



Science

## STUDY OF CRANIAL ULTRASOUND FINDING IN HYPOXIC ISCHEMIC ENCEPHALOPATHY IN TERM INFANTS AND ITS CLINICAL CORELATION

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### Abstract

**Introduction:** Incidence of Hypoxic Ischemic Encephalopathy (HIE) is 2-4 per 1000 live birth in USA, 1.8 per 1000 live births in Sweden, 3.8 per 1000 term live births in Australia. In India the incidence of HIE is 10-15 per 1000 live birth. The survivors from severe HIE develop cerebral palsy and mental handicaps as high as 50%. Concurrent use of cranial ultra sound and clinical staging systems are evolving to predict the prognosis. **Objective:** To study the cranial ultrasonographic finding in HIE Infants and its clinical correlation and prediction of outcome. **Method:** it is a prospective clinical study of 120 baby suffering from hypoxic ischemic encephalopathy. **Result:** Co-relation of initial cranial ultra sonography grading with mortality and sequel showed an increasing trend as the ultrasonography grading increases, with 51.4% mortality in grade –III, 18.5% in grade-II and 15.4% in grade –I. Sequele 48.6% was observed only in grade-III sonographic abnormality. **Conclusion:** Sonographic grading is more accurate than the clinical staging in predicting recovery, mortality and sequel.

**Keywords:** Hypoxic Ischemic Encephalopathy; APGAR Score; Cranial Ultrasound.

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### 1. Introduction

Hypoxic ischemic encephalopathy is the term used to designate the clinical and neuropathologic finding of an encephalopathy that occurs in an infant who has experienced a significant episode of intra-partum asphyxia[1]. It is important to recognise that the child who subsequently will develop cerebral palsy secondary to intra-partum asphyxia will demonstrate unequivocal clinical signs of HIE during the neonatal period, usually during the first 2 to 7 days of life. Cerebral hypoxia-ischemia (asphyxia) occurring in the fetus and newborn infant is a major cause of acute mortality

and chronic neurological disability in survivors,[2] The incidence of perinatal asphyxia is about 1.0 to 1.5 % of live births in most centres and is inversely related to gestational age and birth weight ,lowering considerably in later gestation. It occurs in 9%of infants less than 36 weeks and in 0.5%of infants more than 36 weeks of gestation accounting for 20% of perinatal death[3,4] . The incidence is higher in term infants of diabetic or toxæmic mothers, these factors correlates less well in preterm infants. The Sarnat clinical stages are commonly used to estimate the severity of asphyxia insult to infants more than 36 weeks of gestation age[5].

In recent years ultrasonographic grading and correlation with clinical staging are being increasingly practised. Concurrent use of sonographic grading with clinical staging systems are evolving to predict ultimate prognosis[6]. However certain imaging futures are independently associated with poor prognosis. Since birth asphyxia is one of the leading cause of neonatal mortality in our country and as trasfontanalle ultrasonography is a non invasive relatively inexpensiveand easily repeatable bedside imaging modality, it was decided to take up the study of cranial ultrasound finding in hypoxic ischemic encephalopathy in term infants and its clinical correlations.

## 2. Method

The study was conducted at S.V.P. Post Graduate Institute of peditrcs, S C B Medical College, Cuttack from September 2015 to August 2017. It's a prospective study. We studied 120 number of infants.

### Inclusion Criteria

The inclusion criteria are

- i. Documented APGAR score of 0-3 persisting for longer than 5 minutes.
- ii. Neonatal neurological manifestations like convulsion, coma, hypotonia, lethargy.
- iii. Multiple organ involvement (brain, liver, lungs, heart, kidney, intestine)
- iv. History of difficult labour with poor or no cry immediately after birth.

### Exclusion Criteria

- i. Insult not due to hypoxic ischemia of brain such as complication of pregnancy, labour that do not support the occurrence of asphyxia.
- ii. Injury to brain caused by metabolic derangement, cerebral dysgenesis, infections, prematurity.
- iii. Infants left against medical advice.
- iv. Infants with congenital malformations.
- v. Death within half an hour of admission.
- vi. In infant where at least two cranial ultrasound could not be done.

All the babies were examined on admission physically, detail history was taken in a Performa to avoid bias. Special importance was given to gestational age, nature of delivery, duration of 2<sup>nd</sup> stage of labour and evidence of intra uterine asphyxia. All the babies were clinically graded according to severity of HIE as per Levens clinical grading and "Sarnat and Sarnat" staging. The

baby who became very sick needing Neonatal Intensive Care were being admitted to NICU (Neonatal Intensive Care Unit). The baby who were included in study underwent relevant laboratory investigations as needed. Trans cranial ultra sonogram was done in every neonate within 24 hours, at 4 weeks and at 12 weeks to evaluate the resolution and sequele. All the investigations were done in SVP PG Institute of Pediatrics, S C B Medical College, Cuttack.

## Investigations

The following investigations were done in every baby included in this study.

- i. Complete blood count,
- ii. Random blood sugar,
- iii. Serum electrolytes,
- iv. Sepsis screen,
- v. Serum urea and creatinine,
- vi. Cranial ultrasonography.

Other investigations were done as and when required according to the need.

## Cranial Ultrasound

Using the real time 2 D Scanner with high frequency (7.5Mhz) transducer Cranial ultrasound was done. Scans were performed through anterior fontanelle in both coronal and sagittal planes. Transducer was moved along parasagittal plane and anterior –posterior plane to acquire the image of whole hemisphere. Axial scanning was done through mastoid fontanelle for evaluation of posterior fossa and brain stem. Axial posterior fontanels scanning was done in selective cases for evaluation occipital horns for ventricular clot.

After all the investigation were done and tabulated

Table 1: Incidence of HIE cases among hospitalised children

Sl No	Total no of indoor admission	Total no. of HIE cases admitted	%	Total number of newborns admitted to NICU	Total number of HIE admitted to NICU	%	Number of cases excluded	Number of cases included
1	15071	633	4.2	972	283	29	163	120

The overall incidence of HIE cases among hospitalised children is 4.2% whereas ICU admissions of HIE cases constitute 44.7% of all ICU admissions. After applying exclusion criteria 120 cases included in the study.

Table 2: Clinical presentation of HIE at admission to ICU (n=120)

Sl no	Clinical presentation	No. of cases	Percentage
1	Level of consciousness		
	Hyper alert	44	37
	Coma	34	28.57
	Stuporous	10	8.11

	Lethargic	52	32.8
2	seizures	39	32.8
3	Muscle tone		
	a. Hypotonia	59	49
	b. Flacid	16	13.63
4	Behavioral abnormalities		
	Poor feeding	117	97.4
	Irritability	45	37.33
	Excessive cry	18	15.25
	Sleepiness	30	25.32
5	Reflexes: Neonatal		
	Normal	44	37
	Depressed	59	49.35
	Absent	20	16.63
	Exaggerated	-	-
	Reflexes: Deep Tendon Reflex		
	Normal	41	34
	Depressed	6	4.87
	Absent	10	8.76
	Exaggerated	84	69.8
6	Apnea	45	38
7	Papillary finding		
	Mydriasis	44	37
	Miosis	39	32.8
	Mid position / Unequal	16	13.83
8	Posture		
	Mild distal flexon	72	59.74
	Strong distal flexon	39	32.8
	Intermittent decebration	9	7.46
9	Cranial nerves palsy	0	0
10	Peripheral circulatory failure	3	2.59
11	Irregular respiration	7	6.16
12	Respiratory distress	3	2.27
13	Jaundice	5	4.22
14	Abdominal distention	9	8.11
15	Acute renal failure	2	1.94

Altered sensorium in the form of lethargy was observed in 43.5%, hyper alert state in 37% and coma in 28.6% cases. Seizure occurred in 33% cases. Hypotonia were observed in 49% and complete flaccidity in 13.6% of cases. Behavioral abnormalities in the form of poor feeding was seen in 97.45 cases, irritability in 37.3% and sleepiness 25.3% of cases and excessive cry only in 15% of cases. Almost half of cases have depressed neonatal reflexes and it was absent on 16.6% of cases. Apnea was observed in 38% of cases. 93% of cases had papillary abnormalities and 100% had posture abnormalities including 7.5% with intermittent decerebration. As to other organ involvement irregular respiration was seen in 6.2% of cases, respiratory distress in 2.3% of cases,

circulatory failure in 2.6% of cases, jaundice in 4.2% cases, ARF in 2% and abdominal distention in 8.1% of cases.

Table 3: Transcranial ultra sonogram findings in HIE babies (n=120)

Sl no	USG finding	Pre-term (n=15)	Term(n=105)	Total
1	Normal study	9(60%)	7(6.7%)	16 (13.3%)
2	Cerebral edema		86(81.9%)	86(71.6%)
3	Intra Parenchymal hemorrhage	3(20%)	9(8.6%)	12(10%)
4	Sub Ependymal hemorrhage	1(6.66%)	3(2.8%)	4(3.4%)
5	Periventricular hyperechogenicity	2(13.3%)	-	2(1.7%)

Gross USG findings in HIE cases showed normal study in 13.3%, cerebral edema in 71.6% and periventricular hyperechogenicity in 1.7%.

Table 4: USG grading in HIE CASES

Sl No	Gestational Age	No. of cases	USG GRADING			
			Normal	Grade -I	Grade -II	Grade -III
1	Preterm	15	4	4 (3.33%)	3(2.5%)	4 (3.33%)
2	Term	102	12	9(7.5%)	51(42.5%)	30(25%)
3	Post term	3	0	0	0	3(2.5%)
4	Total n=120	120	16(13.3%)	13(10.8%)	54(45%)	37(30.8%)

By cranial USG 1.8% were in grade -I. 30.8% were in grade -III and majority were in grade -II(45%). Among preterm infants babies majority were in Grade-I and Grade -III each in 3.3 % in term babies majority were in Grade-II 42.5% followed by 25% in Grade-III and all post term infants were in Grade-III.

Table 5: Outcome according to initial USG Grading

Sl. No	USG Grading	No. of cases	Death		Sequele		Recovered	
			No of cases	%	No of cases	%	No of cases	%
1	I	13	2	15.4	-	-	11	84.4
2	II	54	10	18.5	-	-	44	81.5
3	III	37	19	51.4	18	48.6	-	-
4	Total	104	31	29.8	18	17.3	55	52.9

Ultimate outcome of 104 neonates with initial USG abnormality showed recovery in 53% of cases mortality of cases and sequel in 17% of cases. New born infants with grade -I USG abnormality had mortality in 15.4% and the remaining 84.6% had completely recovery. Neonates (n=54) with grade-II USG abnormality showed 81.5% recovery mortality in 18.5% and no sequel. Among 37 neonates with grade-III USG abnormality none recovered, 51.4% died and 48.6% had sequele.

Table 6: Follow up USG in HIE cases at 4 weeks & 12 weeks

SI No	USG Grade	No of Survivor	USG at 4 weeks			USG at 12 weeks		
			Parenchymal echogenicity		Atropy	Parenchymal echogenicity		Atropy
			No resolution	Resolution		No resolution	Resolution	
1	I	11	4♥(36.4%)	7(63.6%)	-	-	4(100%)	-
2	II	44	24♦(54.5%)	20(45.5%)	-	-	24(54.5%)	-
3	III	18	18♣(100%)	-	-	14(77.8%)	-	4
4	Total	73	46(63%)	27(37%)	-	14(30.4%)	28(60.9%)	4

♥ 2 cases had died earlier, ♦ 10 cases had died earlier, ♣ 19 cases had died earlier

Follow up USG at 4 weeks and 12 weeks were done for survivors of HIE cases. Of 11 neonates grade –I USG abnormality (15%), 63.6% had complete resolution and 36.4% had no resolution by 4 weeks, by 12 weeks these infants showed complete resolution and recovered fully. Of 44 neonates with grade-II USG abnormality (18.5%), 45.5% showed complete resolution and 54.5% had no resolution by 4 weeks. Repeat USG at 12 weeks showed complete resolution of all the cases (54.5%). In grade grade-III (n=18) 100% had no resolution by 4 weeks, at 12 weeks 77.8% persisted with parenchymal hyperechogenicity and 22.2% showed cerebral atropy.

### 3. Discussion

The incidence of HIE cases from total hospital admissions is 4.2%. But HIE cases constitute 29% of all new born admitted to ICU. it is reported in the national neonatal database that the incidence of birth asphyxia is around 5%. Prakas J et al [7] reported incidence of birth asphyxia to be 18.85% among hospitalized neonates in National Institute of Child Health, Karachi. Vasudevan A et al[8] in a retrospective study in a PICU in Northern India observed birth asphyxia in 11.2% of all ICU admissions. The total newborn admission to ICU during the study period was 972, of which HIE formed 29% which is much higher than the reported of above authors. Raghvendra Narayan[9] found 25% of admitted case of NICU were HIE. About 18.42% of HIE cases were being reported of all admission of NICU by Preeti R et al, 2018[10].

Snyder ey et al [11]1991 observed poor feeding in 64% abnormal muscle tone in 70%, seizure in 30%, Apnea in 18% of cases and loss of neonatal reflexes in 64% of cases. Pandey VP [12] reported apneic attacks in 66% of affected infants whereas Bergman et al[13] observed apneic spell in 22% of term infants with asphyxia. Brown observed seizures in 50% of asphyxiated cases; Mulligan et al [14] observed seizure in 52% of cases but Leblanc and O Gorman[15] reported 30% with seizures.

The observations of the above authors shows conflicting data on different clinical features due to asphyxia. difference with our figures and the difference between the authors is probably due to different sample size, different levels of obstetric care and differing maternal conditions in the study quoted. Martin ancil et al [16] reported single organ involved in 25% , two organ involved in 34% and 3 organ involved in 9% . Kidney involvement was observed in 50%, CNS in 28%, CVS in 25% and pulmonary system in 23%. Although various organ involvements in our series were not similar to the finding of above authors, 25% of our case had various combinations of

multiple organ involvements. Our under reporting of multiple organ involvement could be due to lack of sophisticated investigations to early organ dysfunctions.

Cranial USG of brain in HIE shows normal study in 13.3%, cerebral edema in 71.6%, intraparenchymal haemorrhage in 10%, sub ependymal haemorrhage in 3.4% and periventricular hyperechogenicity in 1.7% of cases. Cally J. Tann et al [17] found no abnormality in 45.1% (83/184) of cases. Zhu L et al [18] from china reported intracranial hemorrhage 18.5% and 10.4% in which cerebral edema. Our combined figure of hemorrhage 13.4% is lower than observed. Anand N K et al [19] in a study in Safdarjung hospital New delhi observed cerebral edema in 86% and normal study in 14% which is similar to our study. However, the periventricular echogenicity of 6.6% is much higher than our figure 1.7%. Prithviraj, et al [20] found 46% of cases to be normal neuroscan, 38 % to be cerebral edema.

The ultrasonographic grading of HIE found in our study were 10.8% in grade I, 30.8% in grade – III, & 45% were in grade-II. There was no USG abnormality in 13.3% cases. Among preterm infants majority were in grade-I and grade-III each in 3.3%. in term babies majorities were in grade –III (42.5%) followed by 25% in grade –III and all post term infants were in grade-III. Indira Raghupathy[21] in a study of HIE cases in child trust hospital from may 1986 to august 1990 observed grade-I ultrasound abnormality in 46.5% cases, 34.8% in grade-II, 18.6% in grade –III HIE cases which is much different from the present study. This difference is probably due to more severe asphyxiated infants in the present series than those of the author for which grade-II and grade –III numbers were much higher (75.8%) as against 53.4% in the same grades of the author. Clinical stage-II disease had positive co-relation of 58.7% in grade-II Sonographic abnormality. 10% had grade –III sonographic abnormality which shows under diagnosis of clinical staging of these cases. No definite sonographic abnormality was seen in 17.4% cases of clinical stage-II disease showing clinical over diagnosis in these cases. Stage –III clinical disease co-relates well with sonographic grade-III abnormality in 100% cases.

At 4 weeks 2 infants had already died, in grade –I, 4 had no resolution of parenchymal hyperechogenicity, 7 had complete resolution. At 12 weeks there was no USG abnormality in the survivors indicating full recovery. In grade-II, 10 cases had died and by 4 weeks 45.5% had total resolution and 54.5% had no resolution. From these non-resolving cases, all cases had complete resolution of USG abnormality by 12 weeks. In grade-III, 19 infants had died and 100% showed no resolution at 4 weeks. At 12 WEEKS 77.8% of these persisted with no resolution and 22.2% developed cerebral atrophy. Overall out come of 73 survivors 37% had resolution and 63% no resolution at 4 weeks and of these non-resolving cases 30.4% persisted as such, 60.9% showed complete resolution and 8.7% developed cerebral atrophy at 12 weeks.

Anand N K et al [19], 1994 reported cerebral atrophy in 21% and persistent sonographic abnormality in 7% and no abnormality in 51% cases. Mejaski et al [22], 2006 reported in a follow up of 10 infants with grade-III HIE that 100% developed severe cerebral atrophy on follow up of by ultrasound. Our figure of 22% of cerebral atrophy is similar with the study of Anand NK et al [19]. There is no other comparable literature for comparison of our finding.

#### 4. Summary

The Incidence of HIE is 4.2% and constitute 29% of all Neonatal admissions to NICU. Term babies constitute 85% of all HIE cases. Lethargy (43.5%), seizures (33%), hypotonia (49%), poor feeding (97%), depressed neonatal reflex (49.3%), apnea (38%) papillary abnormality (70%) were the major clinical presentation. Clinical stage-II was 79% in term babies and 73% in preterm. Cerebral edema was the major sonographic finding inn 72% of cases and 13% had normal sonographic findings. Sonographic grading of HIE cases reveals grade-II finding in the majority (45%) followed by grade-III in 31%. Complete recovery was observed in 59%, death in 26% and sequel in 15%. Mortality was highest in stage –III in 68% and sequel in 32% without recovery in a single case. In stage-II 13% died there was no sequel, rest 77% recovered.

Correlation of initial USG grading with mortality and sequel showed an increasing trend as the USG grading increases, with 51.4% mortality in grade –III, 18.5% in grade-II and 15.4% in grade-I. Sequele 48.6% was observed only in grade –III sonographic abnormality. In sonographic positive cases from grade-I, 36.4% showed no resolution at 4 weeks but completely resolved by 12 weeks. In grade-II positive cases 54.5% showed no resolution at 4 weeks which completely resolved by 12 weeks. However, in grade-III abnormality 100% showed no resolution at 4 weeks and by 12 weeks 78% had no resolution and 22% showed features of cerebral atrophy. Overall sonographic resolution in 75.3% and persistence of abnormality remained in 24.7%

#### 5. Conclusion

Out of all HIE admission 45% required NICU care, mostly in first 3 days of life. Male, low birth weight babies are at high risk of HIE. 75% of HIE cases were from institutional deliveries, indicating poor delivery management and inadequate neonatal resuscitation. Cerebral edema and stage-II HIE are the major presentation. Sonograpgic grading is more accurate than the clinical staging in predicting recovery, mortality and sequel.

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