

## Original Research Article

# To evaluate the role of MRI in infants with suspected hypoxic ischemic encephalopathy and prognosticating neurological outcome at end of one year

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### ABSTRACT

**Background:** Hypoxic ischemic encephalopathy (HIE) is one of the common causes of neonatal fatality due to perinatal asphyxia. The long-term outcomes of HIE are impaired mental and motor development, hearing loss, recurrent seizures and cerebral palsy. MRI is increasingly becoming the gold standard in diagnosis of HIE as it involves no radiation and can be performed during a neonate's physiological sleep. To evaluate the role of MRI in infants with suspected hypoxic ischemic encephalopathy in prognosticating neurological outcomes at end of one year.

**Methods:** A total of 50 patients were included in the study who underwent MRI of brain. A clinical follow up was done at the end of one year.

**Results:** The sensitivity of MRI in prognosticating clinical outcome was 72% and specificity was 71% while PPV and NPV was 86% and 50% respectively.

**Conclusions:** MRI is a useful modality to assess early changes in HIE and it can prognosticate clinical outcome.

**Keywords:** HIE, MRI, Neurological

### INTRODUCTION

HIE is one of the most common causes of neonatal fatalities. The most common cause of HIE is perinatal asphyxia and its long-term outcomes are impaired mental and motor development, hearing loss, recurrent seizures and cerebral palsy.<sup>1</sup> MRI is increasingly becoming the gold standard in diagnosis of HIE because it involves no radiation and can be performed during a neonate's physiological sleep.<sup>2</sup>

MRI shows more number of lesions in HIE than ultrasound (i.e. cortico-subcortical lesions within the central region, bilateral parasagittal lesions and brain stem, thalamus, cerebellum and hippocampus lesions) and can also predict the clinical consequences of hypoxia.<sup>3</sup> Early findings on MRI include increased T2

signal intensity (SI) within the basal ganglia, the periventricular white matter, the subcortical white matter and the cortex. Bilateral abnormal SI within the basal ganglia and thalamus that is also detected by ultrasonography is associated with a poor outcome in neonates with HIE.<sup>4</sup> MRI helps in defining the nature and extent of perinatal brain injury. Because hypoxic-ischemic (HI) cerebral injury is a dynamic process, the diagnostic and prognostic utility of MRI can be interpreted in the context of the timing of the MRI.<sup>5</sup>

The patterns of brain injury on conventional T1- and T2-weighted MRI at one week after birth predict abnormal neuromotor outcome in early childhood. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) changes with HI injury are most prominent from days two through five and can be

detected earlier than abnormalities detected on the conventional T1- and T2-weighted MRI.<sup>6</sup>

The aim of the study was to evaluate MRI findings in patients with HIE and in prognosticating neurological outcome.

## METHODS

This prospective study was conducted in a tertiary care hospital in south India for a period of 16 month from October 2014 to Aug 2016 after obtaining clearance from the institutional ethical committee. A total of 50 patients with history of birth asphyxia were included in the study who underwent MRI of brain and were followed up clinically at the end of one year to assess the neurological outcome.

### Inclusion criteria

- Full term (>37 weeks of gestation),
- pre-term (<37 weeks of gestation)
- Neonates born with birth asphyxia and APGAR score at 5 minutes after birth <7

### Exclusion criteria

Term or preterm neonates with infection and suspected Metabolic disease.

MRI was done on Philips Achieva 1.5 Tesla MRI system. The neonate was sedated using pedicloryl syrup and was placed in the supine position and the following protocol was followed.

- T1-weighted spin-echo (TR/ TE, 400/13-308),
- T2-FLAIR (TR/TE, 9500/120),
- Axial T2 FSE TR/TE (4000/102) Echo train length 24,
- DWI (TR/TE 8000/100.7)
- SWAN sequence.

The section thickness was 3-4 millimeter. Only plain MRI studies were done without using intravenous contrast. Statistical analysis was done using SPSS version 15 and sensitivity, specificity, positive and negative predictive value of MRI in comparison to clinical follow up at the end of one year was assessed. A grading system was devised for both MRI and clinical follow up for statistical purpose.

### MRI grading

- Grade I- Normal MR findings.
- Grade II- Focal areas showing increased signal on FLAIR/T2WI /DWI.
- Grade III- Punctuate hemorrhages in the white matter.

- Grade IV- Extensive signal intensity changes on FLAIR /T2WI /DWI with or without hemorrhagic or cystic lesion involving the peri ventricular and sub cortical white matter.

### Clinical grading

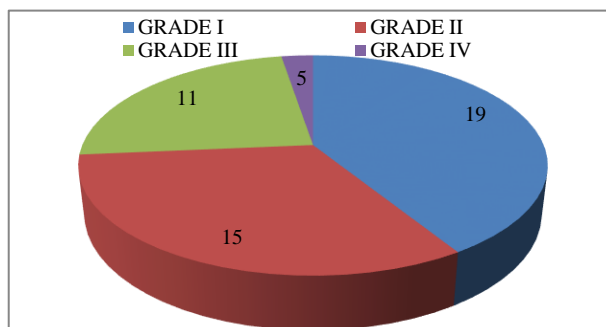
- Grade I- Normal at the end of one year.
- Grade II- Delayed milestones (neck holding, sitting with / without support).
- Grade III- Abnormal tone in limbs (Increased or decreased) with seizures.
- Grade IV- Cerebral palsy.

## RESULTS

In present study, 41 neonates were term infants and nine neonates were preterm with 32 (64%) males and 18 (36%) females. A total of 33 neonates had normal birth weight (>2.5kg at birth), 13 had low birth weight (1.5-2.5kg) and four had very low birth weight.

### Clinical presentation

All infants presented with history of birth asphyxia. 32 neonates presented with seizures and 18 neonates presented with failure to thrive.

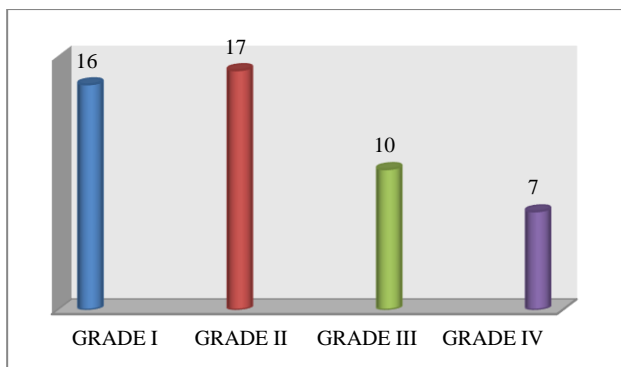


**Figure 1: MRI grading of HIE.**

A total of 19 neonates had normal MRI findings (grade I), 15 neonates showed increased signal intensity on MRI (grade II), 11 showed diffuse signal intensity changes and five showed diffuse cystic/haemorrhagic changes.

The neonates were assessed for milestones, seizures, muscle tone and features of cerebral palsy. 16 neonates were normal at the end of one year (grade I), 17 had delayed milestones (neck holding, sitting with/without support (grade II), 10 had abnormal tone in limbs (increased or decreased) with seizures (grade III) and 7 developed cerebral palsy (grade IV).

All the neonates underwent clinical follow up at the age of 1 year. The sensitivity of MRI in prognosticating clinical outcome was 72% and specificity was 71% while PPV and NPV was 86% and 50% respectively.



**Figure 2: Clinical grading.**

**DISCUSSION**

Neonatal encephalopathy results from a variety of conditions; hypoxic-ischaemic brain injury is most important and is called hypoxic-ischemic encephalopathy (HIE).<sup>7</sup>

HIE is one of the most common causes of cerebral palsy and other severe neurologic deficits in children, occurring in two to nine of every 1000 live births.<sup>8</sup> Perinatal asphyxia is the most important cause of HIE, resulting in hypoxemia and hypercapnia. Hypotension and the resulting decreased cerebral blood flow lead to a cascade of deleterious events, including acidosis, release of inflammatory mediators and excitatory neurotransmitters, free radical formation, calcium accumulation, and lipid peroxidation. These biochemical substances result in loss of vascular auto regulation in the setting of cerebral hypoperfusion. These “events” result in biphasic energy failure, in which initial impairment of cell metabolism is followed by reperfusion prior to eventual neuronal cell death.<sup>9-12</sup>

Accurate identification and characterization of the severity, extent, and location of brain injury rely on the selection of appropriate neuroimaging modalities, including ultrasonography (US), computed tomography (CT), and magnetic resonance (MR) imaging. Newer diagnostic techniques such as diffusion-weighted MR imaging and MR spectroscopy provide further insight into HIE and the potential for possible therapeutic intervention.<sup>13-15</sup>

**Correlation of MRI with long-term outcomes of neuromotor and mental development in one year old subjects**

In present study MRI was performed in neonates with HIE one week after their birth. The neonates were then followed up the end of one year and neurological status was assessed.

Neurological parameters assessed were milestones, neck holding, seizures and cerebral palsy. We found a significant correlation between the MRI findings and

neurological outcome Neonates who had grade III or grade IV MRI changes had a higher incidence of seizures and cerebral palsy. In present study, out of 19 neonates who had normal MRI findings, nine neonates were normal at the end of 1 year while n=10 neonates had delayed milestones.

15 neonates showed increased signal intensity on FLAIR and T2WI and DWI. Out of the 15 seven neonates showed increased intensity in the bilateral frontal lobe and eight showed increased signal intensity in the periventricular white matter. Out of these, three neonates were clinically normal at the end of one year, four had seizures, six neonates had abnormal muscle tone and two neonates developed cerebral palsy.

Six neonates showed microhemorrhages on SWAN. Out of these two neonates were normal at the end of one year. While four neonates had delayed milestones. Diffuse signal intensity changes were seen in six neonates on FLAIR and T2WI in the bilateral frontal, parietal, occipital lobe and corpus callosum. Four neonates who increased signal intensity had an abnormal muscle tone and two neonates developed cerebral palsy at the end of one year two neonates who had cystic changes on MRI developed cerebral palsy.

**Table 1: Overall sensitivity and specificity for MRI in prognosticating the clinical out come at end of one year.**

MRI	Normal	Abnormal
Normal	10 (a)	10 (b)
Abnormal	4 (c)	26 (d)
Total	14	36

We found that MRI had a sensitivity of 72%, specificity of 71% and PPV and NPV of 92% and 50% for detecting HIE and prognosticating the neurological outcome.

A similar study was conducted by Jose A et al to correlate findings on MRI brain with neurological outcome at 12 months in term new-borns with hypoxic ischemic encephalopathy.<sup>16</sup> Term neonates with perinatal asphyxia and hypoxic ischemic encephalopathy underwent MRI at 3 months using flair, T2, T1 and diffusion weighted sequences and neurological assessment was done at 12 months. MRI was normal in 16 (61.5%) neonates. There were abnormal signals (T2WI and FLAIR hyperintensity with diffusion restriction) in basal ganglia in two neonates (7.7%) and scattered signal abnormalities in both cortex and basal ganglia in six (23.1%) neonates. The sensitivity of MRI in prognosticating neurological outcome was 82%, specificity was 93%, PPV was 90% and NPV was 87%.

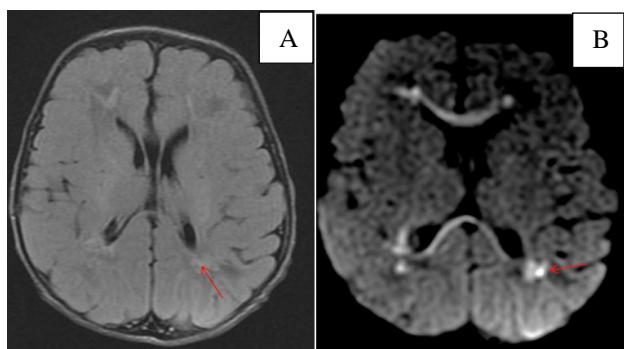
In the present study similar results were seen in terms of sensitivity and positive predictive value when compared to the study conducted by Jose A et al, however present study had a lower negative predictive value.<sup>16</sup>

Another study was conducted by El-Auoty M which correlated MRI findings and clinical outcome in neonates with HIE.<sup>17</sup> A total of 25 neonates with HIE were included in the study out of which three had severe HIE, 19 had moderate HIE and 3 had mild HIE. Only the initial images obtained after the first week after birth (range 7-28 days) were considered in this study because by this time brain swelling present in first days after birth gets cleared and the pattern of lesions is more evident. Early scans can appear relatively normal even with severe insults. All infants survived were followed up for a minimum of 12 months, (range 12-19 months). These infants were seen in the follow up clinic at 3, 9 and 12 months of age and every 3 months thereafter.

**Table 2: Comparison of sensitivity specificity PPV and NPV of current studies vs the studies mentioned.**

	Sensitivity	Specificity	PPV	NPV
Present study	72 %	71%	92%	50%
Jose A et al <sup>16</sup>	82%	93%	90%	87%
Ayouty et al <sup>17</sup>	100%	43%	82%	100%

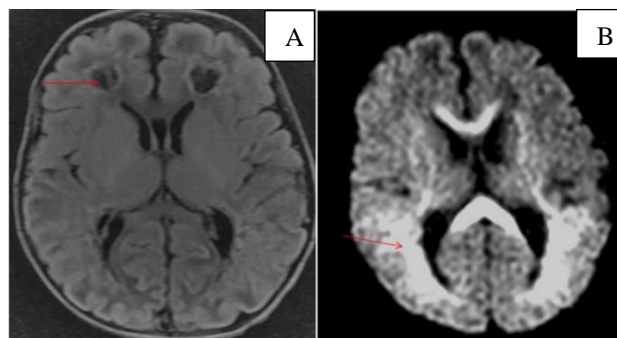
MRI findings were normal in three (12%) neonates, minimal basal ganglia and thalami hyperintensities were seen in three (12%) neonates, moderate basal ganglia and thalami hyperintensities in eight neonates (32%) and moderate white matter hyperintensities were seen in five neonates (20%).



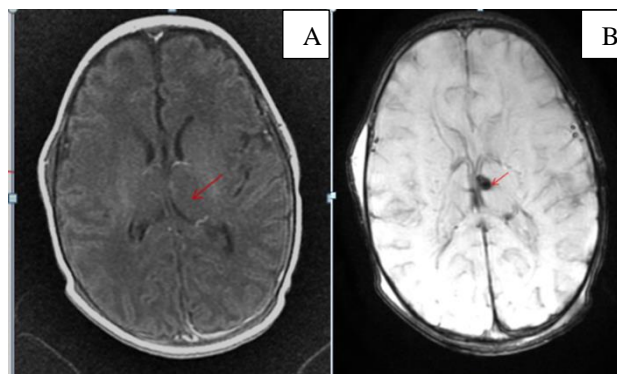
**Figure 3: A 3 day old neonate presented with birth asphyxia and seizures; 3A) Axial FLAIR section showing hyperintensities involving the bilateral peritrigonal region and; 3B) DWI showing restriction involving of corpus callosum. MRI grading- grade III. clinical outcome at the end of 1 year: neonate developed seizures and had poor muscle tone.**

Severe white matter hyperintensities were seen in four neonates (16%) and Severe Basal ganglia and thalami plus diffuse white matter hyperintensities in two (8%) neonates. Their study showed a sensitivity of 100 %, specificity of 42 %, PPV of 81% and NPV of 100%. Clinical follow up at end of 1 year revealed that 19 neonates had seizures and six were normal nine neonates had microcephaly, 16 were normal while seven had normal muscle tone, four developed quadriplegia and 14

developed quadriplegia. They concluded that normal MRI was always associated with normal clinical outcome. Severe abnormalities on MRI (i.e. severe basal ganglia and thalami with diffuse or subcortical white matter lesions) were associated with seizures or quadriplegia. This was in contrast to present study where 10 neonates with normal MRI findings showed delayed milestones.



**Figure 4: A 3 day old neonate presented with birth asphyxia and seizures; 4A) FLAIR sections showing cystic changes in the subcortical white matter in the bilateral frontal lobes and; 4B) DWI showing diffusion restriction involving the subcortical and periventricular white matter of bilateral parietal and occipital lobes, peri Rolandic regions and corpus callosum. MRI grading- grade IV. Clinical outcome at the end of 1 year: neonate developed cerebral palsy.**



**Figure 5: A 4 day old neonate presented with seizures; 5A) Axial T1WI shows subtle hyper intensity in the left thalamus and; 5B) SWAN image shows a punctate focus of blooming in left thalamus- s/o intraparenchymal haemorrhagic focus MRI grading- grade III clinical outcome at the end of 1 year neonate had delayed milestones.**

Genedi EA et al conducted a study on role of magnetic resonance imaging in early identification of cerebral injuries in neonatal encephalopathy. Their study enrolled 38 neonates who presented with HIE. In their study showed positive findings in 33 neonates. Findings at MRI supported hypoxic-ischemic encephalopathy as an etiology in 25 neonates, other aetiologies included metabolic disorders in two, congenital neonatal infection

in one, two cases of neonatal stroke, and congenital brain anomalies in two neonates and cerebral venous sinus thrombosis in one. They found that overall diagnostic accuracy of MRI was 78.9%, while the overall sensitivity and specificity were 81.8% and 60% respectively. They concluded that early MRI is mandatory as it can detect precisely the extent of brain injury.

## CONCLUSION

MRI is a useful modality to assess the early changes noted in HIE. Parenchymal cystic changes noted on MRI had a higher incidence of cerebral palsy. While a normal MRI has a specificity of over 90% in predicting a normal outcome, involvement of the thalamus or basal ganglia indicates a poor outcome. MRI had a good sensitivity (72%) and specificity (71%) and good correlation in predicting neurological outcome.

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