abnormality	64	50.79

Out of the different complications enlisted in the table convulsions (66.7%) is most common followed by Apnea (65.08%) (Table 8).

Table 9: Distribution of long-term complications.

Complications	No. of babies	% response
Auditory abnormalities	6	4.76
Recurrent infection	57	45.24
Gross neuro development delay	24	19.05
Seizure disorders	28	22.63
Failure to thrive	26	20.63

Recurrent infections (45.24%) is the most common complication followed by seizure disorders (22.63%), failure to thrive (20.63%) and gross neurodevelopment delay (19.05%) (Table 9).

DISCUSSION

Perinatal asphyxia is one of the leading causes of perinatal death and a well-established cause of neuromotor disability later in life among survivors. Perinatal asphyxia is known to predispose the baby to develop a large number of neonatal disorders affecting every system of body thus increasing morbidity and mortality. When asphyxia is followed by a symptom complex, a syndrome has been described known as hypoxic ischemic encephalopathy. It is often difficult to determine clinically, the extent and location of lesion. Attempt has been made to diagnose and to evaluate the damage caused by hypoxia clinically by neurological examination with the aid of newer techniques in neuroimaging and neurophysiological studies.

In our study, during the period of data collection 180 asphyxiated babies from Department of Obstetrics and Gynecology were received. Out of 180 babies, 126 had fulfilled the inclusion criteria and hence taken cases. Complication and short-term outcome analysis on the study population was carried out for the first 7 days or till the day of discharge. During the short-term outcome analysis period 12 babies expired. 2 babies expired during long term follow up; one at 6 months and one at 8 months of age.

In the present study, the study population had male predominance which is insignificant for statistical gender preponderance. Maximum neonates were in the 39-40 week of gestational age group. Majority of patient in asphyxiated group were weighing between 2500-3000 kg (64%)

An APGAR score of <7 was recorded in all 126 newborns at 5 minutes and in 40 newborns at ten minutes. Clinical signs of convulsion were observed in 110 infants; and all received anti-epileptic drugs. 12 out of 126 infants died while hospitalized within 7 days after

birth. Death was related to severe neurological problems in all of them.

Hayes BC et al conducted a case control study.[15] Results for 237 case new-born infants (155 newborn infants with grade I encephalopathy, 61 newborn infants with grade II encephalopathy and 21 newborn infants with grade III encephalopathy) and 489 control newborn infants were described. An apgar score of <5 at 10 minutes, a continued need for resuscitation (including endotracheal or mask ventilation) at 10 minutes after birth, and/or acidosis within 60 minutes of birth (defined as any occurrence of umbilical cord, arterial or capillary pH <7.10) was present in 93 of 155 newborn infants (60%) with grade I HIE; 47 of 61 newborns (77%) with grade II HIE, and 21 of 21 newborns infants (100%) with grade III HIE.

In the present study out of 126 asphyxiated infants 2 delivered by forceps. In asphyxiated group maximum numbers of patients were born by LSCS 69% (87). Remaining 29% delivered by vaginal delivery.

Babu AB et al In their study the overall mortality rate was 17.8%.[16] Mortality as per the grade of HIE was significantly higher in stage-III (50%) compared to stage-I (4.1%) and stage-II (21.7%). Average hospital stay was same in cases and controls. Overall 42% cases were recovered without apparent sequelae and 26% had neurological sequelae.

Carli G et al included in their study; fifty-three babies who survived probable moderate HIE were identified.[17] Forty-two of these were seen at 1 year of age. Of these, 22 (52%) had normal development and neurological examination and four (9.5%) had mild developmental delay with normal neurological examination. Thirteen babies (31%) had cerebral palsy, 11 of whom also had developmental delay. Two infants (5%) who had been severely impaired at 6months expired before 1year of age. Overall, 36% of survivors of the neonatal period had significant disability and or had expired by 1 year of age. Duration of anticonvulsant treatment and length of hospital stay were significantly related to adverse outcome.

Dr. Costello's group studied the outcome of those diagnosed as "HIE stage-I, II and III" and found that almost all with stage-III was dead by one year: 25% of stage-II were dead, but 45% were impaired. Of the stage-I cases, 18% were dead and only 5% were impaired.18 Thus there exists a condition which is much more serious and crippling than polio before the nation is declared as "polio free" and there is no marked change in its incidence, risk factors, morbidity and mortality over the past decade.

In the present study, HIE-I had no death. In HIE-II 33% (4) babies expired within 7 days of life 2 babies expired on long term follow up. Where as in HIE-III 67% (8) babies expired within 7 days of life. As grading of HIE increases death rate increases.

Clinical staging of HIE was done as per Sarnat and Sarnat criteria. It is observed in our study that maximum number of patients in asphyxiated group belong to grade HIE I 60% (76), while in stage II there were 30% (38) and in stage III only 10% (12). Leijser L, Vein A et al studies consisted of mostly HIE II (52%) AND III (43%).[19] Biagioni E, Mercuri E et al study population consisted of HIE I (28%), HIE II (60%) and HIE III (4%).[20]

In this study neurosonographic findings are correlated with clinical staging of HIE. In asphyxiated group abnormal CUS scan were seen in HIE-I 30% (10), HIE-II 33% (11) and in stage III HIE 37%. In present study with abnormal CUS finding; 53% (10) have poor long-term outcome. Patients with normal CUS; 77% (72) have good outcome. The P value for this is 0.0076 which is significant. Leiser L, Vein A et al showed severely abnormal CUS finding were highly predictive of an adverse outcome.

CONCLUSION

Hypoxic ischemic encephalopathy is one of the major consequences of perinatal asphyxia. Despite of best care, some babies are likely to develop it. CUS is good modality in predicting outcome. Early diagnosis and appropriate management will not only reduce the morbidity and mortality but also increase the quality of life among these cases.

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