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MRI Brain in Perinatal Hypoxia – A Case Series.

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Abstract:
Background: *HIE is one of the most common cause of neonatal deaths and morbidity in children. Due to limited facilities in India, many a times HIE goes undetected only to present in later stages of life as handicapped children.*
Objective: *To study the Magnetic Resonance Imaging (MRI) brain findings in children having suffered perinatal hypoxia, to analyze MRI findings in brain based on time of perinatal hypoxia.*
Material and Methods: *A prospective Study was conducted on 100 patients suffered with perinatal hypoxia on Siemens 1.5 Tesla MAGNATOM AVANTO machine. Patterns of hypoxic ischemic brain injury in preterm and term infants of were evaluated.*
Results: *Out of 100 cases, 72% were abnormal and 28% were normal studies. 36 %patients were preterms and 64% had term delivery. In patients with term delivery, 28.1 % were normal and 71.8 % were abnormal. In patients with preterm delivery, 72.3% cases were found to be abnormal while 27.7 % cases did not show any significant abnormality.*
Conclusion: *MRI was a definitive diagnostic modality in perinatal hypoxia. Patterns of brain injury were determined by nature, timing and severity of insult. Imaging appearances were influenced by sequences used and time from injury.*

I. Introduction

Hypoxic Ischemic Encephalopathy (HIE) refers to a combination of hypoxia, hypercarbia and metabolic acidosis as a consequence of occlusion of umbilical vessels or interference with placental perfusion in fetal life and/or due to lack of effective breathing after birth. Hypoxia literally means decreased oxygen supply and ischemia is a resultant damage to the tissues.Thus any cause which will lead to lack of oxygen supply to the brain tissues which is extremely necessary for the normal functioning of the brain and thus in turn the other body system; it will give rise to a series of events that will lead to injury to the brain tissues and certain clinical manifestations. Almost 40% of deaths under age 5 years in children occur in the neonatal period. Reported global totals of neonatal deaths due to non-specific conditions of HIE vary from 0.7 million to 1.6 million per year. Mortality rate in children with severe hypoxia is 25–50%. Incidence of prenatal asphyxia is approximately 3.3% in India. It is usually related to gestational age and birth weight. [1] Thus, outcomes of HIE are dangerous and permanent, making it a major burden for the patient, family and the society. Thus, it is very important to identify, evaluate and analyze the effects of HIE on the brain so as to develop better therapeutic strategies to decrease the brain injury in newborns and provide them a better future.

II. Materials and Methods

A prospective study was conducted on 100 patients in the department of Radio-diagnosis, Padmashree Dr. D.Y Patil Medical College from July 2012 over a period of 2years to September 2014. The study included all the patients of paediatric age group (birth to12 years of age) referred for MRI having suffered from perinatal hypoxia. It included neonates with clinical signs of bradycardia, hypotonia and who gave poor response to stimulation. In children; developmental delay, cerebral palsy, seizures, hemiplegia/paraplegia/quadriplegia were the criteria used for performing the MRI. Patients who were on MRI incompatible life support were excluded. Patients were evaluated by Siemens 1.5 Tesla MAGNATOM AVANTO machine. The bore size was 60 cm and the overall length was 160cm. The MRI system used zero Helium boil off technology. A 32 channel head coil with iPAT compatibility was used. The proforma was designed on the objective of the study and it was used after modification.A structured proforma was used to note the detailed clinical history, birth history, developmental history, immunization details, anthropometry, physical examination findings, systemic examination findings and investigation findings.Patient was positioned in the supine position and a head coil was placed around the head to obtain a uniform signal to noise ratio. MRI examination of the brain was performed in axial, sagittal and coronal planes. A Sagittal acquisition through the mid Sagittal plane was used as

an initial localizer for subsequent axial and coronal planes. T1 (TR/ TE, 210–710/6–14 ms, flip angle 90°, matrix- 320 X 320) and T2 (TR/ TE, 1550–5800/90–200ms, 150°, matrix- 320 X 320220 X 320) weighted images were obtained. Fluid Attenuation Inversion recovery (FLAIR) (TR/ TE, 8050/120 –130/1860–2000ms, flip angle -150°, matrix- 256 X 320), Diffusion Weighted, Gradient Echo and IR sequences were also performed. ADC maps of brain were obtained in axial planes. DWI was done by using single-shot spin-echo echo-planar sequences (TR/TE, 5130–5000/74–68 ms with a b-value of 800–1000 s/mm2, matrix- 190 X 190). The conventional MR brain protocol included T1-weighted sequences, T2-weighted sequences and Gradient Echo (GRE) (TR/ TE, 700/26, flip angle-20°, matrix- 132 X 192) sequences. Field of view of 230 mm and slice thickness of 5mm for routine and 3 mm for IR sequences was used. T1-weighted and inversion recovery sequences provided excellent anatomic information as well as high contrast between gray and white matter. T2-weighted sequences provided good contrast resolution between gray matter, unmyelinated white matter and myelinated white matter. Gradient Echo (GRE) sequences provided increased sensitivity for the detection of T2-weighted magnetic susceptibility. Three-dimensional T1 IR sequence (3DT1 IR) (TR/TE, 4000-4120/70-74ms, flip angle-150°,matrix- 154 X 192) and allows thin 1 mm contiguous slices which can be reconstructed in any anatomic plane. T1-weighted IR sequence is helpful as it gives excellent images of brain anatomy and maturation. It helps in differentiating myelinated and unmyelinated WM.

III. Observations and Results

In our study of 100 cases, the lesions which were accurately diagnosed by MRI included pathologies such as germinal matrix hemorrhage, periventricular leukomalacia, cystic encephalomalacia, cerebral and cerebellar atrophy, corpus callosal thinning and agenesis and delayed myelination. Thus, in diagnosis of these conditions MRI was a definitive diagnostic modality. MRI was able to diagnose these conditions in 72% of the patients. However, in rest of the 28 % patients, MRI was normal, even though the patient had a history of perinatal hypoxia or was symptomatic.

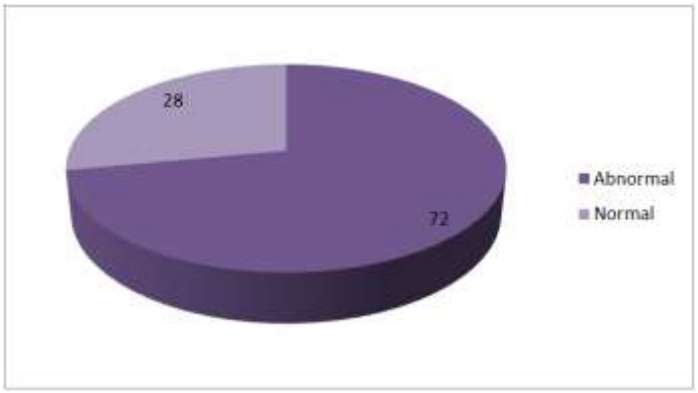

Figure-1 Distribution of total number of cases studied

Sex Wise Distribution

In this study MRI of the brain was done in 100 patients out of whom 56 were males and 46 were females as seen in the chart below. Thus, males were more commonly affected than females.

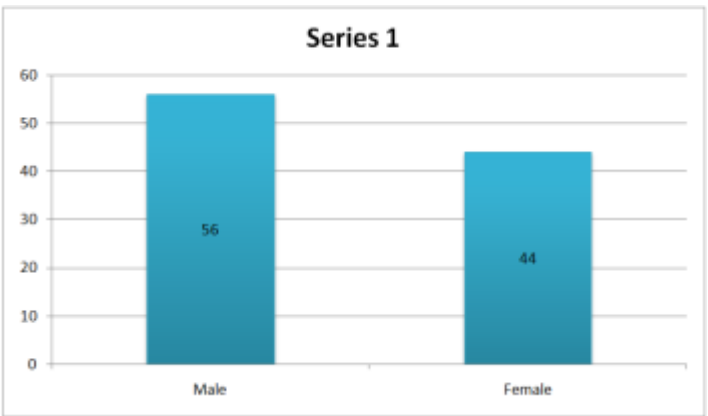

Figure-2: Sex distribution of children suffered with perinatal hypoxia.

Age Wise Distribution

The age of patients ranged from 0 years to 12 years. It is clear from the table below that maximum pathologies were seen in patients who were in the age group of 1 to 5 years.

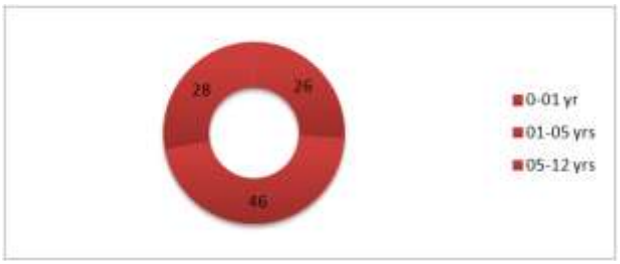

Figure-3 Age wise distribution of children suffered with perinatal hypoxia.

Gestational Age Wise Distribution

In our case study, 36 patients had a history of preterm delivery and 64 patients were term neonates.

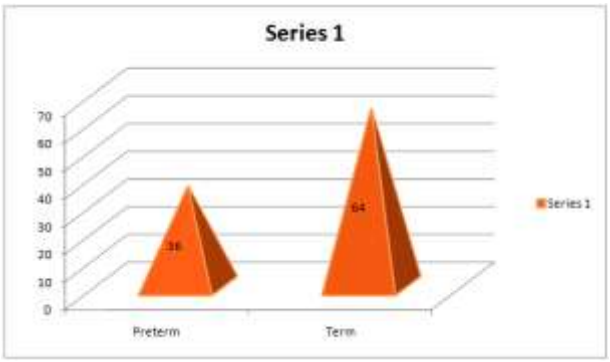

Figure - 4 Distribution of cases according to gestational age.

Distribution of Risk Factors for HIE

There are various risk factors for HIE in a preterm or term neonate. Amongst all maternal and fetal factors no specific cause was found in around 25% of the cases. It was followed by pre eclampsia and anemia. The other causes have been charted below.

Risk Factors	Number	Percentage (n =100)
Indiopathic	25	25 %
Pre eclampsia	20	20 %
Anemia	15	15 %
Placental Factors	10	10 %
Perinatal Infection	8	8 %
Assisted Delivery	7	7 %
Caesarean Section	15	15 %

Table -1 Distribution of risk factors for HIE.

Distribution Of Cases According To The Gravid Status Of The Mothers

Information of gravid status, antenatal examination, hospital or home delivery was obtained of all the mothers of 100 patients.

Gravid status	Distribution (n=100)
Primigravida	55 (55%)
No antenatal examination	44 (80%)
Undergone antenatal examination	11 (20%)
Home deliveries	15 (27.2%)
Hospital deliveries	40 (72.8%)
Multigravida	45 (45%)
No antenatal examination	33 (75%)
Undergone antenatal examination	12 (25%)
Home deliveries	14 (31.1%)
Hospital deliveries	31 (68.9%)

Table-2 Distribution of Cases According To the Gravid Status ofthe Mothers.

Imaging Findings in Term Neonates

64 cases of term neonates who suffered perinatal hypoxia underwent MRI, out of which 46 cases were abnormal (71.8%). Of them, 36 showed white matter (cortical and/or periventricular) T2 hyperintensities, which was the most common abnormality found. Other abnormalities were cerebral atrophy, cystic encephalomalacia, delayed myelination, corpus callosum thinning, cerebellar atrophy, acute infarcts. 18 cases were normal (28.1 %).

Findings	Number	Percentage (n =64)
White matter hyperintensities	36	60 %
Cerebral atrophy	32	50 %
Delayed myelination	20	31.2 %
Corpus callosum thinning	14	21.8 %
Cystic encephalomalacia	24	37.5 %
Acute infarcts	10	15.6 %
Cerebellar atrophy	10	15.6 %
Normal	18	28.1 %

Table-3MRI findings in HIE in term neonates.

Imaging Findings In Preterm Neonates

36 cases of preterm neonates who suffered perinatal hypoxia were evaluated in our study by MRI, out of which 10 were normal (27.7 %) and 26 were abnormal (72.3 %). Of the abnormal studies, the most common were periventricular leucomalacia (12) and cerebral atrophy (12).

Other pathologies which were observed were delayed myelination, corpus callosum thinning, cystic encephalomalacia, acute infarcts and cerebellar atrophy.

Findings	Number	Percentage (n =36)
Periventricular leukomalacia	12	33.3 %
Cerebral atrophy	12	33.3 %
Delayed myelination	8	22.2 %
Corpus callosum thinning	8	22.2 %
Cystic encephalomalacia	8	22.2 %
Acute infarcts	4	11.1 %
Cerebellar atrophy	2	5.5 %
Germinal Matrix Hemorrhage	2	5.5 %
Normal	10	27.7 %

Table-4MRI findings in preterm neonates.

Distribution Of Cases According To Symptom Complex

In this study (n=100), maximum cases were of developmental delay (32). The other symptom complexes with which patients presented were seizures, cerebral palsy, hypotonia and drowsiness.

Sr. No.	Pathology	No. of cases	Percentage
1)	Developmental delay	32	32%
2)	Seizures	28	28%
3)	Cerebral palsy	20	20%
4)	Hypotonia	14	14%
5)	Drowsiness	6	6%
		Total=100	

Table-5 Distribution of cases according to symptom complex

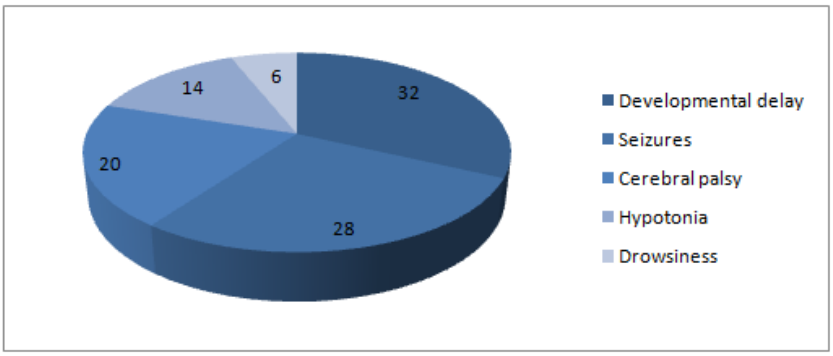

Figure-5 Distribution of cases according to symptom complex

Distribution of Findings on MRI

Out of 72 cases of HIE findings in perinatal hypoxia, maximum number of cases showed generalized cerebral atrophy (61 %), followed by T2WI hyperintensities. The other findings in preterm as well as term neonates were cerebellar atrophy, cystic encephalomalacia, delayed myelination, corpus callosum thinning, acute infarcts.

Sr. No.	Pathology	No. of cases(n=72)	Percentage
1)	T2 hyperintensity	36	50%
2)	Cerebral atrophy	44	61%
3)	Cystic encephalomalacia	32	44%
4)	Delayed myelination	28	39%
5)	Corpus callosum thinning	24	33%
6)	Acute Infarcts	14	19%
7)	Cerebellar atrophy	12	17%
8)	Periventricular leukomalacia	12	17%
9)	Germinal matrix hemorrhage	2	0.3%

Table 6- Distribution of MRI findings.

Distribution of Findings on MRI According to Areas of Brain Involved:

Sr. No.	Site	Preterm/Term	MRI Findings	No. of patients
1.	Cortex	Term	-High signal intensity on T2 and FLAIR	12
			- Infarct	6
			- Atrophy	32
		Preterm	- Atrophy	12
2.	Subcortical white matter	Term	-High signal intensity on T2 and FLAIR	20
3.	Periventricular White matter	Preterm	-High signal intensity on T2 and FLAIR	12
4.	Basal ganglia and thalami	Preterm	-High signal intensity on T2 and FLAIR	4
		Term	-Infarct	3
5.	Hippocampus	Term	-High signal intensity on T2 and IR	4
6.	Cerebellum	Preterm	-High signal intensity on T2 and FLAIR	3
			-Atrophy	2
7.	Insula	Term	-Infarct	1

Table 7- Distribution of findings on MRI according to areas of brain involved

Distribution of Findings on MRI in Patients with Cerebral Palsy

Out of 100 cases of perinatal hypoxia, 20 cases presented with cerebral palsy. Detailed analysis of MRI findings in these 20 cases is done as follows. 6 (30 %) cases were preterm infants and 14 (70 %) cases were term infants. Periventricular leukomalacia was the commonest finding in preterm infants, whereas, hyperintense lesions on T2WI images was the most common findings in term infants. The rest of the findings are given in the table below.

Case No.	Age/ Sex	Preterm/term	CP Type	MR Findings
1	9 Mnths/ M	Preterm	Diplegia	PVL, Cerebral Atrophy
2	1 yr/ M	Preterm	Diplegia	PVL ,Delayed Myelination
3	1yr /M	Preterm	Quadriplegia	PVL, Cerebral Atrophy
4	4 mnths/F	Preterm	Diplegia	Delayed Myelination, Corpus callosum thinning
5	1 mnth/F	Preterm	Hemiplegia	Infarct
6	4mnths/M	Preterm	Diplegia	Normal
7	3 yys/M	Term	Diplegia	Cerebral Atrophy, T2HI
8	6 mnths/F	Term	Diplegia	Cerebral Atrophy, T2HI
9	3 yrs/F	Term	Diplegia	Cerebral Atrophy, T2HI
10	5mnths/M	Term	Hemiplegia	Infarct, Cerebral Atrophy, T2HI
11	1 mnth/M	Term	Quadriplegia	Cerebral Atrophy, T2HI, Delayed Myelination, Corpus callosum Thinning
12	3mnths/M	Term	Diplegia	Cerebral Atrophy, T2HI, Delayed Myelination, Corpus callosum Thinning
13	4 yrs/M	Term	Quadriplegia	Global cystic encephalomalacia, Corpus callosum Thinning
14	2 yrs/M	Term	Diplegia	T2HI, Delayed Myelination
15	1 yr/F	Term	Quadriplegia	Infarct, T2HI, Delayed Myelination
16	4 yrs/F	Term	Hemiplegia	Infarct
17	5 yrs/M	Term	Hemiplegia	Infarct
18	7yrs/M	Term	Hemiplegia	Normal
19	1yr/M	Term	Diplegia	Normal
20	8 mnths/F	Term	Diplegia	Normal

Table 8- Distribution of findings on MRI in patients with cerebral palsy.

Patterns of Hypoxic Ischemic Injury in Term Infants with Acute Presentation

Out of 64 patients with a history of term delivery, infants presented with acute presentation were 10 in number. 5 main patterns of distribution of acute ischemic injury have been recognized. Of them, most showed a watershed predominant pattern.

Sr.No.	Pattern	No. of patients (n=10)
1	Basal ganglia thalamus pattern (BGT)	2
2	Watershed predominant pattern of injury (WS)	4
3	White cerebrum pattern	1
4	Periventricular white matter pattern	2
5	Perinatal arterial ischaemic stroke (PAIS)	1

Table9- Distribution of patterns of hypoxic ischemic injury in term infants.

Patterns of Hypoxic Ischemic Injury in Patients with Acute Presentation

Of the total 100 patients, infants that presented with acute presentation with a history of a term delivery were 10 in number and those with a history of preterm delivery were 4 in number. Risk factors, HIE grades and MRI findings in 14 patients of acute presentation of HIE are analyzed as follows.

Sr. No.	**GA**	**HIE Grade (Sarnat and Sarnat)**	**Risk factors**	**MRI Findings (n=14)**
1	Preterm	I	Idiopathic	Periventricular white matter pattern
2	Preterm	II	PROM	Periventricular white matter pattern
3	Preterm	III	Pre-eclampsia	Basal ganglia- Thalami and Periventricular white matter involvement with
4	Preterm	III	Assessed Deliveries	Basal ganglia- Thalami involvement
5	Term	I	Idiopathic	WM lesions
6	Term	I	Idiopathic	WS predominat injury
7	Term	I	Pre-eclampsia	WM lesions
8	Term	I	Anemia	PLIC , WS predominat injury
9	Term	II	Idiopathic	PLIC , WS predominat injury
10	Term	II	Pre-eclampsia	WM lesions
11	Term	II	Anemia	PAIS
12	Term	II	Antepartum Hemorrhage	WS predominat injury
13	Term	III	Pre-eclampsia	Basal ganglia- Thalami involvement
14	Term	III	Antepartum Hemorrhage	Basal ganglia- Thalami involvement

Table10- Patterns of hypoxic ischemic injury in patients with acute presentation.

IV. Discussion

Hypoxic-ischemic encephalopathy (HIE) in neonates is an important cause of mortality and morbidity and neurodevelopmental delay worldwide. It can lead to permanent brain damage and can also cause damage to other tissues of the body.

Almost 40% of deaths in children under the age 5 years occur in the neonatal period. Decrease in the mortality rate due to HIE observed in the developed countries could be due to the improved neonatal care, however the mortality and morbidity due to HIE in the developing countries still remains high and is a challenge. The total neonatal deaths occurring in the world due to non-specific conditions of HIE vary from 0.7 million7 to 1.6 million per year. In children affected by severe hypoxia, the mortality rate is reportedly 25–50%. The maximum number of deaths occur in the first week of life as a result of multi- system failure or inadequate care. The children having severe neurologic deficit die in their infancy from aspiration pneumonia or various infections. Incidence of prenatal asphyxia is about 3.3% in India and is usually related to gestational age and birth weight. It occurs in 9% of infants less than 36 weeks gestational age and in 0.5% of infants more than 36 weeks of gestational age accounting for 20% of perinatal deaths (or as high as 50% deaths if still births are included). [1]

Treatment for children suffered with hypoxic-ischemic encephalopathy was limited to supportive care for a long time, but now recent advances for effective therapies have been developed. It is a treatable problem and early identification and intervention is necessary to prevent the long term brain damage.Advances in MRI technique have made excellent progress over the last few years.MRI and MRS with the help of DTI is useful in detection of exact patterns of early and late damage in infants with HIE.

Both terminal zones of myelination and perivntricularleukomalacia appear hyperintense on T2WI and FLAIR and their differentiation is extremely difficult. Terminal zones are the persistent areas of high signal intensity in the white matter lateral to the bodies of the lateral ventricles and in the dorsal and superior to the ventricular trigones on T2-weighted images. The difference is best elicited on coronal T2WI and FLAIR images. The periventricular leukomalacia lesions are more sharply defined. They are present more inferiorly; lateral to the trigones and near the optic radiations. They are typically brighter on T2WI and FLAIR sequences than terminal zones of myelination. Periventricular leukomalacia is associated with loss of brain tissue, which results in the irregularity of the ventricular wall, abnormally deep cortical sulci, sometimes extending down to the ventricular surface, and thinning of the body of the corpus callosum. A layer of myelinated white matter is present between the trigone of the ventricle and the terminal zones in normal patients. The very high signal

intensity of the peritrigonal areas compared to surrounding white matter on FLAIR images with the presence of local atrophy favor PVL. [2]

Differentiation of hypoxic-ischemic cerebral injury from normal myelination is important for prediction of neurologic development. T1-weighted images help distinction of infants with hypoxic- ischemic brain damage from those with normal myelination. The posterior limb of the internal capsule (PLIC) is myelinated at birth and appears hyperintense on T1-weighted images. The loss of this normal high signal intensity in the PLIC in infants with HIE, indicates a delay in myelination or insult to previously myelinated tracts. This loss of high SI in the PLIC, though sometimes subtle, is associated with unfavourable outcome. [3]

Patterns of HIE in preterm and term neonates:

An ischemic event lasting for more than 10 minutes is needed to induce parenchymal changes. The extent of injury increases with prolonged duration of the insult. Thus the patterns of injury in infants can be divided into term and preterms depending upon gestational age and being mild to moderate and severe hypoperfusion injuries, depending upon the severity of insult. [4]

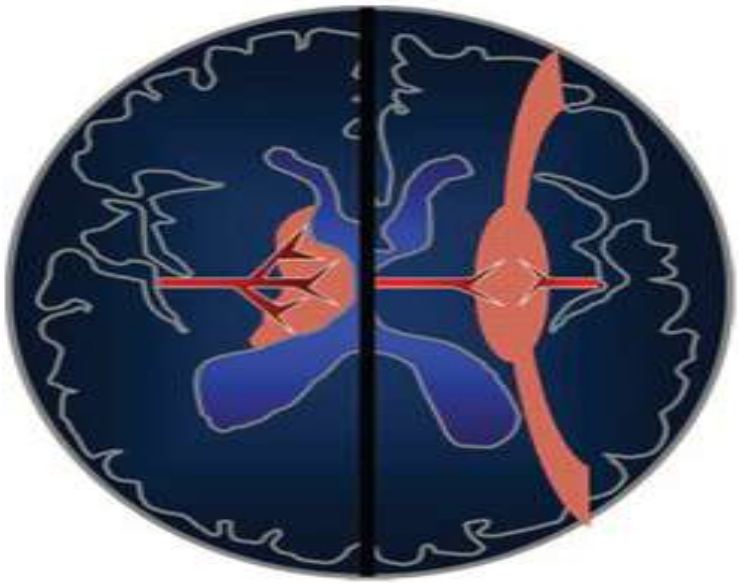

Figure- 6 Patterns of brain injury in mild to moderate hypoperfusion. Schematic of the premature neonatal brain (left) and that of the term infant (right) illustrates how the vascular supply changes with maturation and affects the pattern of brain injury in HIE. The premature neonatal brain (left) has a ventriculopetal vascular pattern, and hypoperfusion results in a periventricular border zone (red shaded area) of white matter injury. In the term infant (right), a ventriculofugal vascular pattern develops as the brain matures, and the border zone during hypoperfusion is more peripheral (red shaded area) with subcortical white matter and parasagittal cortical injury.

(**Source-** Christeine P. Chao et al. Neonatal Hypoxia Ischemic Encephalopathy: Multimodality Imaging. Radiographics 2006; 26:159-172.[5])

Age of Child	Mild to Moderate Hypotension	Profound Hypotension
Premature neonate (up to 34 postconceptional weeks)	Periventricular white matter injury	Thalamic, basal ganglia, and brainstem injury
Term neonate (~36 to ~56 postconceptional weeks)	Parasagittal watershed injury	Dorsal brainstem, ventral cerebellar vermis, thalamus, basal ganglia and perirolandic cortex injury
Older child (more than 4 to 6 postnatal months)	Parasagittal watershed injury	Basal ganglia and diffuse cortical injury

Table-11 Patterns Of Injury In Diffuse Hypoxic-Ischemic Injury

Linda S. de Vries&FlorisGroenendaal in 2014 identified four patterns of acute infarcts in term neonate. [6]

1) Basal ganglia pattern:

It affects bilateral central grey nuclei (ventro lateral thalami and posterior putamina) and perirolandic cortex. It is generally seen following an acute event, such as a ruptured uterus, placental abruption or umbilical cord prolapse, and is also referred to as a pattern following 'acute near total asphyxia. The absence of a normal

high-signal intensity of the posterior limb of the internal capsule (PLIC) on T1WI is highly predictive of severe adverse sequelae. On spin echo MRI sequences, inversion of the signal within the PLIC can be seen from 48 to 72 h onwards. DWI will show early changes in the basal ganglia/thalami. Children with the BGT pattern of injury tend to be severely disabled due to dyskinetic cerebral palsy (CP).

2) Watershed predominant pattern of injury (WS)

t is the type of pattern that can be seen after 'prolonged partial asphyxia'. The vascular watershed zones (anterior–middle cerebral artery and posterior–middle cerebral artery) are involved, affecting white matter and in case of more severe insult also the overlying cortex. The lesions can be uni- or bilateral, posterior and/or anterior. On spin echo MR images loss of the cortical ribbon and thus the grey–white matter differentiation can be seen. DWI is however helpful in making an early diagnosis. A follow up MRI may show cystic evolution with or without atrophy and gliotic changes. This type of insult is usually mild and thus the onset of neurological signs can be delayed. Severe motor impairment is uncommon in this. Symptomatic parieto-occipital epilepsy may occur later in childhood, often associated with reduced intelligence quotients and visuospatial cognitive function.

3) White cerebrum pattern

Marked involvement of the subcortical white matter and cortex is noted with relative sparing of the immediate periventricular white matter and central grey matter. This is referred to as the 'white cerebrum', as DWI shows completely white cerebrum, contrasted to a normal looking cerebellum. This condition tends to be fatal, but in case of survival, muticysticencephalomalacia eventually develops.

4) Periventricular white matter pattern.

It is similar to the punctate white matter lesions in the preterm infant. It is associated with a mild degree of encephalopathy and fewer clinical seizures. Thispattern of brain injury is observed in newborn infants with congenital heart defects.

5) Perinatal arterial ischemic stroke (PAIS), perinatal haemorrhagic stroke (PHS) and sinovenous thrombosis.

It is seen in newborns presenting with encephalopathy and/or seizures. Restricted diffusion at the level of the internal capsule and the middle part of the cerebral peduncle, referred to as 'pre-Wallerian degeneration' can be appreciated. It is then followed by Wallerian degeneration at 6–12 weeks and beyond. Presence of Wallerian degeneration at birth suggests an antenatal onset of the insult.

We carried out a study on 100 patients of perinatal hypoxia presenting with various symptom complexes. Of them, 72% (72) were abnormal and 28% (28) were normal studies. Our study correlates with study carried out by M.A. Rutherford. [7] Our findings correlate well with these studies.

In our study of 100 patients; 56% (56) were males and 46 % (46) were females with a mean age group of 6 years (age range= 0 to 12 years). Maximum patients were of age group 1 to 5 years. In a study carried out by AzharMunir Qureshi et al; 79.6% were males and 20.4% were females. [1] In another study done by D.J.A. Connolly, the age group range taken into consideration was 1 to 24 years. Of them maximum patients were between the age group of 1 to 5 years. [8]Thus, our findings corroborate well this study.

In our study 36 (36 %) patients were preterms and 64 (64%) had term delivery. These findings are in accordance with study performed by R Yin. He carried out the study on 42 patients in whom 12 were premature (28.5%) and 30 were full-term (71. 4%).[9]In another study done by AzharMunir Qureshi et al on 181 infants, out of 181 neonates 77.9% were full term, 19.1% were premature. Thus, overall, our findings correlate with these studies. [1]

Various risk factors for HIE have been proposed over the years. In our study, PIH was commonest risk factor 20 % (20) followed by anaemia 15 % (15). The other risk factors were placental factors 10% (10), perinatal infections 8% (8), and assessed delivery 7% (7). No risk factors were identified in 25 % (25) cases. Caesarean section was done in 15 % (15) of the mothers. In the study carried out by AzharMunir Qureshi et al on 181 patients; the most common risk factor was PIH, observed in 27.7 % of the mothers, followed by anaemia seen in 16%. Placental causes were present in 18.3%. Assessed delivery was done for 7.2 % of the patients and in 15.5% no maternal cause was found. 34.3% were delivered by Caesarean section. [1] Thus, our findings corroborate well with this study.

Inclusion of antenatal examination, home delivery, hospital delivery was taken into consideration in our study. We found that around 55 % (55)cases were primigravida. Of them, around 80% (44) patients had not undergone any antenatal examination. Rest 20 % (11) had undergone antenatal examination. Home delivery was done in 27.2% (15) of primigravida mothers, whereas hospital deliveries were done in 72.8% (40). In the remaining 45 % of multigravida, 75% (33) patients did not undergo any antenatal checkup and the rest of the 25

% (12) underwent antenatal examination. 31.1% (14) of multigravida had undergone home deliveries.Rest of the 68.9 % (31) underwent hospital deliveries. In the study done by AzharMunir Qureshi et al52.5% of the mothers were primigravidaand of them 5% were managed at home. 47.5 % cases were multigravida and of them, 8 % were home deliveries. Thus my study is in accordance with this study. [1]

We evaluated 64 (72 %) patients with a history of term delivery. Out of which 28.1 % (18) were normal studies and 71.8 % (46) cases were abnormal. Out of the abnormal cases cortical and subcortical T2 hyperintensities were noted in 60% (36) cases. Cerebral atrophy was also common and found in 50 % (32) cases. In patients presenting with acute symptoms, 15.6 % (10) cases showed acute infarcts. Delayed myelination was seen in 31.2 % (20) of the patients. Mary Rutherford with his colleagues performed a study on patients with HIE and tried to find the correlation of MR findings with clinical outcome. He found cortical and subcortical T2 hyperintensities in 50 % of the patients and cerebral atrophy in 50 % of the cases. Basal ganglia infarction was observed in 18 % cases and 6 % cases showed insular infarcts. Delayed myelination was present in 50 % of the infants. [10]The difference in the results of our study and other studies can be because of difference in the sample size.

We studied 36 (28%) patients who were born with the history of preterm delivery. Of these, 72.3% cases were found to be abnormal. 33.3% (12) cases showed periventricular leukomalacia and 33.3 % (12) patients showed cerebral atrophy as the commonest findings. Delayed myelination and corpus callosum thinning was observed in 22.2 % (8) cases. 27.7 % cases did not show any significant abnormality on MRI. Acute infarcts were seen in 11.1 % (4) cases. Cerebellar atrophy was present in 5.5 % (2) cases. Germinal matrix hemorrhage was diagnosed in 5.5 % (2) cases. In a study carried out by Gul Serdaroglu et al, 89 children with PVL were evaluated. The aim of this study was to find out neurodevelopmental delay in children with periventricular leukomalacia (PVL). PVL was divided into 3 grades: grade I, unilateral or bilateral areas of periventricular hyperintensity; grade II, hyperintensity more than 3; grade III, hyperintense lesions more than 3 and ventricular wall irregularity; grade IV, diffuse PVL and ventricular dilatation. Thinning of the corpus callosum and cortical atrophy was identified respectively in 73% and 47.2% of the patients. Delayed myelination was noted in 14.3% cases. MRI was normal in 18 % of the infants. [11]In a similar study done by PavithraLogitharajah, the major sites of injury were basal ganglia (BG, 75%), white matter (89%), Cortex was involved (58%) followed by brain stem in 44% cases No abnormality was found in 32%. Significant central gray matter and brainstem injury was found in many preterm infants with HIE. Neonatal MRI findings allowed accurate prediction of neurodevelopmental outcome on follow up studies. [12]The difference in the results of our study and other studies can be because of different age selection criteria of our study compared to other studies.

We came across various symptom complexes with which patients presented. Of them, maximum patients presented with developmental delay 32% (32). This was followed by epilepsy seen in 28 % (28) patients. Cerebral palsy was seen in 20 % (20) cases. Patients presenting with hypotonia were 14 % (14) whereas 6 % (6) cases had an acute presentation in the form of drowsiness or altered sensorium. Maximum cases of developmental delay were noted in the study performed by Gul Serdaroglu et al. Epilepsy was found in 33.7% and cerebral palsy in 30.8% of the patients. Approximately 28 % patients had diplegia. [11] Thus, our findings are in concordance with this study.

In our study, 20 patients presented with cerebral palsy. Out of these 20 cases 30 % (6) cases were preterm infants. The most common finding that we encountered was periventricular leukomalacia seen in 50% (3) of the cases. It was followed by cerebral atrophy and delayed myelination which was seen in 33.3 % (2) cases. Corpus callosum thinning and infarcts were seen in 16.6 % (1) patients. Whereas 16.6 % (1) cases did not show any abnormality. 70% (14) cases of term infants presenting with cerebral palsy were studied. The commonest finding in term infants was hyperintense lesions on T2WI images seen in 64% (8) cases. The next common finding was cerebral atrophy, which was present in 50 % of the cases (7). Delayed myelination and acute infarcts were noted in 28.5 % (4) cases. The less common finding was corpus callosum thinning seen in 21.4 % (3) cases. No abnormality was seen in 21.4 % (3) of the cases. Our findings were similar to those studied by R.Yin. He performed a study of MRI findings in 42 patients, of which 8 were premature (38 %), 13 were full-terms (62%). Periventricular leukomalacia was seen in 66.6%. Cerebral atrophy was seen in 33.3% cases and 33.3% children did not demonstrate PVL. The other group he studied included 30 children who were born between 37 and 42 weeks gestation that is term infants. The MRI findings demonstrated T2 hyperintensities as the most common finding seen in approx. 30 % patients. It was followed by cerebral atrophy seen in 20 % cases and other lesions in 20 % cases. Acute infacrts were noted in 13 % of the patients. Delayed myelination was seen in 7 % cases and corpus callosum thinning in 6 %. [9]Charles L. Truwit did a study on 40 patients with cerebral palsy. Of these, 11 were premature and 29 were term infants. Of the 11 patients born prematurely, MR revealed deep white matter loss, especially in the peritrigonal regions. 81 % of the scans demonstrated thinning of the corpus callosum. No abnormalities were noted in the basal ganglia or thalami. 27% had diminished caliber of the brainstem. MR was done in 29 patients born at term, out of which 66% had diminished deep white matter. 6 % had delayed myelination. In 55 %, the corpus callosum was thinned either focally (involving the

posterior body and/or splenium) or diffusely. Ventricular abnormalities were seen in 41 % with an irregular ventricular contour and ventricular enlargement and cerebral atrophy. Cortical thinning was seen in 10% term patients, one of whom had findings diagnostic of multicysticencephalomalacia.20 % cases had basal ganglia and/or thalami involvement. [13]In another case series, RubaBenini studied 126 patients with cerebral palsy. Of these, 71% had abnormal findings and 36 had normal brain scans. Compared with other CP types, normal-appearing MRI was more prevalent in dyskinetic CP 72% and less prevalent in spastic hemiplegic CP 10%.Thus, genetic or functional, rather than gross structural lesions, may underlie the pathophysiology of CP. [14]Overall our findings corroborate with both the studies.

We evaluated 5 patterns of distribution of acute ischemic brain injury in patients presenting with a history of term delivery. Of the 64 patients with a history of term delivery, 15.6 % presented with acute symptoms. The watershed predominant injury pattern was the most common finding observed in 40 % (4) of the patients. Basal ganglia- Thalami pattern and periventricular white matter pattern was noted in 20 % (2) of the cases respectively. 10% cases showed a white cerebrum pattern and Perinatal Arterial Ischemic Stroke (PAIS) was seen in 10% cases.84Abnormal signal intensity appearing hypointese on T1WI images was noted in the posterior limb of internal capsule (PLIC) was noted in 20 % (2) patients. This sign helped in differentiating the normal myelination from hypoxic injury. [3]

We also studied patterns of acute injury in 11.1% (4 out of 36) patients with a history of preterm delivery. Of them, 50 % (2) had an abnormal signal intensity in the bilateral periventricular white matter. 50% patients showed Basal ganglia –Thalami involvement.

An overall interpretation of patient characteristics and findings on the imaging when compared with the data available according to the review of literature corroborated very well. There are no significant and inexplicable differences in the range/spectrum of MRI findings in patients presented with HIE.

V. Cases

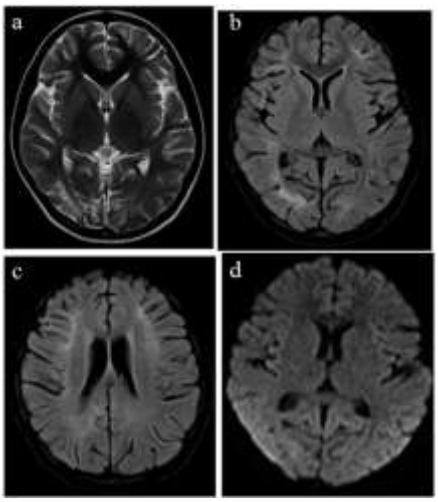

Figure -7 Axial MRI T2WI (a), FLAIR (b) and (c) show hyperintense areas in the bilateral periventricular white matter with no restricted diffusion on DWI (d) suggestive of HIE.

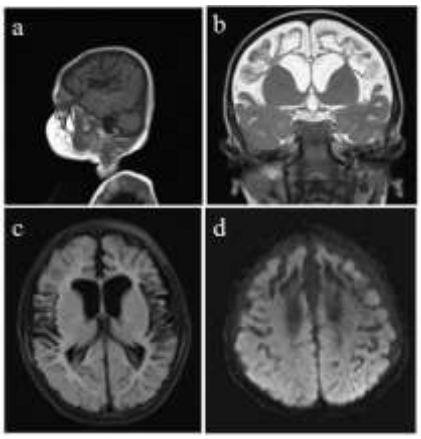

Figure-8 Altered signal is seen in bilateral high fronto-parietal region predominantly along cortex and subcortical white matter and also extending to periventricular white matter appear hypointense on T1WI (a) and

hyperintense in T2WI (b) and FLAIR (c) with no evidence of restricted diffusion (d) suggestive of gliotic changes. Ex vacuo dilatation of both lateral ventricles is also seen.

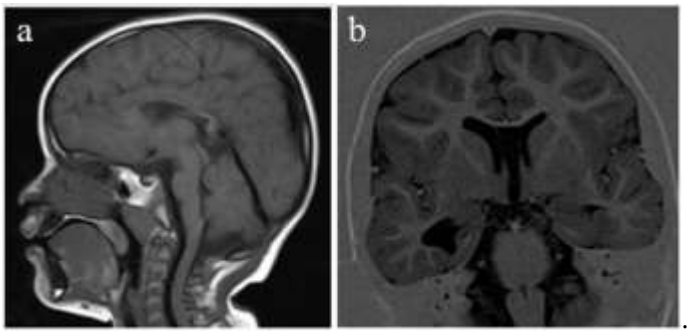

Figure-9 Midsagittal MR T1WI (a) and coronal 3D T1WI IR (b) images showing thinning of corpus callosum.

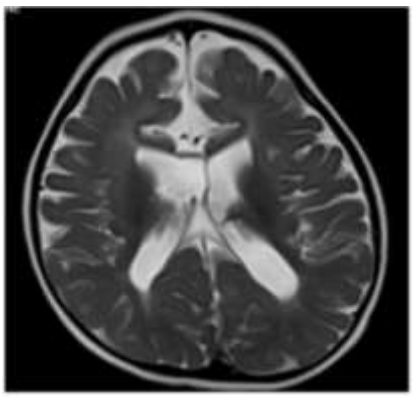

Figure 10 – Axial T2WI MR image showing delayed unmyelinated white matter appearing hyperintense in bifrontal region.

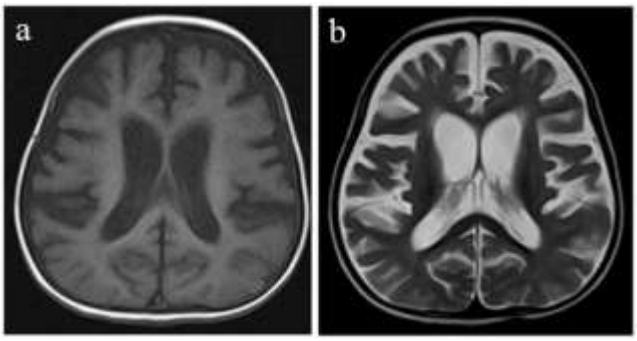

Figure –11 Axial T1WI (a) and T2WI (b) MR images showing prominence of ventricular system and cortical sulci suggestive of generalized cerebral atrophy.

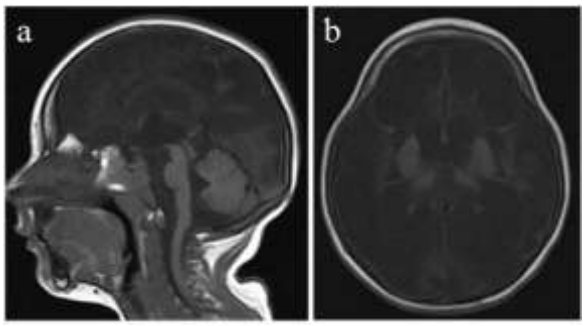

Figure – 12 Mid sagittal (a) and axial (b)T1WI MR at the level of basal ganglia showing changes of cystic encephalomalacia involving both the cerebral hemispheres showing CSF intensity. Note that the deep nuclei are spared.

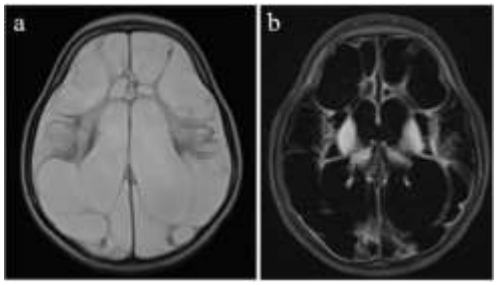

Figure – 13: Multiple areas of cystic encephalomalacia are noted in bilateral cerebral hemispheres appearing hyperintense on T2WI (a) and suppressed on FLAIR images (b). The basal ganglia and thalami are spared in this case, thus confirming that it is a term infant.

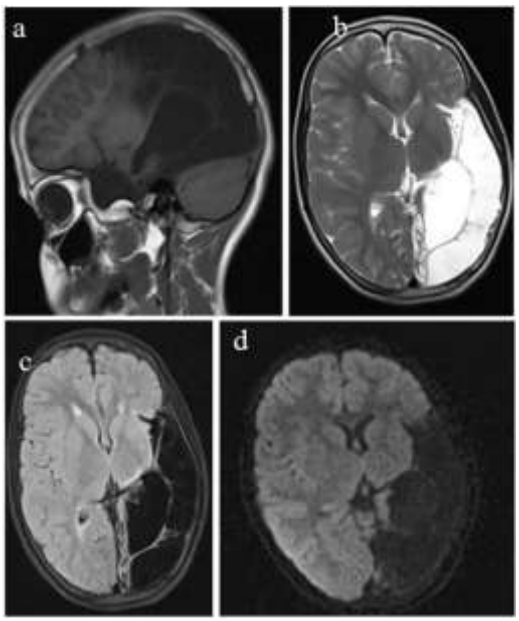

Figure – 14 Left para sagittal T1WI (a), axial T2WI (b), axial FLAIR (c) and axial DWI (d) MR images at the level of lateral ventricles showing area of cystic encephalomalacia involving the left MCA territory appearing hypointense on T1WI and FLAIR, hyperintense on T2WI images with no restriction on DWI.

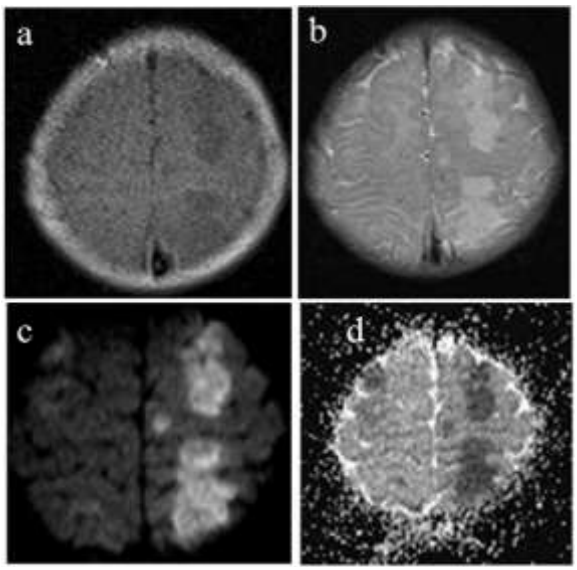

Figure -15 Axial T1WI (a) and T2WI (b) images showing areas of altered signal intensity in left watershed areas appearing hypointense on T1WI and hyperintense on T2WI images. These areas are showing restriction on DWI (c) with corresponding low ADC values (d). This was suggestive of acute infarct in left anterior and posterior watershed areas suggestive of watershed pattern.

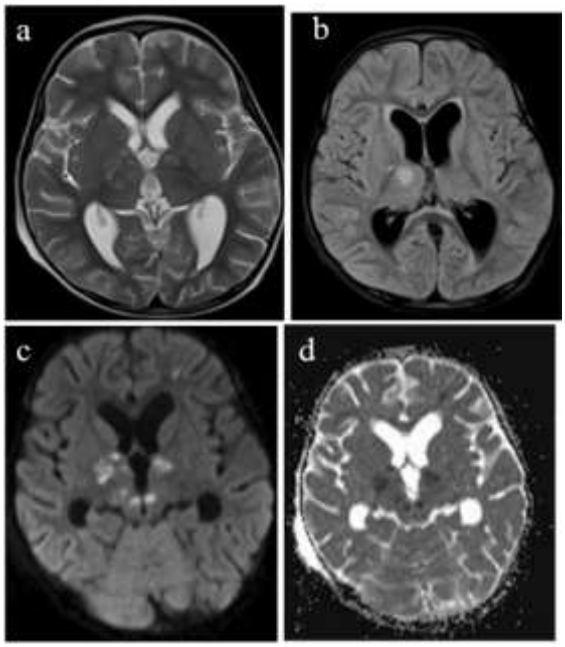

Figure – 16 Areas of altered signal intensity are seen involving deep nuclei in a preterm infant appearing hyperintense on T2WI (a) and FLAIR (b) images, showing restriction on DWI (c) with corresponding low ADC values (d) suggestive of acute infacrts with basal ganglia pattern.

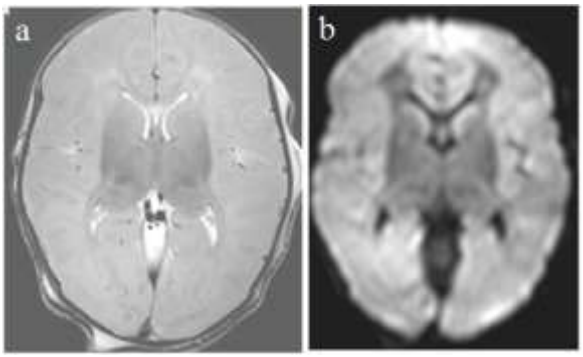

Figure -17 Axial MR T2WI (a) and DWI (b) images at the level of lateral ventricles show areas of altered signal intensity involving the cerebral white matter with relative sparing of the periventricular white matter and deep nuclei appearing diffusely hyperintense on T2WI images with corresponding restriction on DWI. This is suggestive of acute infarct with the white brain pattern of injury.

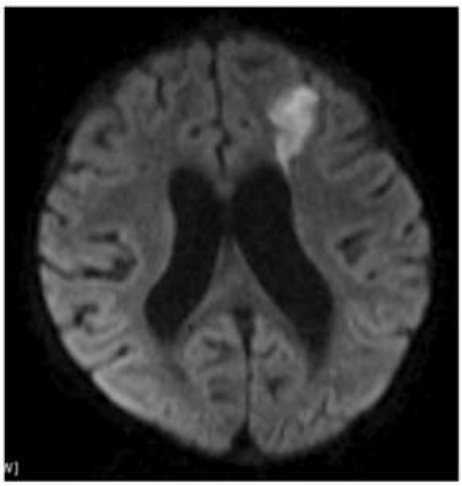

Figure – 18 Axial DW MR Image at the level of lateral ventricles showing focus of restricted diffusion in the left frontal periventricular white matter. This is suggestive of periventricular type of pattern of acute infarct.

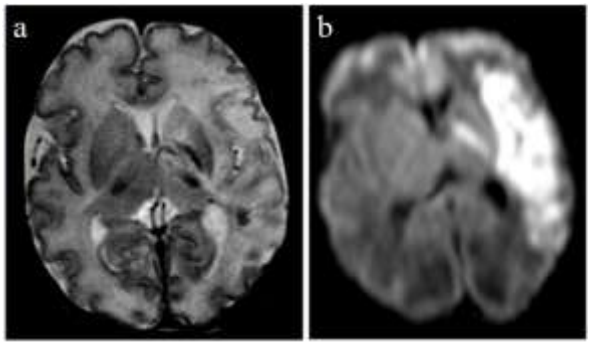

Figure –19 Axial T2WI (a) and DW (b) MR images at the level of lateral ventricles showing acute infarct involving left MCA territory appearing hyperintense on T2WI and showing restriction on DWI. This is the perinatal arterial ischemic stroke pattern.

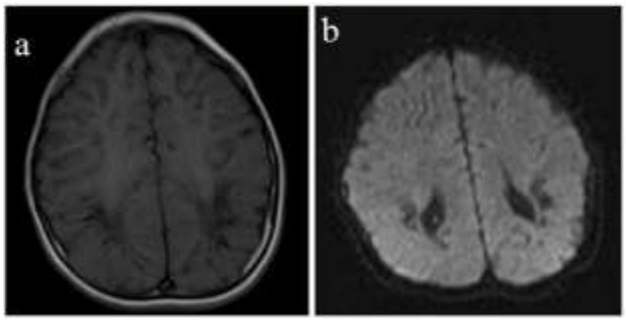

Figure -20 Axial MR images at the level of lateral ventricles showing areas of altered signal intensity in periventricular areas posteriorly appearing hypointense on T1WI (a). These areas do not show restriction on DWI (b) suggestive of HIE.

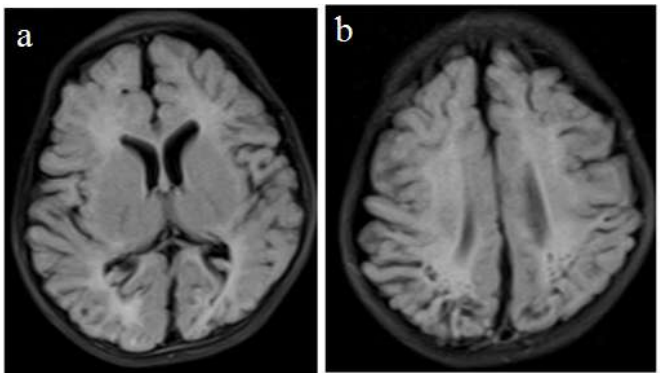

Figure –21 Axial FLAIR MR images at the level of body of lateral ventricles (a) and at the level of corona radiata (b) showing bilateral periventricular hyperintensities with reduced white matter in both occipital lobes (forceps major) suggestive of periventricular leukomalacia.

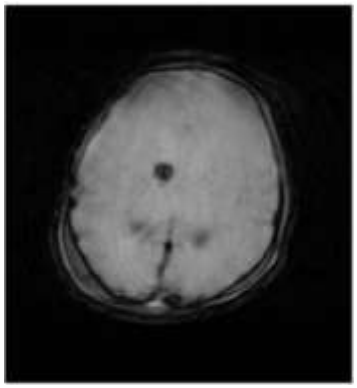

Figure – 22 Axial GRE image shows area of blooming in the right germinal matrix suggestive of germinal matrix haemorrhage.

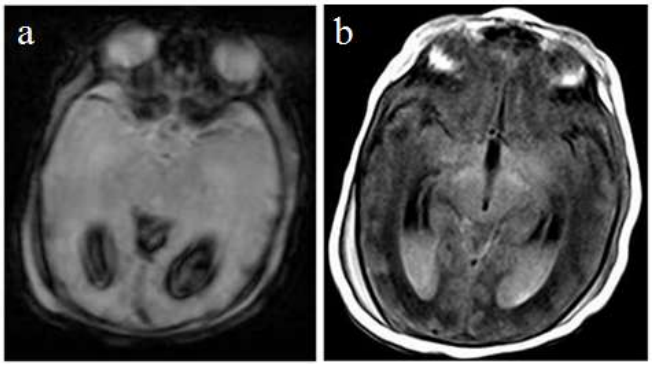

Figure – 23 Axial GRE (a) and T1WI (b) images show intraventricular hemorrhage in bilateral occipital horns of lateral ventricles following germinal matrix haemorrhage with early hydrocephalus, showing area of blooming on GRE images appearing hyperintense on T1WI images.

VI. Conclusion

MRI was able to differentiate between patterns of brain injury, according to the brain maturity, severity and length of the ischemic insult. In our case series, patients presenting late with HIE were more than that of those presenting with acute presentation. This suggests that there is a lack of public health awareness as well as neonatologists in developing countries. Protocol for doing MRI in a suspected case of HIE needs to be formulated.

In our case series, serial follow up of patients suffered with perinatal hypoxia on MRI for the evolution of the lesions and neurodevelopmental outcome was not done due to time constrains. Also, MRI brain was normal in0 few patients who had suffered with perinatal hypoxia. This can be overcome by performing MRS within 2-3 days of insult in patients with normal conventional MRI brain studies. DTI can also be useful for detailed evaluation of the sequelae of HIE in whom conventional MRI brain studies were inconclusive.

Apart from this timely recognition of the risk factors and public health awareness needs to be created. Improvements in maternal health and regular antenatal checkups should be emphasized. Also, follow up MRI studies for those children who have suffered with perinatal hypoxia is extremely important to know the prognosis of the condition.

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