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Original Article

Role of MRI in the Evaluation of Neonatal Hypoxic-Ischemic Encephalopathy

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Abstract

Introduction: Neonatal hypoxic-ischemic encephalopathy (HIE) is one of the most common causes of cerebral palsy (CP) and other severe neurological deficits in children. It is caused by inadequate blood flow and oxygen supply to the brain resulting in focal or diffuse brain injury.

Aim: To study the role of routine MRI findings, MR Spectroscopy in Neonatal Hypoxic-Ischemic Encephalopathy, and the correlation of MRI findings with clinical outcomes.

Methods: This prospective study was done over twelve months, from September 2019 to September 2020. All hemodynamically stable term and preterm neonates with a clinical diagnosis of HIE referred to the department of radiodiagnosis for imaging studies in our hospital were included

Results: Most of the patients with Sarnat and Sarnat clinical stage I HIE had either normal (58%) or mild (38%) changes of HIE on MRI. In the Clinical stage II HIE, most of the patients had either mild (60%) or moderate (30%) changes, and in the clinical stage III, most of the patients had severe (90%) changes on MRI. The findings of MRI were correlated with the final clinical outcome at 1 year, and the diagnostic accuracy of MRI was calculated. MRI has found to have the following values: Sensitivity=83.33%, Specificity=93.94%, PPV=83.33%, NPV=93.94%.

Conclusion: MRI is superior to other imaging modalities in evaluating neonatal hypoxic-ischemic encephalopathy. There is a strong and consistent correlation between the various MRI findings and the clinical outcome. Thus, MRI was very useful in the prognosis of hypoxic-ischemic encephalopathy.

Keywords: Magnetic resonance imaging (MRI), Neonate, central nervous system (CNS), Hypoxic-ischemic encephalopathy (HIE)

INTRODUCTION

Hypoxic-ischemic encephalopathy (HIE) is characterized by clinical and laboratory evidence of acute or subacute brain injury due to hypoxia. The primary cause of this condition is systemic hypoxia and reduced cerebral blood flow. Birth asphyxia causes an estimated 20-24 % of neonatal deaths annually. Neonatal deaths accounted for 46 per cent of all under-five deaths.[1] Despite major advances in monitoring and knowledge of fetal and neonatal pathologies, perinatal asphyxia remains a significant condition that causes mortality and long-term morbidity. MRI is the imaging modality for diagnosing and following up infants with moderate to severe hypoxic-ischemic encephalopathy.[2,3] Conventional MRI sequences (T1W and T2W) provide information on the status of myelination and pre-existing developmental defects of the brain. When performed after the first day (particularly after day 4), conventional images may accurately demonstrate the injury pattern as areas of hyperintensity. Conventional images are most helpful at 7-10 days of age when the diffusion-weighted imaging (DWI) findings have pseudonormalized. DWI allows earlier identification of injury patterns in the first 24-48 hours. This MRI sequence identifies areas of edema and hence injured areas. DWI changes peak at 3-5 days and pseudonormalizes by the end of the first week. In neonates, DWI may most likely underestimate the extent of injury because of

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the importance of apoptosis in the ultimate extent of neurological injury. Abnormal signal intensity in the PLIC (posterior limb of the internal capsule) has been associated with poor neurological outcomes. Severe BGT (basal ganglia-thalamus) lesions on early MRI (performed at a median age of 10 days: 2-42 days) were strongly associated with motor impairment at 2 years. In addition, abnormal PLIC signal was also highly correlated with the inability to walk independently at 2 years with a sensitivity of 0.92 and a specificity of 0.77.[4,5] Both conventional images (T1W and T2W) and DWI have a good specificity (>90%) and positive predictive value (>85%) in predicting death or major disability at age 2 years. However, the sensitivity and negative predictive values are low.[6] MRI is also used for follow up. In a newly diagnosed case of cerebral palsy MRI should be considered because it may help establish the cause. Magnetic Resonance Spectroscopy (MRS) allows for the quantification of intracellular molecules. Proton MRS allows for identifying cerebral lactate, which persists for weeks, to assess cellular metabolic integrity in neonatal brain injury.[3] Studies using 1H- MRS at a distance (>1–2 weeks) to the hypoxic-ischemic event showed a good correlation between reduced NAA ratio with adverse neurodevelopmental outcome.[7] where, as in early-stage (acute) Hydrogen-MRS, NAA ratios are not as well correlated with outcome. In this study, we found the importance of MRI in the neonatal period in babies with HIE as a diagnostic and prognostic tool for assessing neurodevelopmental outcomes at 1 year of life.

AIM

To study the role of routine MRI findings, MR Spectroscopy in Neonatal Hypoxic-Ischemic Encephalopathy, and the correlation of MRI findings with clinical outcomes.

MATERIALS AND METHODS

This prospective study was done over twelve months, from September 2019 to September 2020. All hemodynamically stable term and preterm neonates with a clinical diagnosis of HIE referred to the department of radiodiagnosis for imaging studies in our hospital were included. MRI machines (Philips 1.5T) at our institute were used. Hemodynamically unstable patients who may not tolerate prolonged examination times in the isolated setting of MRI and who are unfit for anesthesia were excluded. MRI findings were categorized into normal, mild, moderate and severe. In addition, in term and preterm neonates' involvement of periventricular white matter and subcortical white matter was classified as mild, signal changes in the posterior limb of the internal capsule, perirolandic white matter, severe multicystic encephalopathy as moderate and abnormal basal ganglia – thalamic lesions in term babies and germinal matrix haemorrhage in preterm babies as severe. In our study, 45 neonates were recruited after getting consent from their parents. Collected data were entered into a Microsoft excel spreadsheet. Continuous variables were presented as mean±SD.". Association between various MRI findings with clinical outcome was assessed by performing the "Chi-square test". Statistical evaluation of diagnostic accuracy of NSG and MRI findings in comparison to the clinical outcome was performed using "McNemar's Chi-square test", and sensitivity, specificity, positive predictive value, negative predictive values and diagnostic accuracy were calculated. P value<0.05 was considered of statistical significance. Statistical software STATA version 14.0 was used for data analysis.

RESULTS

Out of 45 patients, the majority of the patients were in the age group of 26-30 days (37.8%) and 5-10 days (20.0%). Out of 45 patients, 30 patients (67.0%) presented with a chief complaint of seizures and 15 patients (33.0%) presented with lethargy. All of them in this group were preterm babies. (Table 1)

Out of the 45 babies, 5 babies had germinal matrix haemorrhage, and most of them (80%) had abnormal outcomes, which is statistically significant. The one baby who had a normal outcome in this group had only mild intraventricular haemorrhage on MRI.

The majority of the patients with restriction in the corpus callosum had a restriction in the splenium. Isolated diffusion restriction in genu and body of corpus callosum was rare. However, 80% of the babies with diffusion restriction in the splenium and 75% of the babies with diffusion restriction in the genu of corpus callosum showed a statistically significant abnormal clinical outcome. All the patients with thinned out corpus callosum had an abnormal outcome.

Table 1: Distribution of study parameters

Characteristics	Frequency	Percentage
Age group		
<10	9	20.0%
11-15	8	17.8%
16-20	5	11.1%
21-25	6	13.3%
>26	17	37.8%
Gender		
Male	32	71.1%
Female	13	28.9%
Chief complaint		
Seizures	30	67%
Lethargy	15	33%

Out of the 45 babies, 16 babies had periventricular or subcortical white matter involvement, and most of them had abnormal outcomes, which is statistically significant (Fig. 1). Of the 16 babies, about 7 patients had watershed infarcts, and 5 patients had multicystic encephalopathy. 6 patients showed perirolandic white matter involvement. In addition, patients who showed brainstem involvement (100%) showed abnormal clinical outcomes, which is statistically significant. All the patients (25 out of 25) who showed abnormally low NAA peak and decreased NAA/CHO & NAA/CR on MRS showed abnormal clinical outcomes which patients showed elevated lactate levels in MRS, and all of them (100%) showed abnormal clinical outcome which is statistically significant. Elevated lactate was predominantly seen in severe cases of hypoxic-ischemic encephalopathy.

Most of the patients with Sarnath and Sarnath clinical stage I HIE had either normal (58%) or mild (38%) changes of HIE on MRI. In the Clinical stage II HIE, most of the patients had either mild (60%) or moderate (30%) changes, and in the clinical stage III, most of the patients had severe (90%) changes on MRI. Hence clinical staging of HIE is also a very good predictor for assessing the severity of changes in HIE (Table 2). We found that the sensitivity and specificity of MRI in the diagnosis of HIE is around 96%. The negative and positive predictive values were 92% and 97%, respectively. The diagnostic accuracy of MRI is calculated to be around 96% which makes MRI the best imaging modality for diagnosing hypoxic-ischemic encephalopathy. The findings of MRI were correlated with the final clinical outcome at 1 year, and the diagnostic accuracy of MRI was calculated. MRI has found to have the following values: Sensitivity=83.33%, Specificity=93.94%, PPV=83.33%, NPV=93.94%.

DISCUSSION

This study evaluated the various MRI findings in suspected neonatal Hypoxic Ischemic Encephalopathy in term and preterm neonates and compared the different MRI patterns with clinical outcomes. In addition, we also set out to demonstrate the sensitivity of MRI in evaluating birth asphyxia babies.

In a study conducted by Robertson *et al.*,[8], they concluded that 100% of babies with stage I HIE had normal neurodevelopmental outcomes at 3.5 years. For babies with stage II HIE, 71% had normal outcomes, and for stage III HIE babies 0% had normal outcomes at 3.5 years.

In a study conducted by Biarge *et al.*[9] with 175 term babies with birth asphyxia, they found that the severity of BGT lesions was strongly associated with the severity of motor Impairment. These findings were also correlated with the study conducted by Volpe *et al.*[10] He stated that among a group of infants with presumed hypoxic-ischemic encephalopathy, the 25% with predominantly basal ganglia-thalamic injury had a poorer outcome than the 45% with a predominantly parasagittal watershed pattern or the 30% with a normal neonatal MRI.

Mary Rutherford *et al.* (44) conducted studies on infants with a history of birth asphyxia. Only four patients developed cerebral palsy with athetoid movements in their series of 25 patients with hemorrhagic lesions in the basal ganglia region. Out of these four patients, 3 underwent follow up neuroimaging, which disclosed discrete cysts in the putamen region.

In another study conducted by Mary Rutherford *et al.*[11], sixteen infants with HIE were studied using serial MRI upto

Table 2: Crosstabulation clinical staging and MRI findings

Clinical stage	Normal	Mild	Moderate	Severe	P value
I	14	10	1	0	<0.0001
II	1	8	4	1	
III	0	0	1	5	

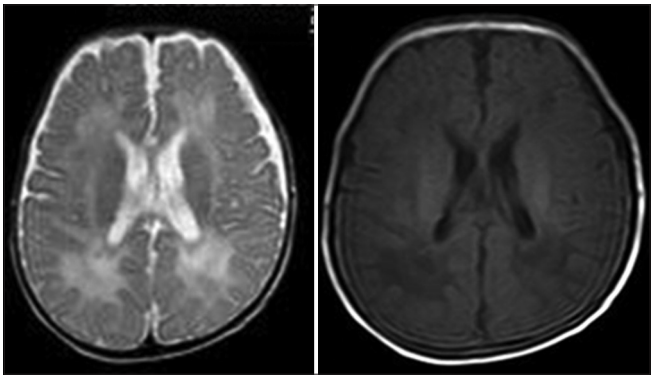

Figure 1: T2 hyperintensity T1 hypointensity PVWM

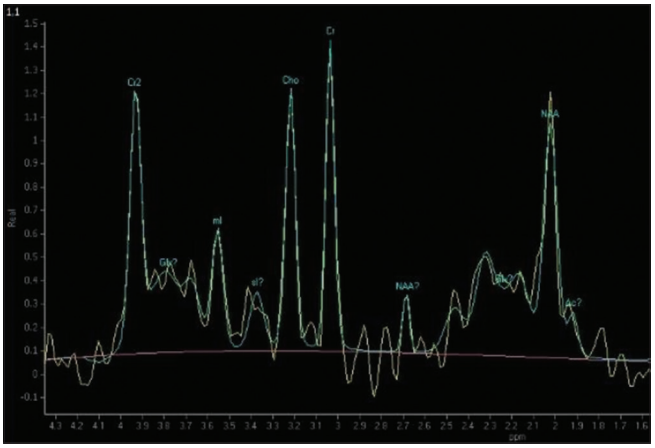

Figure 2: Reduced NAA on MRS

the age of 2 years. The infants had regular neurological and developmental assessments. A nuclear magnetic resonance score was devised to quantify the early and late MRI findings, and a neurological optimality score was used to quantify abnormal neurological signs at the final examination. The follow-up MRI score was compared with the neonatal MRI score and the child's outcome. There was a strong positive correlation between the neonatal and follow up MRI scores and between MRI scores and optimality scores. All infants with a normal outcome had patchy white matter abnormalities. All infants with an abnormal outcome had extensive white matter abnormalities. The outcome was most severe in those infants with additional basal ganglia atrophy with or without cyst formation. Infants with mild HIE who are developmentally normal at the age of 2 years do not have normal MRI scans and may be at risk of minor neurological problems by school age. Bilateral basal ganglia abnormalities are associated with severe developmental delay, but infants with mainly white matter and cortical abnormalities have less severe problems despite extensive tissue loss.

Our study correlated with the findings of Takenouchi *et al*.[12] and Nagy *et al*.[13]

They described patients who demonstrated restricted diffusion within the splenium of the corpus callosum, showed a significantly higher incidence of severe neurodevelopmental delay and worse neuropsychological performance (Fig. 2).

MR spectroscopy itself is a good prognostic indicator in predicting the abnormal outcome. The patients with elevated lactate levels had basal ganglia-thalamus injuries, and they had an abnormal outcome which was statistically significant. Our findings were in concordance with the previous studies conducted by Barkovich *et al*.[14] and Peden *et al*.[15] Barkovich *et al*.[14] mentioned that elevated lactate and diminished NAA were the most common findings in infants with neurologic and developmental abnormalities at age T1W and T2W months and Peden *et al*.[15] described that the NAA/Cho ratios show a clear trend, with the highest value seen in the control infant and the lowest in the infants with an abnormal outcome (Figs. 1 and 2).

CONCLUSION

In this study, Sarnath staging of HIE is a good predictor in identifying poor long-term neurological outcomes, and it also correlates with the findings of MRI. Clinically severe encephalopathy correlated with abnormal basal ganglia–thalamic lesions in term babies and germinal matrix haemorrhage in preterm babies. The diffusion-weighted imaging and MR spectroscopy are useful in identifying hypoxic ischemic encephalopathy early when the conventional MRI findings were subtle. Elevated lactate levels and decreased NAA levels on MRS adds sensitivity in predicting and prognosticating the abnormal final outcome with confidence. MRI has high sensitivity and specificity in the evaluation of hypoxic-ischemic encephalopathy. It is non-invasive and has no radiation hazards. It offers excellent grey-white matter resolution, which the other modalities cannot. In our study, the sensitivity of MRI is calculated to be 96% in predicting the final outcome. MRI should be done in all patients with suspected HIE, thus helping in early identification and initiation of therapeutic hypothermia, thereby preventing the long-term complication of brain injury.

BIBLIOGRAPHY

1. Abdo RA, Halil HM, Kebede BA, Anshebo AA, Gejo NG. Prevalence and contributing factors of birth asphyxia among the neonates delivered at Nigist Eleni Mohammed memorial teaching hospital, Southern Ethiopia: a cross-sectional study. BMC Pregnancy Childbirth 2019;19:536. https://doi.org/10.1186/s12884-019-2696-6.
2. Lawrence RK, Inder TE. Anatomic changes and imaging in assessing brain injury in the term infant. Clin Perinatol. 2008 Dec;35(4):679-93.
3. Bano S, Chaudhary V, Garga UC. Neonatal Hypoxic-ischemic Encephalopathy: A Radiological Review. J Pediatr Neurosci. 2017 Jan-Mar;12(1):1-6.
4. Huang BY, Castillo M. Hypoxic-ischemic brain injury: imaging findings from birth to adulthood. Radiographics. 2008 Mar-Apr. 28(2):417-39.
5. Latchaw RE, Truwit CE. Imaging of perinatal hypoxic-ischemic brain injury. Semin Pediatr Neurol. 1995 Mar. 2(1):72-89.
6. Uzianbaeva L, Yan Y, Joshi T, Yin N, Hsu C-D, Hernandez-Andrade E, *et al*. Methods for monitoring risk of hypoxic damage in fetal and neonatal brains: A review. Fetal Diagn Ther 2022;49:1–24. https://doi.org/10.1159/000520987.
7. Alderliesten T, de Vries LS, Benders MJ, Koopman C, Groenendaal F. MR imaging and outcome of term neonates with perinatal asphyxia: value of diffusion-weighted MR imaging and ^{1}H MR spectroscopy. Radiology. 2011 Oct;261(1):235-42. doi: 10.1148/radiol.11110213. Epub 2011 Aug 9. PMID: 21828190.
8. Robertson C, Finer N. Term infants with hypoxic-ischemic encephalopathy: outcome at 3.5 years. Developmental Medicine & Child Neurology. 1985 Aug;27(4):473-84.
9. Martinez-Biarge M, Diez-Sebastian J, Kapellou O, Gindner D, Allsop JM, Rutherford MA, Cowan FM. Predicting motor outcome and death in term hypoxic-ischemic encephalopathy. Neurology. 2011 Jun 14;76(24):2055-61.
10. Volpe JJ, Herscovitch P, Perlman JM, Kreusser KL, Raichle ME. Positron emmission tomography in the asphyxiated term newborn: Parasagittal impairment of cerebral blood flow. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1985 Mar;17(3):287-96.
11. Rutherford MA, Pennock JM, Murdoch-Eaton DM, Cowan FM, Dubowitz LM. Athetoid cerebral palsy with cysts in the putamen after hypoxic-ischaemic encephalopathy. Archives of disease in childhood. 1992 Jul 1;67(7 Spec No):846-50.
12. Takenouchi T, Heier LA, Engel M, Perlman JM. Restricted diffusion in the corpus callosum in hypoxic-ischemic encephalopathy. Pediatric neurology. 2010 Sep 1;43(3):190-6.

13. Nagy Z, Lindström K, Westerberg H, Skare S, Andersson J, Hallberg B, Lilja A, Flodmark O, Lagercrantz H, Klingberg T, Fernell E. Diffusion tensor imaging on teenagers, born at term with moderate hypoxic-ischemic encephalopathy. Pediatric research. 2005 Nov;58(5):936-40.
14. Barkovich AJ, Baranski K, Vigneron D, Partridge JC, Hallam DK, Hajnal BL, *et al*. Proton MR spectroscopy for the evaluation of brain injury in asphyxiated, term neonates. Am J Neuroradiol. 1999;20(8):1399–405.
15. Peden CJ, Rutherford MA, Sargentoni J, Cox IJ, Bryant DJ, Dubowitz LM. Proton spectroscopy of the neonatal brain following hypoxic-ischaemic injury. Developmental Medicine & Child Neurology. 1993 Jun;35(6):502-10.
16. Barkovich AJ, Kjos B. Normal postnatal development of the corpus callosum as demonstrated by MR imaging. American Journal of Neuroradiology. 1988 May 1;9(3):487-91.

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