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Resistive index (RI) as a prognostic indicator of early morbidities in term neonates with hypoxic ischemic encephalopathy

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Abstract---Background: Hypoxemia and hypoxia sustained by neonates during birth process leads to Hypoxic-ischemic encephalopathy (HIE) which can give rise to immediate and/or long term sequelae of neonatal brain injury, increased neonatal morbidity and mortality worldwide. Material and methods: A prospective observational study done in tertiary neonatal intensive care unit of north Karnataka region. The study was conducted between September 2021 to May 2022. Results: A total of 44 neonates with HIE were studied. There were 26 (61%) male and 18 (39%) female babies and the male to female ratio was 1.4:1. There were 28 cases with grade I, 6 cases with grade II and 10 cases with grade III HIE. The Resistive

index was normal in 30 (68.1%) cases and was abnormal in 14 (31.8%) cases. Common Doppler ultrasound findings were of increased echo density of cerebral parenchyma and increased periventricular density. There were 95% survivors and 5% deaths due to HIE. The most common complications were of acute kidney injury (34%) and seizures (11.4%). Conclusion: Resistive index was found to be a good prognostic factor for neonatal outcome in cases of hhypoxic-ischemic encephalopathy. It will help in counselling, education of parents about early morbidities, about expected long term sequelae and need for follow up. Also colour Doppler can be a useful and safe diagnostic tool to assess the degree of HIE in neonates.

Keywords---resistive index, hypoxic ischemic encephalopathy, term neonates, neonatal morbidity, colour doppler cranial ultrasound.

Introduction

The incidence of HIE in the developed countries is 1.5 per 1000 live births whereas it is higher in developing countries and around 26.5 per 1000 live births.[1] Highly sensitive techniques like neuroimaging are not easily available as they are expensive and also require experts to report who may not be available in all hospitals. Hence, there is a need for an easily available, objective, non invasive, point of care transcranial doppler ultrasonography based prognostic tool that can predict neonatal morbidities at the earliest.[1] Birth asphyxia is one of the most important causes of hypoxic-ischemic brain injury in term neonates. Correct assessment of the degree of asphyxia is important for planning optimum treatment and prevent brain damage. Various modalities of imaging are available like computed tomography (CT), magnetic resonance imaging (MRI), spectroscopy, and ultrasound exam of brain to assess the effect of asphyxia and to prognosticate the neurodevelopmental milestones which may be delayed and detected at later stage of life. A good noninvasive method that can be carried out at bedside is the Doppler test which is convenient for the parents and comfortable for the newborn too.[2]

Survivors of severe hypoxic-ischemic encephalopathy (HIE) may have life long disabilities of cerebral palsy, epilepsy; and a large majority of infants with moderate HIE have cognitive problems, which affect quality of life.[3]. Hypoxic ischemic encephalopathy (HIE), in its immediate effects has a death rate of 15-20% and among the survivors almost 25% develop permanent neurological deficits.[1]. Almost 35-85% of infants who experienced birth asphyxia undergo injury to the deep nuclei in the cerebrum and end up having poor neurologic outcome. Applying color Doppler sonography during this early period to check the brain perfusion provides information that correlates with reperfusion injury.[1]

More severe brain injury is observed in HIE neonates with higher levels of cerebral blood flow measured at 12-24 hr of life, attributable to reperfusion injury. The more severe the HIE, more is the risk of poor neonatal outcome and early morbidities like death before discharge, acute kidney injury, seizures, coagulation derangements, prolonged NICU stay, liver dysfunction, bone marrow

dysfunction, cardiac and respiratory dysfunction, sepsis and shock [4] American Academy of Neurology and Practice Committee of the Child Neurology Society has recommended that the measurements of resistive index (RI) and end diastolic flow velocity (EDFV) in the anterior cerebral artery are to be performed in order to assess cerebral perfusion and early prediction of outcome.[5]

Studies from developed countries have observed decreased cerebral RI to differentiate asphyxiated neonates from healthy controls and this can be used to predict the risk of future neurodevelopmental impairment.[6] Transcranial Doppler (TCD) Ultrasonography is a noninvasive technique and does not use any ionizing radiation. TCD uses the acoustic windows present in the skull to assess the intracranial vascular structures. Some difficulties or contraindications for TCD are lack of sonographic window for evaluation and also restless patients who cannot remain still during the TCD examination procedure.[7] In neonates with perinatal depression, TCD is a good tool for early and initial assessment, monitoring, for selection of treatment and to prognosticate outcomes. Major concern of perinatal hypoxia is the development of permanent neuromotor disability, which can be reduced by early prognostication by using transcranial Doppler ultrasonography, counselling, intervention and management. In the present study we have tried to determine Doppler changes in anterior cerebral artery of neonates with perinatal hypoxic insult and to evaluate early outcome in HIE neonates.

Aim and objectives of the study

Role of resistive index value evaluated by color Doppler transcranial ultrasonography in Hypoxic Ischemic Encephalopathy (HIE) Neonates within 72 hr of life in predicting early morbidities and to evaluate cranial ultrasound findings in HIE**.**

Materials and Methods

A prospective observational study done in tertiary neonatal intensive care unit of north Karnataka region. The study was conducted between September 2021 to May 2022. The inborn neonates with ≥ 37wk period of gestation and history of having not cried at birth, or APGAR score ≤ 5 at 5 minor need for PPV for ≥ 1min admitted to NICU within 72 hours of life were included. Neonates with evidence of HIE based on Modified Sarnat and Sarnat classification. **-** Outborn neonates, neonates with major congenital malformation and neonates with severe illness and unstable vitals were excluded. At the time of enrollment for study, written informed consent was taken from parents. Detailed clinical history and clinical examination findings were noted for all the cases. Modified Sarnat and Sarnat [8, 9| scoring was done for HIE staging and the neonates were grouped into mild HIE, moderate HIE, and severe HIE. Using Sonosite ultrasound device, transcranial doppler ultrasound examination was done using curvilinear (8-5MHz) and linear probes (8-4MHz) with neurosonography settings for the enrolled neonates within 72 hour of life.

In all subjects, cerebral blood flow parameters of RI was measured in right and left anterior cerebral artery (ACA) located in front of the genu of corpus callosum.

Imaging of ACA was done bilaterally on parasagital plane through anterior fontanel. RI value between 0.56 to 0.80 was considered normal and RI value of <0.56 and >0.80 was considered abnormal. Other cranial ultrasound findings of HIE were also evaluated at the same time. Transcranial Doppler ultrasound was performed by Fellow in Neonatology, Senior Pediatrician and findings were confirmed by Radiologist. All the neonates were assessed for early morbidities like death before discharge, seizure, AKI, sepsis, shock, abnormal neurological findings. All enrolled neonates received standard respiratory, hemodynamic and other supportive care as per the unit protocol.

Statistical analysis

The data was entered in a Microsoft Excel sheet, and results were as counts and percentages.

Observations and Results

A total of 44 neonates with HIE were studied. There were 26 (61%) male and 18 (39%) female babies. According to Sarnat and Sarnat grading of HIE, there were 28 cases with grade I, 6 cases with grade II and 10 cases with grade III HIE.

Table 1
The Resistive Index distribution (n=44)

Resistive Index	No. of patients	Percent (%)
Right ACA		
< 0.56	10	22.7%
0.56 to 0.80	30	68.1%
>0.80	4	9.0%
Left ACA		
< 0.56	12	27.2%
0.56 to 0.80	30	68.1%
>0.80	2	4.5%

The Resistive index was normal in 30 (68.1%) cases and was abnormal in 14 (31.8%) cases. All these 14 cases with abnormal RI had grade II and III of HIE of Modified Sarnat and Sarnat satging.

Table 2
Cranial Ultrasound findings

Ultrasound findings	No. of patients	Percent (%)
Normal	29	65.9%
Increased periventricular density	8	18.1%
Intraventricular hemorrhage	3	6.8%
Increased echodensity of cerebral parenchyma	11	25%

Table 3
Neonatal Immediate Outcome

Neonatal outcome*	No. of patients	Percent (%)
Survivors	42	95.4%
Death	2	4.5%
Improved	26	59.0%
Acute kidney injury	15	34.0%
Seizures	5	11.3%
Coagulopathy	3	6.8%
Sepsis	2	4.5%
Shock	3	6.8%
Prolonged NICU stay	7	15.9%

*The findings are not mutually exclusive and more than one finding was present in given patient.

Outcome

It was observed that among the 44 neonates with HIE, 95.5% survived and 4.5% had mortality. Most common acute complication was of acute kidney injury seen in 34% cases, followed by seizures seen in 11.3% cases. Both the deaths occurred in the HIE III grade.

Discussion

Hypoxic-ischemic encephalopathy (HIE) occurs in asphyxiated preterm or term neonates with high mortality in the early neonatal period. The focus is on new imaging and biomarkers for early recognition, treatment, and appropriate neuroprotection of high-risk term and premature infants.[10] Perinatal asphyxia, causes hypoxia and ischemia leading to loss of normal cerebral autoregulation and diffuse brain injury which depends on the severity of hypotension and the degree of brain maturation, ie whether the baby is preterm or term. The myelinated areas are more metabolically active and hence, more susceptible to HIE.[11] In the present study, a total of 44 cases of HIE were studied with a male to female ratio of 1.4:1 which is similar to the study by Likhitha et al [12] wherein there were 50 neonates with HIE with M:F ratio was 1.6:1and Jain H et al [13] wherein there were 40 cases of HIE with M:F ratio of 1.5:1. However, they had studied the RI in renal blood flow vessels.

Resistive Index

Sonography is sensitive for the detection of hemorrhage, periventricular leukomalacia, and hydrocephalus. RI of the middle cerebral arteries, is a good index and give additional information on HIE severity. In severe HIE there is loss of autoregulation which causes increased RI. [11] In the present study, RI was normal in 30 (68.1%) cases and was abnormal in 14 (31.8%) cases whereas Kumar AS et al [14] in their study on prognostic value of RI in neonates with HIE had a population of 50 neonates of which 25 (50%) had abnormal resistive index (<0.56 or >0.80). Jain H et al [13] in their study observed lower Resistive index values in asphyxiated infants, more so in grade II and III of HIE and concluded

that Colour Doppler USG is of practical importance in evaluating the cerebral blood flow velocity in neonate with HIE. In our study, all 14 cases with abnormal RI correlated with grade II and III of HIE of Modified Sarnat and Sarnat satging. The findings of our study correlated with the study by Barseem et al [3] wherein 48.5% cases showed normal findings, 10% showed intraventricular hemorrhage, 20% showed increased periventricular density and 22.5% showed increased parenchymal echogenicity.

Conclusion

Resistive index was found to be a good prognostic factor for neonatal outcome in cases of hhypoxic-ischemic encephalopathy. It will help in counselling, education of parents about early morbidities, about expected long term sequelae and need for follow up. Also colour Doppler can be a useful and safe diagnostic tool to assess the degree of HIE in neonates.

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