

Study of neuro developmental outcome of hypoxic ischemic encephalopathy of less than one-year infant in a tertiary care institute

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Abstract

Introduction: Perinatal asphyxia can lead to hypoxic ischemic encephalopathy (HIE). The mortality due to hypoxic ischemic encephalopathy is as high as 28.8% and morbidity is 30% of surviving new-born due to hypoxic ischemic encephalopathy. **Aim & Objective:** To study the neuro developmental outcome of surviving neonate with hypoxic ischemic encephalopathy till one year of age and to give early stimulation to such baby to decrease the morbidity. **Material & Method:** It is a hospital based prospective study done in tertiary care hospital in SCB Medical College Hospital & SVP PG Institute, Cuttack from July 2015 to June 2017. **Result:** The incidence of asphyxia neonatorum among the babies in normal delivery was very high compared to the babies of lower section caesarean section (LSCS) delivery. Severity of birth asphyxia was high in face presentation, followed by breech than normal vertex presentation. Respiratory distress was found to be associated with neonatal asphyxia in this study. Mortality is highest in severe encephalopathy and least in mild variety. In follow, up study neuro developmental abnormality is found to be 100% in HIE-III. 34.4% in HIE-II and normal development in stage- I HIE. **Conclusion:** Institutional delivery with trained personal with neonatal resuscitation at first golden minute will prevent birth asphyxia. Timely screening of asphyxiated babies and early sensory stimulation decreases the morbidity in asphyxiated newborn.

Keywords: Hypoxic Ischemic Encephalopathy, APGAR score, Gross Developmental Delay .

Introduction

Perinatal asphyxia is one of the most common primary causes of mortality (28.8%) and morbidity among neonates in India and is the commonest cause of stillbirths (45.1%) [1]. Birth asphyxia is the most common and important cause of preventable cerebral injury occurring in the neonatal period [2]. Full recovery may not occur and many children are left with lifelong neurological impairment and in some cases, incapacitating disability[3].

WHO has defined perinatal asphyxia as failure to initiate and sustain breathing at birth. The NNPD, 2000 defined moderate asphyxia as slow gasping breathing or an APGAR score of 4-6 at 1 minute of age [4,5]. Hypoxic ischemic encephalopathy (HIE) is a term that describes encephalopathy as defined above, with objective data to support a hypoxic ischemic mechanism as the underlying cause for encephalopathy [6]. An estimated one million children who survive

birth asphyxia live with chronic neuro developmental morbidities including cerebral palsy, mental retardation and learning disabilities[7].

Material

After getting ethical committee clearance, the study has been organised with prior written informed consent from the parents of new-born babies suffered from HIE. It is a hospital based prospective study done in SNCU, NICU & New-born ward of SCB Medical College Hospital from July 2015 to June 2017.

Newborn babies admitted newborn ward, SNCU, NICU satisfying the inclusion and exclusion criteria were taken into the study.

Inclusion criteria: a. Gestational age ≥ 37 weeks, b. APGAR Score ≤ 6 at 1 min of birth [8], c. Requirement of ≥ 1 min positive pressure ventilation (PPV) before sustained respiration occurred, d. Need for mechanical ventilation at birth.

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Exclusion criteria: a. Gestational age <37weeks, b. APGAR Score \geq 7 at 1 min of birth, c. Major congenital diseases & alformation, d. Intraventricular heamorrhage. Total 151 new-borns were enrolled in our study and were counselled for regular follow up.

Methods

new-borns enrolled were studied according to pre-structured Performa together with the result of physical examination at the time of admission, discharge and on subsequent follow up and routine investigation done at the time of admissions are haemoglobin, differential count, total leucocytes count, band cell count, blood culture and sensitivity, C-reactive protein (CRP) (Quantitative), serum sodium, potassium, calcium and random blood sugar (RBS), serum urea, creatinine. On each of follow up at every 3-month interval following assessment was done.

1. Neurological assessment done using Amiel Tison scale at the time of discharge, 1 month, 3 month, 6 month, 9 month, 12 month.

Observation

Table-1: Maternal age in relation to birth asphyxia

Maternal age in years	Number of birth asphyxia	Percentage
< 20	80	53.3
21-35	30	19.8
>35	41	26.49

The birth asphyxia is highest (53.3%) in mother below 20 years and high maternal age of 35 years, which is also a risk factor.

Table-2: Parity in relation to birth asphyxia

Parity	Number of birth asphyxia	Percentage
1	55	36.42
2	30	19.8
3	17	11.2
4	13	8.6
5	36	23.7

The birth asphyxia is maximum in primipara (36.42%) followed by grand multipara (23.7%).

Table-3: Place of delivery in relation to birth asphyxia.

Place of delivery		No of birth asphyxia
Home	Mild	2 (2.7%)
	Moderate	54 (75%)
	Severe	16(22.3%)
Hospital	Mild	15(19%)
	Moderate	56(71%)
	Severe	8(10%)

The severe asphyxia was higher in-home delivery (22.3%) as compared to hospital delivery (10%).

2. Developmental assessment done: assessment of milestones in all 4 domains of development done. Milestones are development are divided into 4 domains—gross motor, fine motor, language and social/ personal/cognition.
3. Growth and nutrition, immunisation assessment by clinical and WHO Growth charts during each follow up visits.
4. Ophthalmologic assessment for squint and refractive error.
5. Hearing screening by BERA.
6. Transcranial USG, CT Scan and MRI of Brain were done.

The data obtained were analysed with respect to standard statistical methods. The data were noted in tabulated form, necessary statistical procedure was applied to observe the percentage outcome.

Statistical analysis:

Statistical analysis was done by statistical software SPSS for windows version 21. P values were calculated using chi- square test.

Table-4: Mode of delivery in relation to birth asphyxia.

Mode of Delivery	No of birth asphyxia	Degree of Asphyxia
Normal Vaginal	111(73.5%)	Mild 13 (11.7%)
		Moderate 79 (71.2%)
		Severe 19 (17.1%)
Breech both(both)	25	Mild 1 (4%)
		Moderate 14 (56%)
		Severe 10 (40%)
Face (both)	7	Mild 1 (14.3%)
		Moderate 1(14.3%)
		Severe 5(71.4%)
LSCS	40(26.5%)	Mild 4 (10%)
		Moderate 31 (77.5%)
		Severe 5 (12.5%)

The occurrence of severe degree of asphyxia is highest in face presentation (71.4%) followed by 40% in breech presentation and 17.5% in vaginal delivery & 12.5% in caesarian section.

Table-5: Incidence of complication of Birth Asphyxia.

Complication	No of birth asphyxia	Percentage
Apnea	34	22.5
Respiratory distress	80	52.9
Hypoglycemia	26	17.2
Neurological abnormality	134	88.7
Sepsis	51	33.8
Neonatal jaundice	34	22.51
Renal failure	44	29.1
Coagulopathy	24	15.9

The above table shows that neurological abnormality (88.7%) is maximum in asphyxiated babies followed by respiratory distress (52.9%) followed by sepsis (33.8%).

Table- 6: Mortality in different grade of birth asphyxia.

Grade of HIE	No of HIE	Percentage	No of death	Percentage
I	17	11.25	0	0
II	110	72.84	9	8.2
III	24	15.89	10	41.7

The above table shows that mortality is maximum in HIE-III followed by HIE-II & least in HIE-I.

The difference observed in mortality in different stage of HIE was found to be statistically significant ($p < 0.05$) by applying Chi-squared test.

Follow up

Out of 151 babies 19 died in the hospital. Rest 132 discharged & Counseled for regular follow up. Out of them 18 lost to follow up, rest 114 came for regular follow up every 3-month interval till 1 year of age. Out of 114, 5 in HIE –I, 96 in HIE-II, 13 in HIE-III came for regular follow up.

Table-7: Head circumference of babies on follow up.

Head circumference	Normal for age	In between 2SD-3SD	More than - 3SD	Percentage of microcephaly
I	5	0	0	0
II	54	9	33	34.4
III	0	0	13	100

The above table shows that all babies of HIE- I showed normal head circumference and all babies of HIE- III showed small for age head circumference.

Table-8: Different type of reflexes found in HIE.

Grade of HIE		Tone			DTR		Primitive Reflex	
		Normal	Hypertonia	Hypotonia	Normal	Increased	Abnormal & persistent	Absent
I	3M	5	0	0	5	0	0	0
	6M	5	0	0	5	0	0	0
	9M	5	0	0	5	0	0	0
	12M	5	0	0	5	0	0	0
II	3M	61	31	4	54	42	35	0
	6M	61	33	2	61	35	35	0
	9M	61	33	2	61	35	35	0
	12M	61	33	2	61	35	33	2
III	3M	0	10	3	0	13	11	2
	6M	0	12	1	0	13	13	1
	9M	0	12	1	0	13	13	0
	12M	0	12	1	0	13	13	0

On follow up we have seen that all the HIE-I babies had normal tone, reflex & no persistence primitive reflex. Out of 96 HIE-II babies by the age of 3 month 61 were having normal tone, 31 were having hypertonia & 4 were having hypotonia. Out of 61 normal, 7 were having increased DTR. Subsequently on 6 months 2 hypotonic baby became hypertonic & 7 normal tone babies became normal in reflex & 35 babies those were having abnormal tone were having abnormal & persistence of primitive reflexes. Out of 13 HIE-III all were having abnormal tone & persistence of primitive reflexes.

Table-9: Relation of developmental delay with HIE.

Grade of HIE	No of cases	Normal developmental milestone	Delayed developmental milestone		Percentage of GD
			MD	GD	
I	5	5	0	0	0
II	96	54	9	33	34.4
III	0	0	0	13	100

From the above table it is seen that all HIE-III babies suffered from gross delayed developmental milestone & all HIE-I babies had normal development. About 56.25% of HIE-II were having normal development & 9.37% having mild developmental delay & 34.4% were having gross developmental delay. The difference observed is statically significant ($p < 0.05$) by chi-squared test

Table-10: Relationship of HIE with different abnormality.

Grade of HIE	No of cases	Neurological abnormality			Vision abnormality	%	Hearing abnormality	%
		Absent	present	%				
I	5	5	0	0	0	0	0	
II	96	61	35	36.4	9	9	6	
III	13	0	0	13	3	27	15.3	

The above table shows that all most all surviving HIE-III developed neurological abnormality, 36.4% of HIE-II developed neurological abnormality. out of 35,33 HIE-II were having gross developmental delay & another 2 were having mild delay. The Percentage of cerebral palsy was found to be 36.4%. The difference observed in different stages of HIE is statically significant ($p < 0.05$) by Chi-squared test. 27% of HIE –III suffered from squint /cortical blindness & 9% of HIE –II had squint. Hearing defect was observed in 6% of HIE-II & 15.3% of HIE-III newborn.

Discussion

The incidence of birth asphyxia in relation to maternal age was found to be highest 53.3% in below 20 years of maternal age. Rise in birth asphyxia of 26.49% in age group of 35 years. Our study is similar to the observation done by Sharma V et al [9] and Lee et al [10] who stated that the risk of birth asphyxia mortality was 88% in young mothers of age <20years. We observed birth asphyxia to be highest in primipara (36.42%) followed by in grand multipara (>5) that is 23.7%. The study by Lee et al [10] showed that primipara has more risk of asphyxia. In contrast delivery related complications were minimum in primipara & maximum in multipara stated by Iian Arad et al [11].

Mode of delivery is an important predisposing factor in Asphyxia neonatorum. Only 6.5% of newborn delivery by LSCS had asphyxia at birth where as it was as high as 73.5%. Present study corroborates with the study of Kumar et al[12] who reported higher incidence of neonatal asphyxia in vaginal delivery. Dweck et al reported 60% asphyxiated babies born out of abnormal labour and delivery[13]. Chandra et al also observed caesarean section and breech delivery to be significantly associated with asphyxia [14]. A higher association of vaginal breech deliveries with asphyxia has been reported by Chaturvedi et al[15]. A higher incidence of asphyxia (38.5%) in caesarean deliveries and attributed it to higher number of unbooked cases and high-risk indication for caesarean section has been reported by Batra et al [16].

These results are somewhat at variance to our finding. The incidence of neonatal asphyxia in asphyxia in the present study was 52.3% among the hospital deliveries whereas the incidence of asphyxia among home delivery was 69.5%. Due to NRHM & JSY trained delivery has increased drastically. So, the percentage of hospital delivery has increased. But severe birth asphyxia is definitely higher in-home delivery than institutional delivery. Bhandari et al reported high incidence of birth asphyxia in rural area could be due to 96% deliveries were conducted at home in rural areas [17]. Incidence of respiratory distress in the present study group following neonatal asphyxia were 52.9%. Other complications occurring in asphyxiated neonates

were neonatal jaundice, hypoglycemia, convulsion, sepsis, renal failure, coagulopathy. 22.5% asphyxiated babies developed hyper bilirubinemia. 15.9 asphyxiated newborns had consumption coagulopathy. Perlman JM et al stated that in asphyxiated term infants renal, CNS, Cardiac and lung dysfunction occur in 50%, 28%, 25% and 25% cases respectively [18]. Martin-Ancel et al reported that the Central Nervous System (CNS) was most frequently involved (72%)[19]. Severe CNS injury always occurred with involvement of other organs. Renal involvement occurred in 42%, pulmonary in 26% and gastrointestinal in 29% of the infants, 15% neonates had renal failure and 19% had respiratory failure.

The babies who had HIE in the present series were grouped into 3 grades of severity according to Sarnats's clinical staging. 11,3% were HIE-I, 72.8% in HIE-II and 15.9% in HIE-III. As most of HIE-I are not coming for regular follow up & most of the HIE-III in rural area are neglected, their percentage of follow up is less compared to HIE-II. Mortality in HIE –I was 0%, which is similar to Dawn E. Elder et al, who reported no death in HIE –I group [20]. Mortality in HIE-II was 8.2%. Levene et al reported very low mortality in this group (4.34%) [21]. Mortality in HIE –III was 41.7%, which was low as compared to Dawn E. Elder et al, who reported 80 % mortality in this group. On regular follow up in the present study, 20% of HIE-I showed nutritional deficiency I. e. <3 SD below the mean & 80% had normal growth. 45.83% of HIE –II had nutritional deficiency <3SD. Majority of HIE-III had nutritional deficiency (84.6%).

Due to regular follow up it has increased immunization coverage 80-100%. Exclusive breast feeding in follow up babies upto 6 month is 50.33%. Coverage evaluation survey (2009) reportedly only 36.8% of infants aged 6-9 months received exclusive breast feeding until 6 months of life. Head circumference was small for age in 100% of HIE-III, 34.4% of HIE-II. All most all HIE-I were having normal head circumference. 59% of HIE-II were having HC in normal range & 9.3% were having HC between 2SD & 3SD below the mean. Charlene MT Robertson et al reported that the head circumference is an important baseline parameter, measurement below the third percentile may indicate that the brain

pathology preceded the intrapartum asphyxia, whereas a normal baseline with the subsequent decelerated growth suggest a peripartum cause [22]. A decrease of head circumference growth in early months, as determined by serial measurements, is associated with adverse outcome. In the present study all most all (100%) HIE-III showed delayed developmental milestone. 34.4% of HIE-II had grossly delayed development and all most all HIE-I had normal development.

Dixin et al stated that 62% of those with severe encephalopathy had poor developmental outcome compared to 25% of those with moderate encephalopathy [23]. In the present study no HIE-I baby showed neurological abnormality. 100% of HIE-III had neurological abnormality. 36.4% of HIE-II developed neurological abnormality. Out of 35 HIE with abnormal neurology, 33 HIE-II were having gross developmental delay & another 2 were having mild delay.

Percentage of cerebral palsy was found to be 36.4%, which is quite similar to study result by G Carli et al that among HIE-II survivor (52%) had normal development and neurological examination and four (9.5%) had mild developmental delay with normal neurological examination [24].

Thirteen babies (31%) had cerebral palsy, 11 of whom also had developmental delay. In the present study 27% of HIE-III and 9% of HIE-II found to have vision problem in the form of squint and cortical blindness which is similar to Shankaran et al 2008[25] & Marlow et al 2005[26]. In their study 13-25% of HIE-III had blindness (often cortical blindness).

About 15.3% of HIE-III and 6% of HIE -2 found to have abnormal hearing screening on follow up BERA, which is quite similar to Shankaran et al 2008 [25] & Marlow et al 2005 in their study 6-18% of HIE-III had hearing impairment [26].

Conclusion

The incidence of asphyxia neonatarum was high among mother less than 20 years of age and above 35 years. It was common among the infants of primi mothers and parity of 5 or above.

Birth asphyxia is a preventable cause of morbidity and mortality. Not only the period of labor, delivery but also many prenatal factors & intranatal factors plays a vital role in birth asphyxia. Lack of antenatal screening, home delivery by untrained persons pose a greater risk of asphyxia.

Abbreviation

BERA: Brainstem Evoked Response Audiometry, **CNS** : Central Nervous System, **CRP:** C- reactive protein

CT Scan: Computerized Tomography Scan, **DTR:** Deep Tendon Reflex, **GDD:** Gross Developmental Delay

HIE: Hypoxic ischemic encephalopathy, **JSY:** Janani Surakhyayojana, **LSCS** : Lower Section Caesarian Section, **MD** : Mild Developmental Delay, **MRI** : Magnetic Resonance Imaging, **NICU** : neonatal intensive care unit, **NNPD:** national neonatal perinatal database, **NRHM** : National Rural Health Mission, **PPV:** Positive Pressure Ventilation, **RBS:** Random Blood Sugar, **SD** : Standard Deviation, **SNCU:** Special Neonatal Care Unit

USG: Ultrasonogram, **WHO:** World Health Organisation.

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