Original Research Paper

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Radio Diagnosis

PROGNOSTICATING CLINICAL OUTCOME IN NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY BY MRI

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ABSTRACT **Background:** MRI is an unparalleled study in the evaluation of hypoxic ischemic encephalopathy. But the literature regarding the clinical correlation of MRI findings with the final clinical outcome using DDST II (DENVER DEVELOPMENTAL SCREENING TEST) are lacking.
Objective: To correlate the MRI findings in hypoxic ischemic encephalopathy with clinical outcome after one year.
Methodology: 75 patients were subjected to 1.5T MR imaging followed by which patients were examined for growth & development and a detailed neurodevelopmental assessment according to DDST II for one year.
Observations: Sensitivity, specificity, PPV, NPV and accuracy of MRI compared to clinical outcome at the end of one year.
Conclusion: MRI is superior imaging modality in the evaluation of neonatal hypoxic ischemic encephalopathy. There is a strong and consistent correlation between the various MRI findings and the clinical outcome.

KEYWORDS : Hypoxic ischemic encephalopathy, HIE, MRI in HIE.

INTRODUCTION:

Perinatal asphyxia, more appropriately known as 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/or reduced cerebral blood flow. Birth asphyxia causes an estimated 598,000 deaths or 23% of all neonatal deaths annually.[1] Neonatal deaths accounted for 46 per cent of all under-five deaths.

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 of choice for the diagnosis and follow up of infants with hypoxic ischemic encephalopathy. In a newly diagnosed case of cerebral palsy MRI should be considered because it may help to establish the cause.

In this study we have made an attempt to know the importance of MRI in the neonatal period in babies with HIE as a diagnostic and prognostic tool for assessing neurodevelopmental outcome at 1 year of life.

METHODOLOGY:

Type of Study- Observational
Study Setting- Tertiary Care Hospital
Study Period- October 2016- October 2018
Sample Size-75 patients.
Study Instrument- 1.5 Tesla, Philips MR Achieva (head coil)

Inclusion criteria: All hemodynamically stable term and preterm neonates with clinical diagnosis of HIE.

Exclusion criteria:
Suspected congenital infections.
Those who are unfit for anesthesia.
General contraindications to MRI examination such as pacemakers, metallic implants or metallic foreign body.

MRI PROTOCOL:

- T1 weighted 3D images in axial, sagittal and coronal planes.
- T2 weighted images in axial and coronal plane.
- T2 weighted FLAIR axial images.
- Diffusion weighted axial images.
- T2W Gradient axial images.

METHOD OF COLLECTION OF DATA AND INTERPR ETATION:

All hemodynamically stable term and preterm neonates with a clinical diagnosis of HIE, referred for imaging studies were taken up.The study requires that the patients be adequately sedated to tolerate the prolonged examination time inside the MRI machine.

The basic history of the patients including age, sex, mode of delivery, parity of the mother, whether cried immediately after birth, meconium stained amniotic fluid, birth weight, APGAR score at 5 mins, term/preterm, clinical stage of HIE according to Sarnat & Sarnat grading and preliminary NSG findings whether normal/abnormal/not performed were taken.

Following MRI patients were followed up for a period of 1 year. - Babies were examined for growth & development and a detailed neurodevelopmental assessment was done according to DDST II (DENVER DEVELOPMENTAL SCREENING TEST) once in a month for 3 months and then once in 2 months for next 8 months.

DDST II test is designed to compare a given child's performance on a variety of tasks to the performance of others of the same age. It consists of 125 tasks/items which are arranged on the test forms in 4 sectors. Personal-social, Fine motor-adaptive, language and gross motor.

Denver II is interpreted as follows.
Normal: No delays and a maximum of one caution in the various items.
Suspect: 2 or more cautions and or more delays.
At one year, child was diagnosed as having abnormal outcome if,

1. Cerebral palsy of any severity.
2. Microcephaly.
3. Suspect according to DDNS II.

MRI findings were categorized into normal, mild, moderate and severe. In term and preterm neonates' involvement of periventricular white matter and subcortical white matter was classified as mild, signal changes in posterior limb of internal capsule, perirolandic white matter, severe multicystic encephalopathy as moderate and abnormal basal ganglia – thalamic lesions in term babies and germinal matrix hemorrhage in preterm babies as severe. In our study 75 neonates were recruited after getting consent from the parents.

STATISTICAL METHODS:

Association between various MRI findings with clinical outcome was assessed by performing “Chi square test”. For small number “Fischer exact test” was performed whenever applicable. Statistical evaluation of diagnostic accuracy of MRI findings in comparison to 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 as of statistical significance. Statistical software STATA version 14.0 was used for data analysis.

RESULTS:

Out of 75 patients, majority of the patients were in the age group of 26-30 days (37.0%) and 5-10 days (20.0%). 54 patients (72.0%) were males and 21 patients (28.0%) were females.

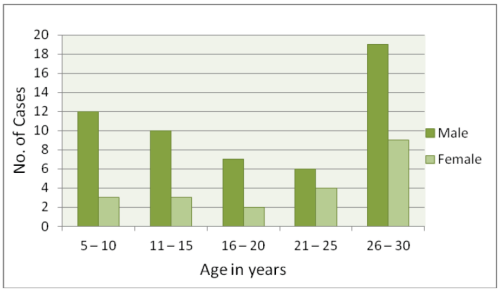

FIG 1: AGE AND SEX DISTRIBUTION

Chief complaint was seizures in 50 patients (67.0%) and 25 patients (33.0%) presented with lethargy. Out of 75 babies, 64 babies (85.33%) were born to primi mothers and 11 babies (14.67%) were born to multiparous mothers. In Our study majority of the patients (80.0%) were normal weight babies. Amniotic fluid was meconium stained in 11% of the cases. Most of the patients were of normal vaginal delivery (78.67%). The second common mode of delivery was LSCS (10.67%).

Out of the 75 patients 45 (60%) had APGAR >7 and 30 (40%) had <7 at the end of 5 minutes. Severe hypoxic ischemic changes were noted mostly in APGAR <7 patients. Out of the 75 patients, 41 patients (55%) were clinical stage I, 24 patients (32%) were stage II and 10 patients (13%) were stage III. 63 patients (84%) were term and 12 patients (16%) were preterm out of the 75 patients. Out of the 75 examined patients, 50 patients (67%) had abnormal outcome at the end of one year. The rest (33%) had normal outcome.

Out of the 75 babies, 7 had hyperintensity of thalamus in T1W images, 6 had loss of T1W hyperintensity of PLIC, 8 had hyperintensity of basal ganglia in T1W images, 8 babies had periventricular leukomalacia, 5 babies had germinal matrix hemorrhage, 26 babies had periventricular or subcortical white matter involvement in the 11 had watershed infarcts, 5 had multicystic encephalopathy and others had mild white matter involvement, 6 patients showed perirolandic white matter involvement, 3 patients showed brainstem involvement, 7 patients showed generalized cerebral atrophy. White matter abnormalities were the most common finding in our study. Few of the patients showed overlap of findings also.

Most of the patients with Sarnath and Sarnath clinical stage I HIE had either normal (58%) or mild (39%) changes of HIE on MRI. In the Clinical stage II HIE most of the patients had either mild (58%) or moderate (29%) 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 of HIE.

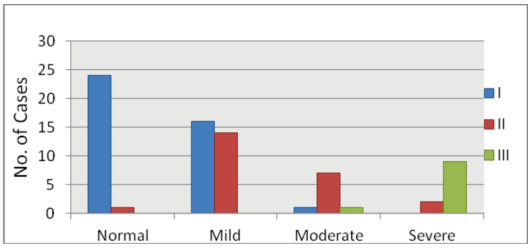

Fig 2: Correlation Of Clinical Staging And Mri Finding

Table 1: Diagnostic Evaluation Of Mri In Comparison To Clinical Outcome

	Clinical outcome		
MRI Finding	Normal	Abnormal	Total
Normal	24	2	26
Abnormal	1	48	49
Total	25	50	75

We found that the sensitivity and specificity of MRI in the diagnosis of HIE is around 96%. The negative predictive value and the 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 the diagnosis of hypoxic ischemic encephalopathy.

DISCUSSION:

This study was directed to evaluate the various MRI findings in suspected neonatal Hypoxic Ischemic Encephalopathy in term and preterm neonates and also to compare the various MRI patterns with clinical outcome. We also set out to demonstrate the diagnostic accuracy of MRI in evaluating birth asphyxia babies.

72% of the patients included in our study were male, the rest were female. The presence of changes of HIE in MRI did not showed any significant association with the sex. [p value 0.17]. Severe involvement of HIE is common in males compared to females. But there is no statistically significant association between sex of the patient and chance of finding an abnormal MRI pattern for severe in patients with HIE. These observations were found in study conducted by **Sajitha et al.**[2]

In our study 85% of the babies with HIE were born to primi parous mother and rest were multi parous. In a study conducted by **Nilufar Shireen et al,**[3] they concluded that more of asphyxiated babies were born to primi mothers.

The number of subjects with grade III injuries who could be included in the study was less due to the unstable clinical picture associated with the same and difficulties in obtaining MRI in patients on respiratory support. In our study we found that there is a significant correlation with stage of HIE and final outcome. Most of the babies (25 out of 41) with stage I HIE had normal final outcome at the end of one year. All the patients with Stage II and III had abnormal final outcome. In a study conducted by **Robertson et al**,[4] they came to a conclusion 100% of babies with stage I HIE had normal neurodevelopmental outcome at 3.5 years. For babies with stage II HIE 71% had normal final outcome and stage III HIE babies 0% had normal outcome at 3.5 years.

Out of the 75 babies, 7 babies showed abnormality in the thalamus and 8 babies showed abnormality in the basal ganglia in conventional MRI. All patients with the involvement of basal ganglia and thalamus had abnormal final outcome which was statistically significant. (p value <0.005). This was in concordance with study conducted by **Biarge et al.** [5]

In our study out of 75 patients 6 babies had loss of T1w hyperintensity in PLIC and 83% (n=5) had abnormal final outcome which is statistically significant (p=0.0005). In a study conducted by **Rutherford M.A et al** [6] to establish whether abnormal signal intensity in the posterior limb of the internal capsule on MRI is an accurate predictor of neurodevelopmental outcome at 1 year of age in infants with HIE, they found that abnormal signal intensity in the PLIC is an accurate predictor of neurodevelopmental outcome in term infants suffering from HIE.

In our study the largest group demonstrated changes in the white matter. Periventricular and subcortical white matter was affected more commonly. The classical periventricular leukomalacia was seen predominantly in the preterm neonates. Thinned out corpus callosum was noted in 20 patients those who showed loss of white matter. The perirolandic white matter involvement was seen in 6 patients which was seen in moderate hypoxia. All the patients with white matter involvement showed abnormal outcome in our study. In a study conducted by **Sajitha et al**, stated that term babies with mild encephalopathy shows more involvement of periventricular white matter than subcortical white matter. In our study subcortical involvement was noted more commonly than the periventricular involvement. Our study findings were correlated with the studies conducted by **Ramachandran et al.** [7]

In our study 3 patients had brainstem abnormalities. All three had abnormal outcome at the end of one year. Brainstem involvement is exclusively seen in patients with severe prolonged ischemia who were stage III HIE. These finding were correlated with the study conducted by **M. Martinez-Biarge et al.** [5] No cerebellar involvement is noted in

our study as cerebellum is relatively resistant to hypoxia. This finding was in concordance with the study conducted by **Jouvet P et al.** [8]

In our study 5 patients had germinal matrix out of them 4 patients had abnormal clinical outcome and one patient who had mild intraventricular hemorrhage had a normal neurodevelopmental outcome at the end of one year. Germinal matrix hemorrhage was specifically seen in the preterm neonates only. Our study findings were in concordance with the study conducted by **Pauline Reubsaet et al.** [9] They found that the very preterm infants with low-grade GMH-IVH on cranial US have a similar early neurodevelopmental outcome compared with controls.

From all the data we acquired we came to a conclusion regarding MRI in HIE. 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=96.0%, Specificity=96.0%, PPV=92.31%, NPV=97.96%, Diagnostic accuracy=96.0%. Ramachandran et al** [7] conducted a study in 50 patients with suspected history of hypoxic ischemic encephalopathy and the results of their study was sensitivity of MRI in prognosticating clinical outcome was 72% and specificity was 71% while PPV and NPV was 86% and 50% respectively. A similar study was conducted by **Jose A et al** [10] to correlate findings on MRI brain with neurological outcome at 12 months in 16 term newborns with hypoxic ischemic encephalopathy. In their study the sensitivity of MRI in prognosticating neurological outcome was 82%, specificity was 93%, PPV was 90% and NPV was 87%. The study conducted by **El-Auoty M** [11] which correlated MRI findings and clinical outcome in 25 neonates with HIE, showed a sensitivity of 100%, specificity of 42%, PPV of 81% and NPV of 100%. In comparison with the above studies our study showed higher sensitivity, specificity, PPV, NPV and diagnostic accuracy. The reason for high sensitivity, specificity, positive predictive value, negative predictive values and diagnostic accuracy in our study may be due to late referral for MRI in our setting and being a tertiary care center, the chances of positive patients is found to be high.

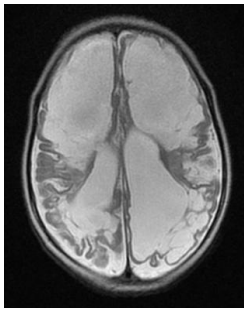

Fig 3: Multicystic Leukoencephalopathy

CONCLUSION :

From the present prospective study of 75 neonates with suspicion of HIE certain inferences were drawn regarding the MR evaluation that this study attempted to evaluate the various magnetic resonance imaging changes in hypoxic ischemic encephalopathy in term and preterm neonates.

Sarnath staging of HIE is a good predictor in identification of poor long-term neurological outcome and it is also correlating with the findings of MRI. This study highlighted the importance of MRI in neonates with low Apgar at 5 mins, as these cases showed severe involvement in MRI and there is statistically significant association between low APGAR score and severe brain injury in birth asphyxia.

Clinically severe encephalopathy correlated with abnormal basal ganglia–thalamic lesions in term babies and germinal matrix hemorrhage in preterm babies. There is a strong and consistent correlation between the various MRI findings and the clinical outcome. Lesions involving basal ganglia and thalamus on MRI predicted adverse neurological outcome at the end of one year. Lesions involving white matter also predicted abnormal final outcome. MRI has a high sensitivity and specificity in the evaluation of hypoxic ischemic encephalopathy. It is non-invasive and has no radiation hazards. It offers excellent gray 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 longterm complication of brain injury.

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