

To study the role of MRI of hypoxic ischemic encephalopathy

S Vinoth Kumar^{1*}, B. M. Monisha²

¹Associate Professor, Department of Radiology, Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem.

²Assistant Professor, Skin and STD Department, Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem

Corresponding Author: S Vinoth kumar

hi_hi_sandy@yahoo.co.in

ABSTRACT

Background: Hypoxic-ischaemic encephalopathy in adults and older children (i.e. not neonates), also known as global hypoxic-ischaemic injury, is seen in many settings and often has devastating neurological sequelae. Magnetic Resonance imaging—has the potential to play a significant role in diagnosis and early intervention in cases of HIE. In addition, imaging studies performed in the subacute stages of injury provide information on the severity and extent of injury and can be helpful in predicting long-term outcome.

Material and Methods: This prospective study was conducted in a tertiary care teaching hospital, over a period of 1 year. A total of 70 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.

Result: A total of 70 patients who fulfilled the selection criteria during the study were enrolled. Of the 70 babies, 46 were males and 24 females, which correspond to 65.7% of male and the rest female babies. The maximum number of patients were in the age group of <1 year which were 47.1% (n =33) of total followed by age group 2–12 months having 34.2% (n = 24) in this group and 18.5% were more than 1 year. In our study, maximum patients, i.e., 48.5% (n = 34) were having Apgar score of 4-6 followed by ≤3 score were 32.8% and least were > 7 score were 18.5%. In HIE 2 cases, 28.5% had involvement of corpus callosum. 27.1% had PVL, 18.5% had basal ganglia or thalamus lesion. There was no MRI evidence of HIE in 25.7%.

Conclusion: HIE is an important cause of morbidity and mortality in the neonatal period. MRI show characteristic pattern of brain injury and help to exclude other causes of encephalopathy. Imaging plays an important role in early diagnosis and timely intervention, thereby reducing the severity of neonatal brain injury.

Keywords: Magnetic Resonance imaging, Hypoxic ischemic encephalopathy, Neurological impairment

Introduction

Hypoxic-ischaemic encephalopathy in adults and older children (i.e. not neonates), also known as global hypoxic-ischaemic injury, is seen in many settings and often has devastating neurological sequelae. [1] Hypoxic-ischemic injury (HII) to the brain is a devastating

occurrence that frequently results in death or profound long-term neurologic disability in both children and adults. Treatment of HII consists largely of supportive care, which does little to prevent the ongoing injury that occurs in the hours immediately following the causative insult. [2]

Regardless of the specific cause of injury, the common underlying physiologic processes that result in HII are diminished cerebral blood flow (ischemia) and reduced blood oxygenation (hypoxemia). In general, infants and children are more likely to suffer asphyxia events, which result in hypoxemia and brain hypoxia. [3] With prolonged hypoxemia, cardiac hypoxia occurs, leading to diminished cardiac output and, ultimately, to brain ischemia. Thus, brain injury resulting from asphyxia is the consequence of ischemia superimposed on hypoxia. In fact, acute hypoxemia without superimposed ischemia is less likely to cause injury, unless the hypoxic state is prolonged. [4] On the other hand, adults more frequently suffer brain ischemia as a result of cardiac arrest or cerebrovascular disease, with secondary hypoxia due to reduced blood flow. [5]

Neuroimaging with ultrasonography (US), computed tomography (CT), and magnetic resonance (MR) imaging has become increasingly valuable in the work-up of patients with HII. [6] As more effective treatment options become available, imaging—particularly MR imaging—has the potential to play a significant role in diagnosis and early intervention in cases of HII. In addition, imaging studies performed in the subacute stages of injury provide information on the severity and extent of injury and can be helpful in predicting long-term outcome. [7]

Imaging findings in HII are highly variable and depend on a number of factors, including brain maturity, severity and duration of insult, and type and timing of imaging studies. Early imaging findings can be subtle and are often overlooked. [8] Therefore, it is essential to be familiar with the many patterns of injury that may be observed and to focus attention on areas that are most likely to be injured when interpreting studies performed for suspected HII.

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

Material and Methods

This prospective study was conducted in a tertiary care teaching hospital, over a period of 1 year. A total of 70 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

Exclusion criteria

Term or preterm neonates with infection and suspected Metabolic disease.

Patients with prosthesis, heart valve prosthesis, artificial/prosthetic limb, surgical staples, clips or metallic sutures and claustrophobia.

A 1.5 T MR scanner was used, with a gradient system that can reach a maximum gradient strength of 21 m T/m in each main direction. The imaging protocol consisted of a spin-echo T1-weighted series (568/18 TR/TE), a turbo spin-echo T2- weighted series (4381/120), and an inversion-recovery series. (3436/18/400 TR/TE/IR). Standard 8-channel birdcage (volume) coil was used. Anaesthesiologists using intravenous Propofol according to weight, after pre-anaesthesia check, sedated the neonates.

Images obtained were analysed on the workstation. Images were assessed for the presence of ischemic damage by the investigators. The extent of ischemic damage in each subject was determined according to MRI findings. Three plane anisotropic diffusion weighted images were examined for signal changes not accounted for by normal white matter anisotropy. Conventional MR studies were examined for the findings of HIE, blinded of the diffusion-weighted imaging appearances. The location and extent of involvement (by volume) of ischemic damage on each sequence were noted.

Statistical analysis

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.

Result

A total of 70 patients who fulfilled the selection criteria during the study were enrolled. The data were analysed, and the final observations were tabulated as below.

Table 1: Distribution of Gender

Sex	No. of patients	Percentage
Male	46	65.7
Female	24	34.2
Total	70	100

Of the 70 babies, 46 were males and 24 females, which correspond to 65.7% of male and the rest female babies in table 1.

Table 2: Distribution of the number of children according to age group

Age group	No. of patients	Percentage
< 1 month	33	47.1
2-12 months	24	34.2

> 1 year	13	18.5
Total	70	100

In table 2, the maximum number of patients were in the age group of <1 year which were 47.1% (n =33) of total followed by age group 2–12 months having 34.2% (n = 24) in this group and 18.5% were more than 1 year.

Table 3: Clinical profile distribution among study population according to Apgar score

Apgar score	No. of patients	Percentage
Score > 7 Generally Normal	13	18.5
Score of 4-6; fairly low	34	48.5
Scores \leq3; critically low, needs intervention	23	32.8
Total	70	100

In our study, maximum patients, i.e., 48.5% (n = 34) were having Apgar score of 4-6 followed by \leq 3 score were 32.8% and least were > 7 score were 18.5% in table 3.

Table 4: Distribution of MRI changes in study population with stage2 HIE

Site of Lesion	Frequency	Percentage
Corpus Callosam	20	28.5
BG/thalamus	13	18.5
No Change	18	25.7
Periventricular leucomalacia	19	27.1

In HIE 2 cases, 28.5% had involvement of corpus callosam. 27.1% had PVL, 18.5% had basal ganglia or thalamus lesion. There was no MRI evidence of HIE in 25.7%.

Table 5: Distribution of MRI changes in study population with stage 3 HIE

Site of Lesion	Frequency	Percentage
Bilateral BG	37	52.8
Bilateral thalami	24	34.2
Subcortical white matter	9	12.8

Out of 6 babies with stage 3 HIE, 52.8% had involvement of bilateral basal ganglia. 34.2% had bilateral thalami lesion and the rest showed subcortical white matter lesion.

DISCUSSION

HIE occurs when the oxygen and blood supply to a baby's brain is cut off or severely limited. This deprivation causes cells in the brain to break down, eventually leading to cell death if deprivation continues. When cells in the brain die, brain damage results. This damage can often be identified with an MRI. [9]

During an MRI of the brain, images are taken from the top of the baby's skull down to the base, from the front of the skull to the back, and across the skull from side to side. [10] When the results come back, each image represents a unique slice of the brain, ensuring that all areas of the baby's brain are imaged. Often, when a baby has brain damage, it will show up in one or more of these images in areas with increased signal intensity. [11]

In our study, out of the 70 patients who were enrolled in the study, our study shows male preponderance. According to a study by Flodmark O et al, there was no gender predilection. [12] Male gender being a risk factor for HIE has also been reported by other studies. [13] Our study shows, that term babies are more affected by MRI than preterms it may be because neonatal brain injury is difficult to diagnose in premature infants because either obvious signs are absent or if present, are attributed to developmental immaturity. [14] Preterm infants can also suffer from hypoxic ischemic encephalopathy, but, most often the change is not recognized early. For preterms findings will be obvious when MRI is done at corrected gestational age. Significantly higher numbers of primi gravida mothers in the affected babies are seen. It may be because the first delivery is more difficult than the subsequent ones. This points to the importance of intrapartum factors in the causation of HIE. [15]

In our study, 86% of term babies had changes in basal ganglia and/or thalamus. Other authors have also observed this finding. [16-21] This is because basal ganglia and thalami are metabolically very active in the immature brain. Occasionally severe basal ganglia lesions are seen with less obvious precipitating events. This may reflect failure to recognize the severity of asphyxia or due to individual susceptibility to damage because of previous hypoxic ischemic events or underlying metabolic or thrombotic disorders.

Term infants who develop HIE following a well-defined acute hypoxic injury typically sustain bilateral lesions within the basal ganglia and thalami. In this study, out of the six babies with clinical stage 3 HIE 52.8% of them had bilateral basal ganglia involvement and 34.2% had bilateral thalami involvement. In stage 2 HIE no stage specific change in MRI could be found. Preterm brain is highly susceptible to injury including periventricular leucomalacia, intraventricular hemorrhage/ germinal layer hemorrhage and parenchymal hemorrhagic infarction. In this study 27.1% of preterm babies had periventricular leucomalacia.

Conclusion

HIE is an important cause of morbidity and mortality in the neonatal period. MRI show characteristic pattern of brain injury and help to exclude other causes of encephalopathy. Imaging plays an important role in early diagnosis and timely intervention, thereby reducing the severity of neonatal brain injury. We can predict the infant development based on the MRI pattern of hypoxic-ischemic lesions, however, we cannot forget about the amazing malleability/flexibility of the child brain that can surprise both radiologists and clinicians.

Reference

1. Bonifacio SL, Glass HC, Vanderpluym J et al: Perinatal events and early magnetic resonance imaging in therapeutic hypothermia. *J Pediatr*, 2011; 158: 360–65 21.
2. Martinez-Biarge M, Bregant T, Wusthoff CJ, Chew AT, Diez-Sebastian J, Rutherford MA, et al. White Matter and Cortical Injury in Hypoxic-Ischemic Encephalopathy: Antecedent Factors and 2-Year Outcome. *J Pediatr*. 2012;161:799–807.
3. Rutherford M: The asphyxiated term infant. In: TMR of the neonatal brain. Rutherford M (ed.), W.B. Saunders, London-Toronto, 2002; 99–128.
4. Miller SP, Ramaswamy V, Michelson D, Barkovich AJ, Holshouser B, Wycliffe N, et al. Patterns of brain injury in term neonatal encephalopathy. *J Pediatr*. 2005;146:453–60.
5. Burns CM, Rutherford MA, Boardman JP, Cowan F M. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycaemia. *Pediatrics*. 2008;122:65–74.
6. Wu YW, Miller SP, Chin K, Collins AE, Lomeli SC, Chuang NA, et al. Multiple risk factors in neonatal sinovenous thrombosis. *Neurology*. 2002;59:438–40.
7. Armstrong-Wells J, Johnston SC, Wu YW, Sidney S, Fullerton HJ. Prevalence and predictors of perinatal hemorrhagic stroke: Results from the Kaiser Pediatric Stroke Study. *Pediatrics*. 2009;123:823–8.
8. Bonifacio SL, Glass HC, Vanderpluym J et al: Perinatal events and early magnetic resonance imaging in therapeutic hypothermia. *J Pediatr*, 2011; 158: 360–65.
9. Zupan-Simunek V, Rutkowska M, Bekiesińska-Figatowska M: Wartość predykcijna rezonansu magnetycznego (MR) w nabytych uszkodzeniach mózgu u noworodków. *Med Wieku Rozwojowego*, 2011; 15(3 Pt 2): 385–93
10. Norton L., Hutchison R.M., Young G.B., Lee D.H., Sharpe M.D., Mirsattari S.M. Disruptions of functional connectivity in the default mode network of comatose patients. *Neurology*. 2012;78:175–181
11. Els T., Kassubek J., Kubalek R., Klisch J. Diffusion-weighted MRI during early global cerebral hypoxia: a predictor for clinical outcome? *Acta Neurol Scand*. 2004;110:361–367.
12. Forbes K.P., Pipe J.G., Bird R. Neonatal hypoxic ischemic encephalopathy: detection with diffusion-weighted MR imaging. *Am J Neuroradiol*. 2000;21:1490–1496.
13. Schulzke S, Weber P, Luetsch J, Fahnenstich H. Incidence and diagnosis of unilateral arterial cerebral infarction in newborn infants. *J Perinat Med*. 2005;33:170–5.
14. Siskas N., Lefkopoulos A., Ioannidis I., Charitandi A., Dimitriadis A.S. Cortical laminar necrosis in brain infarcts: serial MRI. *Neuroradiology*. 2003;45:283–288.
15. Triulzi F, Baldoli C, Righini A: Neonatal hypoxic-ischemic encephalopathy. In: *Pediatric Neuroradiology*. Brain. Tortori-Donati P, Rossi A, Biancheri R (eds.), Springer, Berlin-Heidelberg, 2005; 234–55.
16. Zupan-Simunek V, Rutkowska M, Bekiesińska-Figatowska M: Wartość predykcijna rezonansu magnetycznego (MR) w nabytych uszkodzeniach mózgu u noworodków. *Med Wieku Rozwojowego*, 2011; 15(3 Pt 2): 385–93

17. Sie LTL, van der Knaap MS, Oosting J et al: MR patterns of hypoxicischemic brain damage after prenatal, perinatal or postnatal asphyxia. *Neuropediatrics*, 2000; 31: 128–36.
18. Valk J, Vermeulen RJ, van der Knaap MS: Post-hypoxic-ischemic encephalopathy of neonates. In: *Magnetic resonance of myelination and myelin disorders*. van der Knaap MS, Valk J. Springer-Verlag Berlin Heidelberg, 2005; 718–48.
19. Flodmark O, Barkovich AJ: Imaging of the infant brain. In: *The newborn brain*. Lagercranz H, Hanson M, Evrard P, Rodeck C (eds.), Cambridge University Press, 2002; 289–316.
20. Tong KA, Ashwal S, Obenaus A et al: Susceptibility-weighted MR imaging: a review of clinical applications in children. *Am J Neuroradiol*, 2008; 29: 9–17 14.
21. Lynch JK, Hirtz DG, DeVeber G, Nelson KB. Report of the National Institute of Neurological Disorders and Stroke Workshop on Perinatal and Childhood Stroke. *Pediatrics*. 2002;109:116–23.