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The spectrum of magnetic resonance imaging (MRI) patterns in hospitalised hypoxic ischemic encephalopathy babies in a tertiary care hospital of Odisha

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***Abstract*---**Background: Hypoxic ischemic encephalopathy (HIE) refers to the CNS dysfunction associated with Perinatal Asphyxia (PA) which is an important causes of permanent damage to CNS tissue. MRI imaging methods attributes to better understanding of pathological events and disease progression that may provide decision regarding intervention. MRI has a higher sensitivity and is extremely valuable in assessing the extent of hypoxic-ischemic brain damage during the early postnatal period and later infancy. It is also more specific which clearly differentiates fluid filled cavities, oedema, gliosis and hemorrhage. On this background this study was undertaken to evaluate the MRI changes of all grades of HIE patients. They were also followed up at different time intervals for upto 1 year to correlate the MRI changes and neurodevelopmental outcome. Objectives: To find

out different MRI findings in hypoxic ischemic encephalopathy babies. Assesment of severity of HIE from MR imaging and correlate these findings with clinical & neurodevelopmental outcome. Methods: All hemodynamically stable HIE babies irrespective of their severity were subjected to MRI between day 7 and day 21 of life and their findings were interpreted. Results: Out of total 124 HIE babies, abnormal MRI was found in 60% cases. Majority were HIE –II babies and abnormal MRI was detected in 55.5% of them. Predominant watershed pattern of involvement led to developmental delay in 41% of babies and death in 15% at 12 months of age. Babies with basal ganglia/thalamic patterns, 73% had delayed development. In diffuse patterns all were having delayed. Conclusion: MRI is a definite diagnostic modality in Hypoxic Ischemic Encephalopathy. Patterns of brain injury were determined by nature, timing and severity of injury. This study will attribute to proper diagnosis of hypoxic ischemic events of HIE patients by using MRI. This may prevent neurodevelopmental delay and seizure recurrence frequencies.

***Keywords*---**HIE, MRI, perinatal asphyxia.

Introduction

As per World Health Organization (WHO) Perinatal asphyxia (PA) defined as Failure to initiate and sustain breathing [1]**.** Perinatal asphyxia is a multi-organ disorder affecting virtually every organ system in the body including brain, heart, lungs, kidneys and intestine. Care of asphyxiated neonates therefore should be oriented towards determining the severity of dysfunction of critical organ-system and providing appropriate support to allow recovery to happen. Hypoxic ischemic encephalopathy (HIE) refers to the CNS dysfunction associated with perinatal Asphyxia. It is often the prime concern while managing asphyxiated neonates because it is not only associated with high risk of mortality but also carries a significant risk of serious long term neuromotor sequelae among survivors [2]. PA is one of three most common causes of neonatal deaths[3,4]. Manifestations of hypoxic ischemic encephalopathy (HIE) were seen in approximately 1.4% of live births [5]. The diagnosis of hypoxic-ischemic encephalopathy in the newborn is based principally on a detail history and neurological examination. The history should include details of complications of pregnancy, labour and delivery. Details of APGAR scores, presence of meconium and placental pathology condition should be documented [6].

Early EEG is now being well recognized as a reliable predictor of neurodevelopment outcome in HIE[7]. EEG can provide confirmation that any suspicious phenomena are seizure. Not all clinically observed seizure is detected by EEG and many neonatal seizures are subclinical. Ultrasound scanning is an easily applicable bedside tool and has been used extensively as screening method in preterm infants[8,9]. It is less sensitive for smaller and more subtle abnormalities. It has low sensitivity in term infant with HIE [10,11]. Cranial ultrasonography has a low sensitivity (50%) for the detection of anomalies associated with HIE. Head CT scanning is a rapid mode of screening and is very

effective in detecting hemorrhage with the added advantage of limited sedation need. However, evident suggests that even a single CT scan exposes children to potentially harmful radiation [12]. CT scanning is not a sensitive modality for evaluation of HIE because of the high content of the neonatal brain and high protein content of cerebrospinal fluid, which result in poor parenchymal contrast resolution[13]. MRI overcomes many of the shortcomings of ultrasonography and CT scannings [14,15]. It has a higher sensitivity and has been extremely valuable in assessing the extent of hypoxic-ischemic brain damage during the early postnatal period and later infancy [16,17]. It also is more specific, clearly differentiating fluid filled cavities, oedema, gliosis and hemorrhage [18].

Materials and Methods

This is a prospective Observational Hospital based Study done in SNCU of Department of Paediatrics, M.K.C.G. Medical college and Hospital, Berhampur from November 2019- October 2021. Taking the prevalence of perinatal asphyxia as 8.4%, sample size calculated was 118. Taking 10% of non response rate, the sample size came to be = 118+12 =130. As 6 patients were lost during the period of follow-up due to noncompliance of parents, Final sample size is 130-6=124. Therefore the sample size for our study purpose is 124 (n=124). All hemodynamically stable HIE babies irrespective of their severity were included in the study. And those babies with neuro-infection, congenital malformation, chromosomal disorders and proven or suspected inborn error of metabolism were excluded.

Informed consent was obtained from parents. Relevant data of both mother and the babies were collected in predesigned proforma. Details of mother including mother's age, parity, complete antenatal history, place of delivery, mode of delivery, and place of residence were recorded. Details of babies include weight, sex, history of cry after birth, abnormal movements(seizure) in past or during admission, APGAR score at 1 min and at 5 min, need for resuscitation, foetal distress, meconium stained liquor. Complete clinical examination done during admission includes levels of consciousness, neuromuscular control (muscle tone, posture, stretch), complex reflexes (suck, Moro, oculovestibular, tonic neck reflex), autonomic function (pupils, heart rate, bronchial or salivary secretions, gastrointestinal motility), seizure, head circumference. Routine blood investigations were done after hospitalization.

Newborns were classified as HIE-I, HIE-II and HIE-III according to Sarnat and Sarnat staging [19] of hypoxic ischemic encephalopathy.130 cases were subjected to conventional MRI within 7 to 21 day of life [20]. Stable HIE babies were subjected for MRI. MRI scans were performed when the newborns were in physiological asleep condition (in some cases, they required sedatives like inj lorazepam or cloral hydrate syrup) which allow to obtain diagnostic images free from motion artefacts associated with the child awakening. MRI scan was done by using 1.5 tesla mechine using appropriate head coil. MRI sequence were T1W (Axial, sagittal), T2W (axial, coronal) and FLAIR (axial). Different pattern of MRI scan obtained. They were categories into 4 according to area of involvement.

Regular follow-up done at 3 month, 6 month, 9 month and 12 month at Pediatrics OPD of M.K.C.G medical college and hospital Berhampur. In each follow-up child's weight, length, head circumference, occurrence of seizure in any time during follow-up, number and type of antiepileptic drugs, immunization status, feeding history were recorded. For developmental assessment we used TRIVANDRUM DEVELOPMENTAL SCREENING CHART (TDSC) designed and developed by Child Developmental Centre, SAT Hospital, Medical college, Trivandrum. According to it a vertical line is drawn or a pencil is kept vertically at the level of chronological age of the child being used. If the child fails to achieve any item that falls short on the left side of the vertical lines, the child is considered to have developmental delay. After measurement of head circumference, it was analyzed using WHO Multicentre Growth Reference Study chart.

Statistical Analysis

Data were analysed using statistical software SPSS version 21. The categorical variables were analysed using frequency and percentage. The continuous variables were analysed by using mean +/- standard deviation. The difference between 2 catagorical variable were analysed by using chi-sq^2 test, and Fisher exact test. The group difference was found to be significant if p value < 0.05.

Table -1: Sociodemographic Parameters Of Hie Babies (n=124)

		TOTAL (%)	HIE-I	HIE-II	HIE – III
GENDER	MALE	72(58%)	3	43	26
	FEMALE	52(42%)	6	38	8
PLACE OF DELIVERY	INBORN	36(29%)	5	21	10
	OUTBORN	88(71%)	4	60	24
MODE OF DELIVERY	NVD	109(88%)	8	71	30
	LSCS	15(12%)	1	10	4
PARITY	PRIMI	88(71%)	7	56	25
	MULTI	36(29%)	2	25	9
AREA	RURAL	110(88.7%)	8	71	31
	URBAN	14(11.3%)	1	10	3

Table -1 shows male predominance. Majority of the cases were outborn. Normal vaginal delivery 88%, primi gravida 77% and multigravida 21%.

Table-2: Distribution Of Cases According To MRI Findings (n = 124)

MRI IMAGE	NUMBER	PERCENTAGE
NORMAL MRI	51	40%
ABNORMAL MRI	73	60%

Table-2 shows that, among all HIE cases, 73(60%) showed abnormal MRI findings.

Table-3: Distribution Of Mri Findings In Relation To Hie Cases (n = 124)

HIE types	Normal MRI	W	B	D	TOTAL	□**2**
I -	7(13.2%)	2(3.9%)	0(0%)	0(0%)	9(7.3%)	□^{2} =16.682
II	36(67.9%)	37(72.5%)	6(40%)	2(40%)	81(65.3%)	
III	10(18.8%	12(23.5%)	9(60%)	3(60%)	34(27.4%)	p- 0.011
TOTAL (N= 124)	53(100%)	51(100%)	15(100%)	5(100%)	124	

N = Normal MRI, W = Predominat water shed area of brain involvement, B = Basal ganglia and thalamus predominant and D = Diffuse / Summation of both W and B patterns.

Table –3 shows MRI finding of pattern N = NORMAL is maximum seen in HIE-I. Pattern W = PREDOMINAT WATER SHED AREA is maximum seen in HIE-II compared to HIE-I and HIE-III. MRI pattern B = BASAL GANGLIA AND THALAMUS PREDOMINANT and D= DIFFUSE/ SUMMATION OF BOTH W AND B PATTERNS were maximum seen in HIE-III. The association between the two groups is found to be significant with p value of < 0.05.

Table-4: Association Of Mri Patterns With Neurodevelopmental Outcome At 3 Month (n=124)

	NEURODEVELOPMENTAL OUTCOME			Chi-sq^2 □^{2} p-value
MRI	N(NORMAL) [n=53]	D (DELAY) [n= 63]	DT(DEATH) [n= 8]	
N	31(58.5%)	21(33%)	1(12.5%)	
W	21(39.6%)	25(39.7%)	5(62.5%)	
B	1(1.9%)	12(19.6%)	2(25%)	
D	0(0%)	5(7.9%)	0(0%)	□^{2}=20.067 P=0.003

Table – 4 shows the group difference between neurodevelopmental outcome and MRI patterns was found to be significant with p value of < 0.05.The maximum delay was seen with pattern of B and D which was found to be significant.

Table-5: Association Of MRI Patterns With Neurodevelopmental Outcome At 12 Month. (n=124)

MRI	NEURODEVELOPMENTAL OUTCOME			
	N(NORMAL) n=58	D(DELAY) n=54	DT(DEATH) n=12	□^{2} P- value
N	34(58.6%)	18(33.3%)	1(8.3%)	
W	22(37.9%)	21(38.9%)	8(66.7%)	□^{2}=21.241 P=0.002
B	2(3.4%)	11(20.4%)	2(16.7%)	
D	0(0%)	4(7.4%)	1(8.3%)	

The group difference between neuro-developmental outcome and MRI patterns was found to be significant with p value of < 0.05. At the end of 12 months, 54 cases showed neuro-developmental delay and death was reported in 12 babies.

Table-6: Association Of MRI Patterns With Seizure Recurrence (n=112)

MRI	SEIZURE RECURRENCE			χ^2 P=value
	YES	NO		
N	10	42		χ^2=24.855 P=0.003
W	22	21		
B	6	7		
D	4	0		

The association between MRI pattern and recurrence of seizure was found to be significant with p –value < 0.05. Here maximum seizure was seen in W- pattern, followed by in D- pattern which is significant as compared to Basal ganglia/thalamic pattern.

Discussion

The present study showed slightly male (58%) preponderance. Most of the HIE babies were from Primigravida (71%) compared to multigravida (29%) similar to other studies [21,22]. Out of 124 babies, 81(64%) Hypoxic ischemic encephalopathy babies belonged to HIE-II category followed by 34(28%) HIE-III and rest 9(8%) were HIE-I. Vrious studies had shown majority belonged to HIE II[21,23]. Depending on the various areas of involvement of brain, the MRI findings were divided into four categories as 1. N = Normal, 2. W = Predominant Watershed Areas, 3. B = Predominant Basal Ganglia And Thalamic Areas and 4. D = Diffuse involvement of areas of both watershed and basal ganglia thalamic areas. Normal MR imaging was seen in 40% cases and abnormal (distinct MR imaging) was found in 60% cases out of total 124 HIE participants in our study. In our study abnormal MR imaging was seen in majority cases HIE –III (70%) followed by HIE –II (56%) babies similar to other studies [24,25].In our study Watershed predominant pattern is most common MR patterns (42%) and 12% have basal ganglia/thalamic pattern which is comparable to a study**[26]**.

Neuro-developmental delay (according to TDSC) was seen in 63 babies (51%) at 3 month of age, 56 babies (46%) at 6 month age, 54 babies (44%) at 9 and 12 month of age. There is reduction in number of babies with neuro-developmental delay at 12 month compared to 3 month age which is probably due to normal maturation and myelination of brain in some HIE babies. These babies had MR imaging belongs to Predominant watershed patterns. During our study period, all the HIE babies (n=124) were followed up at different intervals like 3 month, 6 month, 9 month and 12 month of ages. 12 babies had lost their lives at different period during our follow up period of 12 month. The remaining HIE babies (n=112) were followed up for seizure recurrence and anti-epileptic drug (type and number of drug) therapy. In our study seizure recurrence was seen in 28.5%, similarly to the other study[22,27].

Conclusion

Majority of our study cases were from primigravida mothers. Most of them belonged to HIE-II category and they showed abnormal MRI patterns (Watershed predominant pattern is most common MRI patterns). In follow up of these cases,

majority showed neuro-developmental delay at 3 & 6 months, but later on at 9 & 12 months there was reduction in neuro-developmental delay. Seizure recurrences were more common with abnormal MRI findings especially with diffuse type and predominant water shed pattern type.

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