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A Profile of Hypoxic Ischaemic Encephalopathy in Neonatal Intensive Care Unit, Gauhati Medical College and Hospital, Guwahati.

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Abstract

Objective: To study the incidence, risk factors and outcome of HIE in NICU of Gauhati Medical College and Hospital (GMCH).

Design: Prospective study.

Setting: Tertiary care Hospital.

Participants: 228 term inborn babies who met the inclusion criteria were studied over a period of 12 months.

Intervention: None

Outcome measures: Incidence of HIE, Risk factors of HIE and Outcome among babies with HIE.

Results: The incidence of HIE was 19.97/1000 term live births or 1.9%. The statistically significant antepartum, intrapartum risk factors were primigravida (p=0.0092), fetal distress (p=0.005) and prolonged labour (p=0.0003). When the antepartum and intrapartum risk factors were distributed in the three grades of HIE (HIE I, II, III) statistically significant risk factors were Spontaneous vaginal delivery/Assisted vaginal delivery (p=0.0177), fetal distress (p=0.0024) and prolonged labour (p=0.0264). Out of 228 babies with HIE 87(38.15%) were discharged, 71(31.14%) had expired and 70(30.71%) were taken away against medical advice by the attendants. There was no deaths in babies with HIE I, however 10(15.62%) babies with HIE II and 61(93.84%) babies with HIE III were expired. 59(60%) babies with HIE I was discharged, whereas 25(39%) babies with HIE II and only 3(4.6%) babies with HIE III were discharged.

Conclusion: Incidence of HIE is very high .Some simple but important measures which will help to bring down this are: Early detection of high risk pregnancy and early referral to higher centre with proper facility, early detection of fetal distress, management of fetal distress, vigorous resuscitation at birth.

Keywords: Hypoxic ischemic encephalopathy, Incidence, Risk Factors, outcome.

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Introduction

Failure to initiate and sustain breathing immediately after delivery has been associated with hypoxic-ischemic injury to the central nervous system (CNS) and the clinical manifestations of this injury have been termed as Hypoxic Ischemic Encephalopathy (HIE). In the immediate newborn period many factors can produce neurologic symptoms mimicking HIE, including prepartum and postpartum ischemia/hypoxemia, genetic factors, metabolic disease, and maternal and fetal drug use. Since establishing the relationship between asphyxia and HIE is not always possible the term Neonatal Encephalopathy was proposed (NE) as an alternative to remove the medicolegal implications of HIE[1]. Hypoxic-ischaemic encephalopathy (HIE) is reserved for the subgroup of the term NE who have convincing evidence of intrapartum hypoxia [1]; the criteria of which have been outlined by the International Cerebral Palsy Taskforce [2].

Inspite of major advances in monitoring technology and knowledge of fetal and perinatal medicine, and the introduction of therapeutic hypothermia, HIE is one of the significant causes of neonatal mortality and permanent neurological disability worldwide. Hypoxic Ischaemic Encephalopathy (HIE) occurs at a rate of approx.1-2 /1000 full term live birth in high income countries [3,4] ,in low income countries the incidence is much higher

[5,6]. HIE is of concern because it can lead to serious long-term neuro-motor sequelae among survivors. Between 20% and 50% of newborn infants affected by perinatal brain injury die during the newborn period, and 25–60 % of the survivors suffer from permanent neurodevelopmental handicaps, including cerebral palsy, seizures, mental retardation, and learning disabilities [7-11] sequelae of hypoxic-ischaemic brain injury require significant resources [11].

In spite of the fact that birth asphyxia is the major killer of neonate in the first 24 hour very few studies are available across North-east India including Assam. Under this backdrop the present study has been undertaken with the following aims and objectives**:**

1. To study the incidence of HIE in NICU in Gauhati Medical College and Hospital (GMCH).
2. To study the risk factors for occurrence of HIE.
3. To study the correlation of risk factors with the severity of HIE.
4. To study the outcome among babies with HIE.

Materials and Methods

The present study was conducted during a period of one year from 1st September 2014 to 31st August 2015) in Neonatal Intensive Care Unit (Level IIB accredited by National Neonatology Forum) of Department of Pediatrics, of Gauhati Medical College & Hospital. The study was a prospective study and approved by Institutional Ethical Committee.

Selection of Sample

Inclusion Criteria

Out of all asphyxiated Inborn babies ,admitted to neonatal unit from September 2014 to August 2015 who developed HIE according to Sarnat classification were included in this study. Babies were labelled as asphyxiated on the basis of the definition laid down by NNF, i.e. when a baby had gasping and inadequate breathing or no breathing at 1 minute after birth. A total of 228 newborns who met the inclusion criteria were enrolled in the study.

Exclusion Criteria

1. Newborns with major congenital malformations involving central nervous or cardiovascular system.
2. Dysmorphism (obvious chromosomal abnormalities).
3. Severe hyperbilirubinemia bordering on kernicterus [Total serum bilirubin (TSB) ≥20 mg/dl].
4. Evidence of meningitis or bleeding disorders.
5. Those who are older than 15 days will be excluded. 6. Prematurity <37 weeks. 7. Out born babies those babies born outside GMCH).

Plan of Study

Babies with a gestational age of 37 weeks or more that were admitted with the clinical picture of HIE at birth on the basis of changes in the level of consciousness, muscle tone, neonatal and deep tendon reflexes and development of seizures were included. The cases were assessed and followed closely to assign a stage of HIE according to the criteria of Sarnat and Sarnat. A specially designed proforma was used, to assess the role of maternal factors and neonatal presentation of Hypoxic ischemic encephalopathy. Status of the baby on admission, resuscitation required, Apgar score, course in the hospital and maternal characteristics and antepartum history were obtained using a structured proforma. Maternal history was taken, regarding their age, gestational age, and complications. Special emphasis was on presentation other than cephalic. Anemia, hypertension, oedema, and vaginal bleeding were enquired about. Prolonged rupture of membrane, meconium stained liquor and fever was noted. Prolonged rupture was labelled when rupture of membranes was more than 18 hours before the birth of baby. Antenatal care was enquired about in detail. Mode of delivery and instrumentation, if any, was also noted.

Outcome was noted and on the basis of outcome, two groups were formed, a group who survived and a second group of babies who expired. Factors (maternal age, antenatal check-up, parity, mode of delivery, gestational age, birth weight, sex, Anemia, fetal distress, PIH, Prolonged labour. APH, Malpresentation, obstructed labour) affecting both groups were compared. Group of survivors included babies who were discharged successfully, were taking feeds and had stable vital signs.

Data analysis

The data thus collected was subsequently scrutinized individually and analysed manually. Proportions were compared by Chi square test and Fischer Exact test if needed and ‘‘p’’ value was obtained by software INSTAT. ‘‘p’’ value was considered as significant when it is less than 0.05.

Results and Observations

During the study period there were 15328 live births and 11416 (74.47%) full term live births in the Institution. Of these 437 (2.85%) babies had Perinatal Asphyxia. So incidence of Perinatal Asphyxia was 28.5/1000 live births or 2.85%. Among these 275 (63%) were full term perinatal asphyxia babies. So the Incidence of Perinatal Asphyxia among full term live births were 24.08/1000 term live births or 2.40%. HIE was observed in 228 (83%) of full term perinatal asphyxia babies. So the incidence of HIE was 19.97/1000 term live births or 1.9%. Among these 228 babies, 71 were expired, so the mortality rate was 31%. At admission 99 (43.42%) cases were in Stage I HIE, 64(28.07%) were in stage II HIE and 65(28.91%) were in stage III HIE. (Table I)

Table I. *Hypoxic Ischemic Encephalopathy (HIE)-Incidence and Mortality*

Variable	*Frequencies*
Deliveries during study period	16415
Live births	15328
Full term live births	11416(74.47%)
Preterm live births	3912(25.53%)
Babies with Perinatal asphyxia(Inborn)	437(2.85%)
Full term babies with Perinatal Asphyxia (Inborn)	275(63%)
Preterm babies with Perinatal Asphyxia	162(37%)
HIE in full term babies with Perinatal asphyxia(Study Population)	228 (83%)
Deaths in full term neonates with HIE	71(31%)
Incidence of Perinatal Asphyxia	28.5/1000 live births or 2.85%.
Incidence of Perinatal Asphyxia among full term live births	24.08/100 term live births or 2.40%
Incidence of HIE	19.97/1000 term live births or 1.9%.

The male to female ratio was 2.35:1 in the discharged group and 1.95:1 in the expired group. The mean age of mothers in the discharged group and the expired group were comparable (23.385 vs 24.296 yrs.). Most of the mothers (81.62%) in the discharged group and in the expired group (91.54%) belong to the age group of 20-35 yrs. Most of the neonates were term (99% vs 94% in the discharged and expired group) and percentage of SVD was higher in both the groups (66% vs 62%). The background demographic characteristics of both the groups such as maternal age, no. of antenatal check-up, mode of delivery, gestational age of the baby, birth weight and sex of the baby were not statistically significant. (Table II).

More of the HIE babies who expired were born to primi mothers (93%) as compared to those who were discharged (69%) (p=0.0092). Most of the babies who required prolonged resuscitation in the form of bag and mask or bag and tube ventilation were expired (44% vs 27%) p=0.006. (Table II)

Out of 228 cases, in 87.71% cases mothers were suffering from anemia. In 57.46% cases, there was history of antenatal fetal distress. In 29.38% deliveries were associated with meconium stained liquor. In 15% cases duration of labour was prolonged. In 7.45% cases mothers were suffering from Preeclampsia. In 6.14% cases mothers had history of inadequate antenatal check-up (either < 3 or no antenatal visit). In 4.82% cases deliveries were associated with prolonged rupture of membrane. In

Table II. Baseline data of the study patients

SVD: Spontaneous Vaginal Delivery, LSCS: Lower segment caesarean section, SGA: Small for gestational age, LGA: Large for gestational age, AGA: Appropriate for gestational age

Maternal	*Parameters*	*Discharged (%) (n=87)*	*Expired (%) (n=71)*	*P Value*
Age	(Mean ± *SD*	23.38 ± *4.4*	24.30 ± *4.3*	
Age (years)	20-35	86(81.62)	69(91.54)	0.5882*
	>35	1(1.14)	2(2.83)	
Antenatal check up	No	6(7)	4(5)	1.000*
	Yes	81(93)	67(95)	
Parity	Primi	60(69)	34(93)	**0.0092#**
	Multi	27(31)	37(7)	
Mode of delivery	SVD	57(66)	44(62)	0.3677*
	LSCS	28(32)	26(37)	
	Ventouse	0(0)	1(1)	
	Forceps	2(2)	0(0)	
Resuscitation steps needed	Initial Steps	14(16)	0(0)	**0.006#**
	Oxygen	50(57)	40(56)	
	Bag & mask/tube	23(27)	31(44)	
		Baby		
Gestational Age of Baby	Term	86(99)	67(94)	0.1747*
	Post term	1(1)	4(6)	
Birth Weight	SGA	23(26)	24(34)	0.5731*
	LGA	2(3)	2(3)	
	AGA	62(71)	45(63)	
Sex	Male	61	47	0.6105*
	Female	26	24	

*- not significant, #- significant

3.07% cases mothers were suffering from PIH. In 2.63% cases mothers had history of antenatal vaginal bleeding suggestive of APH. In 2.63% cases mothers were suffering from eclampsia. In 2.19% cases mothers had history of obstructed labour. In 2% cases presentation was other than cephalic. In 2% cases mothers had history of fever within 2 weeks of delivery. Among these statistically significant risk factors were fetal distress (p=0.005) and prolonged labour (p=0.0003). (Table III) When the antepartum and intrapartum risk factors were distributed in the three grades of HIE (HIE I, II, III) statistically significant risk factors were Spontaneous vaginal delivery/Assisted vaginal delivery (p=0.0177), fetal distress (p=0.0024) and prolonged labour (p=0.0264). (Table IV)

Out of 228 babies with HIE 38.15% were discharged, 31.14% had expired and 30.71% were taken away against medical advice by the Attendants. There was no deaths in babies with HIE I, however 15.62% babies with HIE II and 93.84% babies with HIE III were expired. 60% babies with HIE I was discharged, whereas 39% babies with HIE II and only 4.6% babies with HIE III were discharged. (Table V)

Discussion

This study was undertaken to know the incidence, risk factors and outcome of babies with HIE in Neonatal Unit of GMCH. 228 babies with HIE who met the inclusion criteria in the period of 1 year were included in the study. The incidence of Perinatal Asphyxia was 28.5 /1000 live births or 2.85% and the incidence of HIE was 19.97/1000 term live births or 1.9%. The statistically significant risk factors were primigravida, spontaneous/Assisted vaginal delivery, fetal distress and prolonged labour. Deaths in full

Table III. *Risk factors of HIE and their distribution in two groups (discharged & expired).*

Risk factors	***Number***	***Percentage***
Maternal Anemia	200	87.71%
Fetal distress	131	57.46%
Meconium stained liquor	67	29.38%
Prolonged Labour	34	15%
Preeclampsia	17	7.45%
No Antenatal check up	14	6.14%
Prolonged rupture of membrane >18 hours	11	4.82%
Pregnancy induced hypertension	7	3.07%
Antepartum haemorrhage	6	2.63%
Eclampsia	6	2.63%
Obstructed labour	5	2.19%
Malpresentations	4	2%
Maternal Fever	4	2%

Risk Factors	**Parameters**	**Discharged**	**Expired**	**P value**
Prolonged rupture of membrane >18 hours	No	83(95)	64(90)	0.2231*
	Yes	4(5)	7(10)	
Meconium stained liquor	No	59(68)	47(66)	0.8659*
	Yes	28(32)	24(34)	
Parity	Primi	60(69)	34(48)	**0.0092#**
	Multi	27(31)	37(52)	
Anemia	Yes	81(93.11)	64(91.55)	0.7676*
	No	6(6.89)	6(8.45)	
Pregnancy induced Hypertension	Yes	17(12.64)	11(15.49)	0.5374*
	No	70(87.36)	60(84.51)	
Fetal Distress	Yes	44(50.57)	55(77.47)	**0.005#**
	No	43(49.43)	16(22.53)	
Prolonged Labour	No	68(78.17)	69(97.19)	**0.0003#**
	Yes	19(21.83)	2(2.81)	
Antepartum hemorrhage	No	85(97.7)	69(97.18)	1.0000*
	Yes	2(2.30)	2(2.82)	
Obstructed Labour	No	85(97.7)	68(95.77)	0.6578*
	Yes	2(2.3)	3(4.23)	
Malpresentation	No	86(98.85)	69(97.18)	0.5882*
	Yes	1(1.15)	2(2.82)	

*-not significant, #- significant

Table IV. *Antepartum & Intrapartum risk factors among grades of HIE (HIE I, HIE II, HIE III)*

Sl. No.	*Factors*	*HIIE I (n=99)*		*HIE II (n=64)*		*HIE III(n=65)*		*p value*
		No.	%	No	%	No	%	
1.	No or <3 antenatal visit	6	6.06%	3	4.69%	5	7.69%	0.7760*
2.	Antenatal Vaginal bleeding	3	3.03%	1	1.56%	2	3.07%	0.9584*
3.	Fever within 2 weeks of delivery	1	1.01%	1	1.56%	2	3.07%	0.3347*
4.	Anaemia	83	83.83%	57	89.06%	60	92.3%	0.2514*
5.	Pregnancy induced hypertension	4	4.04%	1	1.56%	2	3.07%	
6.	Pre-Eclampsia	8	8.08%	2	3.125%	7	10.76%	
7.	Eclampsia	4	4.04%	0	0%	2	3.07%	0.0606*
8.	Mode of delivery SVD	67	67%	52	82%	38	58.46%	
9.	Mode C-Section	29	29%	10	15%	27	41.54%	
10.	Assisted Vaginal Delivery (Forceps/ Ventouse)	3	4%	2	3%	0	0%	**0.0177#**
10.	Meconium stained liquor	25	25.25%	16	25%	26	40%	0.0847*
11.	Prelabour rupture of membrane	3	3.03%	3	4.69%	6	9.23%	0.0889*
12.	Presentation other than cephalic	2	2.02%	0	0%	2	3.07%	0.7185*
13.	Multigravida	37	37.37%	24	37.5%	33	50.76%	0.1812*
17.	Fetal distress	51	51.51%	31	48.44%	49	75.38%	**0.0024#**
18.	Prolonged labour	21	21..21%	9	14.06%	4	6.15%	**0.0264#**
19.	Obstructed labour	2	2.02%	0	0%	3	4.62%	0.3859*

*- not significant, #-significant, SVD: Spontaneous vaginal delivery

Table V. *Grade of HIE vs Immediate Outcome*

Sl. No	*Factors*	*HIIE I (n=99)*		*HIE II (n=64)*		*HIE III(n=65)*		*Total*	*p value*
		No	%	No	%	No	%		
1.	Discharged	59	60%	25	39%	3	4.6%	87	
2.	Expired	0	0%	10	15.62%	61	93.84%	71	
3.	Left against Medical Advice (LAMA)	40	40%	29	45.38%	1	1.56%	70	**<0.0001#**

*- not significant, #-significant

Table VI. *Incidence of HIE in various studies*

Author	*Location*	*Year of Birth*	*Number of cases/live births*	*Incidence per 1000*
Hospital Based Study				
Itoo et al [14]	Madina Maternity and Children's Hospital Madina-Al-manawara Kingdom of Saudi Arabia	1995-1996	70/12,730 term live births	5.50(4.29-6.94)
			70/15,005 all live births	4.67(3.64-5.89)
Airede [15]	Joe University Teaching Hospital Nigeria	1987-1989	166/6181	26.2(22.7-30.8)

term neonates with HIE were 31%, majority of which was contributed by HIE III (93.84%), none of the babies with HIE I was expired.

In our study the incidence of Perinatal Asphyxia was 28.5 /1000 live births or 2.85% and the incidence of HIE was 19.97/1000 term live births or 1.9%.This is similar to study by Ekta AD [12] (6.6% and 1.9% respectively) and Vijai Anand babu (6.6%, 2.8%) [13].The reported incidence of Perinatal asphyxia and HIE in the developing world is varied [14-17] (Table VI) because some of these studies have included all the live born babies in their study while only term or post term babies are included in some study. Various definitions of perinatal asphyxia also play a part. Higher incidence of HIE in our study could be explained by the fact that this study was conducted in a tertiary care hospital where many of the high risk pregnancies are referred and bound to be managed. In this study male to female ratio was 1.5:1 which was almost similar to other studies. Babies delivered by Spontaneous or assisted vaginal delivery and babies who required prolonged resuscitation in the form of bag & mask or bag & tube ventilation developed HIE more often. Incidence was maximum in mothers of 20-35 yrs. Primiparity, evidence of fetal distress and prolonged labour were found

to be important risk factors. Primi mothers are more prone to deliver asphyxiated babies may be due to prolonged labour prematurity and low birth weight which are common in primi. These findings are similar to previous studies [12,13,17]. No statistically significant correlation were found in between Antenatal check-ups, PIH, Pre-eclampsia, eclampsia, PROM, APH and the occurrence of HIE. This can be explained by the fact that many of the infants who developed HIE have an uneventful fetal course after which they experience a hypoxic-ischemic event sometimes associated with infection that compromises the fetus. In this study anemic mothers were equally distributed in both groups (Discharged and Expired), hence no positive correlation has been found. In our study the overall mortality rate was 31%. Mortality was higher in HIE III (93.84%) as compared to HIE II (15.62%).This is high in comparison to other studies [12,13,17]. This reflects the high need for early diagnosis and prompt referral of High risk pregnancies. Limitations of the study were 1) Lack of control population, so proper matching cannot be done.

Conclusion

The most frequently cited definitions of HIE do not successfully identify all infants who are affected; consensus standardised definitions and the benchmarking of HIE against a comparable definition is a global priority. Research in low-resource settings is difficult because of lack of infrastructure, but this baseline data is needed before the benefit of neuroprotective strategies can be established. Future research should focus on: 1) what is the optimal time period and depth of therapeutic hypothermia? 2) How can cooling be facilitated in a low resource setting and during transport? 3) Is cooling effective when started after 6 hours or given to infants < 36 weeks? 4) Do infants with mild HIE have impaired cognitive functions and would they benefit from Hypothermia Therapy?

What is already known?

Hypoxic ischemic encephalopathy is a significant cause of mortality and long term neurological disability

What this study adds?

Incidence of HIE is very high and it has not reduced despite various measures.

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