Role of Magnetic Resonance Imaging in Assessing Morphometry of Corpus Callosum in Patients with Hypoxic Ischemic Encephalopathy and Its Ability to Predict the Clinical Outcome

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ABSTRACT

BACKGROUND

Hypoxic ischemic encephalopathy (HIE) is one of the major causes of mortality and morbidity in neonates in India. In spite of advancements in the field of medicine with respect to HIE, there is no satisfactory standard test for HIE. HIE can present with a multitude of manifestations in the infant brain, but one of the most obvious abnormality is the thinning of corpus callosum, which is more evident on MRI than other imaging modalities. This study was done to qualitatively assess and quantitatively measure the corpus callosum and correlate with APGAR score at birth. We wanted to correlate the morphology of corpus callosum on MRI in patients with HIE with APGAR scores and evaluate the prognostic ability of morphometric changes in corpus callosum.

METHODS

This is a prospective and cross-sectional study conducted in a tertiary care center in Bangalore from September 2017 to December 2018. A total of 18 clinically proven cases of HIE of age less than 10 years were included in the study. The study was carried out on T1 & T2 mid-sagittal sections of brain. The changes in corpus callosal morphometry were studied and correlated with APGAR scores and clinical outcomes.

RESULTS

The correlation between various dimensions and age was statistically significant for APD ($p < 0.05$), LCC ($p < 0.05$), GT ($p < 0.05$), BT ($p < 0.05$), ST ($p < 0.05$) and FOD $p < 0.05$).

CONCLUSIONS

Preterm birth adversely affects the development of corpus callosum as most of the patients were born preterm. Most common site of injury was posterior part including isthmus and body. Quantitative measurement helps in prediction of the clinical outcome of the disease. In spastic cerebral palsy, corpus callosum is diffusely thinned out, predominantly affecting posterior body, isthmus and splenium, whereas choreoathetoid cerebral palsy shows focal thinning of posterior body and isthmus of corpus callosum.

KEYWORDS

APGAR Score, Athetotic, Cerebral Palsy, Preterm, Spastic

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DOI: 10.18410/jebmh/2020/213

Financial or Other Competing Interests: None.

How to Cite This Article:
Alemao NN, Pahwa S, Gowda S. Role of magnetic resonance imaging in assessing morphometry of corpus callosum in patients with hypoxic ischemic encephalopathy and its ability to predict the clinical outcome. J. Evid. Based Med. Healthc. 2020; 7(20), 975-979. DOI: 10.18410/jebmh/2020/213

Submission 18-03-2020,
Peer Review 24-03-2020,
Acceptance 22-04-2020,
Published 14-05-2020.

BACKGROUND

Hypoxic ischemic encephalopathy (HIE) is one of the major causes of mortality and morbidity in neonates in India. In spite of advancements in the field of medicine with respect to HIE, there is no satisfactory standard test for HIE. Foetal distress, acidaemia, APGAR score and other clinical markers of possible intrapartum injury are the parameters that are used regularly in clinical practice but have a low positive predictive value. Brain hypoxia and ischemia due to systemic hypoxemia and reduced cerebral blood flow (CBF) are the primary physiological processes that are attributable to HIE.[1–2] Incidence of HIE is approximately 2.5 per 1000 live births.[3] This incidence is much higher in preterm births (7 per 1000 preterm births).[4] Among the affected newborns, 15-20% die in the postnatal period, and about 25% suffer from disabilities.[5,6] The presence of an abnormal neurologic examination in the first few days of life is the single most useful indicator that a brain insult has occurred. Identification and characterization of the severity, extent, and location of brain injury in HIE infants rely on the selection of appropriate neuroimaging modalities. Ultrasonography used to be the first-line imaging technique for the evaluation of the new-born brain. Though ultrasonography is easily available and cheaper, it is less sensitive and operator dependent. Magnetic Resonance Imaging (MRI) has been more useful in the detection of early lesions and much higher sensitivity and Positive Predictive Value (PPV).

HIE can present with a multitude of manifestations in the infant brain, but one of the most obvious abnormality is the thinning of corpus callosum, which is more evident on MRI than other imaging modalities. Such injury may be partly explained by the intrinsic vulnerability of immature oligodendrocytes in corpus callosum.[7] Corpus callosum(CC) is the primary white matter commissure of the brain and the significance lies in the fact that damage to the CC during development has been found to be associated with poor neurological outcome and neuropsychological performance.[8] The study was done to evaluate the morphology of CC in patients with HIE and quantitatively measure the corpus callosal dimensions and correlate the same with APGAR scores and clinical course of the patients. One of the evaluative measures of a newborn's condition at birth is APGAR score. It provides the clinician an alarm for immediate attention. The Apgar score is performed at 1 and 5 minutes of life. But the score in itself lacks sensitivity and specificity, unless used with other parameters.[9] Cerebral Palsy (CP) refers to a clinical set of static encephalopathies comprising a broad array of neuropathologies that are linked by their expression of variable disabilities of movement and posture consequent to a nonprogressive lesion of the immature brain. Several types of CP have been classified, of which spastic CP is the dominant type. In addition, choreo athetotic, hypotonic, and ataxic varieties have been described. In the present study, we sought to establish a role of corpus callosum morphometry in correlation with CP.

We wanted to correlate the morphology of corpus callosum on MRI in patients with HIE with APGAR scores and evaluate the prognostic ability of morphometric changes in corpus callosum.

METHODS

This prospective and cross-sectional study was conducted in the Department of Radiodiagnosis, M.V.J. Medical College and Research Hospital, Bangalore from September 2017 to December 2018. A total of 18 patients of age less than 10 years with a clinical diagnosis of HIE were included in the study. Patients aged more than 10 years, patients with metallic implants, patients with space occupying lesions and inherited metabolic disorders were excluded. Informed consent was taken from the guardians of the patients for the MRI scans. The study was carried out on T1 mid-sagittal sections of brain. The changes in corpus callosal morphometry was studied. All the MRI scans were done using Siemens Magnetom Essenza 1.5 T machine using head coils. Patients were imaged in the supine position. The protocol included acquisition of spin echo images with parameters of 529/9.7/1 (repetition time/echo time/excitations), 5 mm contiguous axial sections, a matrix of 256 x 256, and a field of view of 230 mm.

Evaluation of corpus callosum was done on mid sagittal T1 & T2 weighted image by following C Garel et al method.[10]

A. Thickness of the CC- At the level of the genu (GT) {Normal: 5 ± 0.7 mm}, body (BT) {Normal: 2.7 ± 0.4}, isthmus (IT) { Normal: 2.5 ± 0.4 mm} and splenium (ST) {Normal: 4.9 ± 0.8 mm} (Figure 1).
B. Anteroposterior diameter (APD) of the CC {Normal: 2.7 ± 0.3} -The distance between the anterior aspect of the genu and the posterior aspect of the splenium (Figure 2)
C. True length of CC (LCC) {Normal: 42.9 ± 2.7 mm} - The curvilinear distance between the rostrum and the splenium at mid thickness of the CC (Figure 2).
D. Fronto-occipital diameter (FOD) {Normal: 2.7 ± 0.3 mm} -The distance between the extreme points of the frontal and occipital lobes (Figure 2).

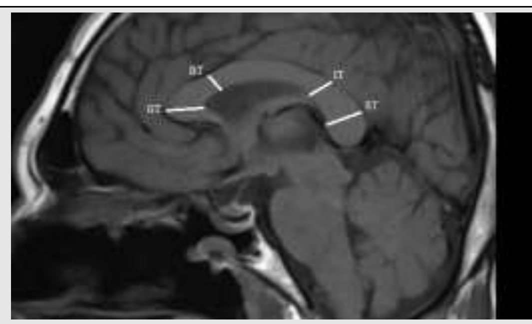

Figure 1. Measurement of the Corpus Callosum Parameters on a Mid-Sagittal T1 Weighted Image (GT, BT, IT, ST)

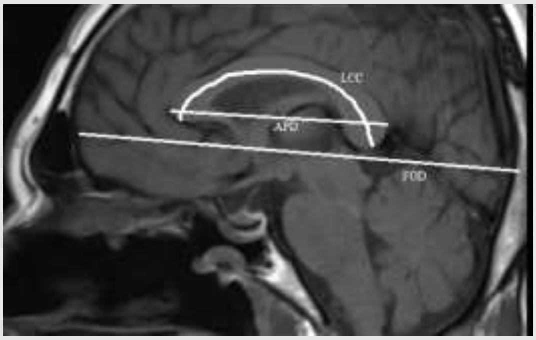

Figure 2. Measurement of the Corpus Callosum Parameters on a Mid-Sagittal T1 Weighted Image (FOD, APD, LCC)

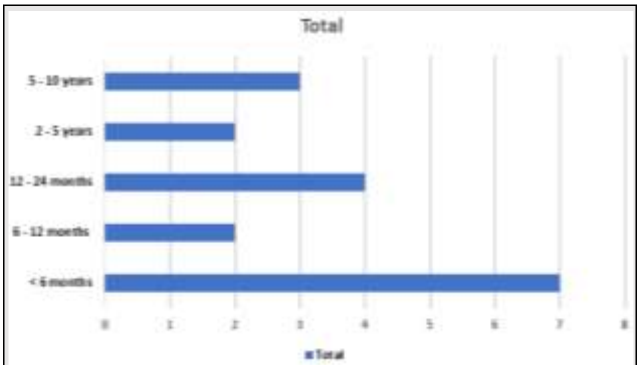

Figure 3. Age Distribution of the Study Subjects

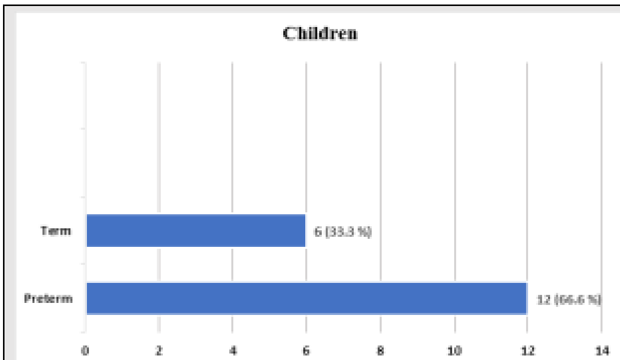

Figure 4. Distribution of the Number of Children as a Function of Birth History

Variable	N	Mean (mm)	SD (mm)	p-value
APD	18	42.43	4.46	< 0.05
LCC	18	56.42	8.54	< 0.05
GT	18	4.94	2.02	< 0.05
BT	18	2.02	1.13	< 0.05
IT	18	1.21	0.59	< 0.05
ST	18	2.97	1.52	< 0.05
FOD	18	102.59	14.32	< 0.05
IT/ST	18	0.49	0.27	< 0.05
APD/FOD	18	0.40	0.03	< 0.05

Table 1. Corpus Callosum Parameters on MRI

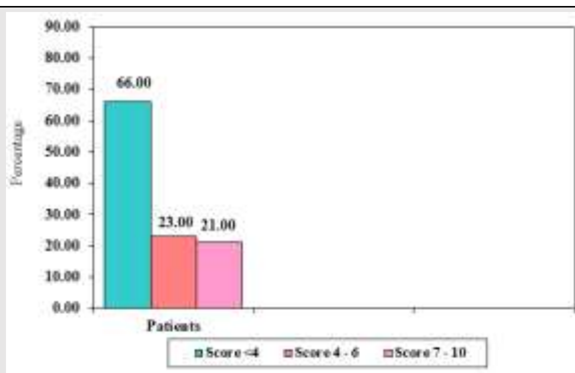

Figure 5. Distribution of the Number of Children by APGAR Scores

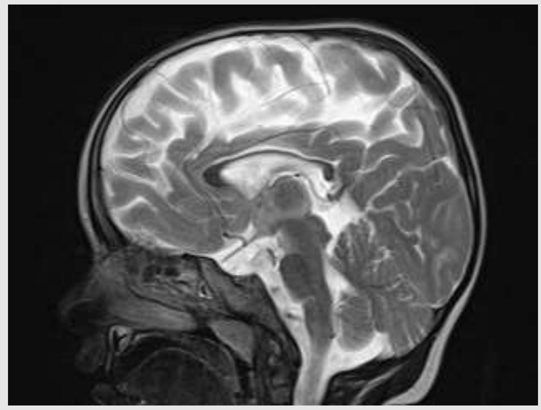

Figure 6. Sagittal T2WI Showing Focal Thinning in Posterior Part of Corpus Callosum Including Isthmus and Body in a 9-Year-Old Male Who Came with Complaints of Delayed Milestones, Difficulty in Walking and Speech, and Jerky Movements Since 1 Year

Correlation with APGAR Scores

APGAR score at 1 minute after birth was retrospectively obtained from all the patients and the individual score was correlated with the extent of involvement of corpus callosum.

Statistical Analysis

Statistical Analysis of results was carried out by means of the statistical package (SPSS) version 20. A descriptive statistic frequency, Chi-square test and t-test were performed to analyse the data. P value< 0.05 was considered significant. The data was analysed and the final observations were tabulated.

RESULTS

In this study, the maximum number of patients were in the age group of less than 6 months which were 38.8% (n = 7) of total. (Figure 3). In the present study, majority were males 61.1% (n = 11) and females 39.9% (n=7). The male to female ratio was 1.57:1. Preterm constituted 12 cases (66.6%) and post term constituted 6 cases (33.33%). (Figure 4). In the present study, dimensions of different parts of corpus callosum were in order of isthmus < body <splenium <genu. Thus, the thickest part was genu followed by splenium and thinnest part was isthmus (Table 1). In the present study, the correlation between various dimensions and age was statistically significant for APD (p < 0.05), LCC (p <0.05), GT (p <0.05), BT (p <0.05), ST (p <0.05) and FOD p <0.05). For isthmus, the difference of age groups was insignificant. (Table 1)

Correlation with APGAR score shows that majority of the patients of HIE with corpus callosal involvement had a low APGAR score of less than 7, of which most had a score less than 4. This shows that low APGAR scores are associated with HIE and such newborns must be put on close follow-up. In the present study, majority (72%) had varying degrees of spastic CP; two (11%) with hypotonic CP and three (16%) with choreoathetoid CP. It was observed that corpus callosum was diffusely thinned out predominantly affecting posterior body, isthmus and splenium in patients with spastic CP. In patients with choreoathetoid CP, focal thinning was predominant.

DISCUSSION

Our study shows that preterm birth adversely affects the development of corpus callosum as most of the patients were born preterm. Most common site of injury was posterior part including isthmus and body. The corpus callosum originates at 10–11 weeks' gestation and genu is the first part to develop. Initially, the genu grows faster than the splenium which does not show a rapid growth until after birth.[11] Thus, the later development of the splenium and posterior part of corpus callosum make them particularly susceptible to damage in the third trimester and perinatal period. Other parts including the rostrum and splenium are formed after the trunk is developed, and the development is near complete by 16 weeks when it resembles that of an adult.[12]

In 1952, Dr. Virginia Apgar, an anaesthesiologist at Columbia University developed the Apgar score. The score is a rapid method for assessing a neonate immediately after birth and following resuscitation. Apgar scoring is accepted by both the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics. Apgar score contains 5 components which includes color, heart rate, reflexes, muscle tone, and respiration. Apgar scoring is designed to assess for signs of hemodynamic compromise such as cyanosis, hypoperfusion, bradycardia, hypotonia, respiratory depression or apnoea. Each component is scored 0, 1, or 2. The score is recorded at 1 minute and 5 minutes in all infants. Maximum score is 10 and score below 3 are considered critical and needs immediate resuscitation, scores 4 to 6 are considered fairly low, while scores above 7 are considered reassuring.[13]

In the present study, majority {13 out of 18 (72%)} had varying degrees of spastic CP; two (11%) with hypotonic CP and three (16%) with choreoathetoid CP. It was observed that corpus callosum was diffusely thinned out predominantly affecting posterior body, isthmus and splenium in patients with spastic CP. In spastic cerebral palsy, corpus callosum is diffusely thinned out, predominantly affecting posterior body, isthmus and splenium, whereas choreoathetoid cerebral palsy show focal thinning of posterior body and isthmus of corpus callosum. This probably due to preferential involvement of white matter in spastic CP, thereby causing a diffuse involvement. The other types of CP are known to have both grey and white matter involvement and the reason for focal involvement is unknown.[14]

A study done by Cristina Mañeru et al[15] show that measures of corpus callosum dimensions are altered in children with HIE. In a study by Sheth et al, the correlation between the size of corpus callosum and the cause of cerebral palsy was highly significant.[16] Epelman, M et al showed that corpus callosal involvement was highly positive in majority of patients with hypoxic ischemic injury. These outcome of these studies are in tandem with results of our study.

Limitations

The study included only patients under the age of 10 and hence the long-term follow-up was not ascertained. Also, the sample size of the study was very small to obtain statistical significance between the types of cerebral palsy. A larger study with more sample size and longer-term follow-up is likely to throw more light onto the disease pathogenesis and the imaging implications.

CONCLUSIONS

Early identification of the pattern and severity of injury in HIE patients depends on the use of appropriate imaging modality and timing of the study. Use of MRI at an early life will aid in early diagnosis and appropriate management of the patient with history of HIE. Measurements of corpus callosum morphometry will help in quantitative analysis and prediction of the clinical course and prognosis of the patient.

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