

Comparison Between Transcranial Ultrasound And Magnetic Resonance Imaging In The Evaluation Of Neonatal Hypoxic-Ischemic Encephalopathy

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Received: 10-04-2022 / Revised: 15-05-2022 / Accepted: 05-06-2022

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Conflict of interest: Nil

Abstract

Background: Hypoxic-ischemic encephalopathy (HIE) is the condition that is diagnosed based on specific clinical findings of profound acidosis, poor Apgar score (0–3) at birth, seizure, coma, hypotonia, and multi-organ dysfunction and it is the most common cause of cerebral palsy. The essential role of neuroimaging in the evaluation of the early cerebral injury in neonatal encephalopathy (NE) is to establish the time, severity, extent, location, and pattern of injury, and the probable neurological outcome. Ultrasound is an ideal screening modality in the neonate because it is widely available, non-ionizing, painless, and no need for sedation or intravenous contrast. Magnetic Resonance Imaging (MRI) is the most sensitive and specific imaging technique for examining infants with suspected HIE of the brain. MRI can demonstrate better soft-tissue contrast differentiation, the exact extent, and site of brain injury.

Aim: The goal of this study is to compare the Transcranial ultrasound (TCUS) with MRI in the evaluation of HIE in neonates.

Methods: This is an observational cross sectional study conducted in the Department of Radiology, Silchar Medical College and Hospital, Silchar for one year from 1st of June 2019 to 30th of May 2020. Forty-nine neonates with HIE have undergone TCUS and MRI brain examinations, and the findings were compared using suitable statistical methods.

Result: Out of 49 HIE cases, MRI detected basal ganglia-thalamus injury in 23 (46.9%), cortex and subcortical white matter predominant in 14 (28.6%), white matter injury in 5 (10.2%), Germinal matrix hemorrhage (GMH) in 4 (8.2%), and mixed pattern in 2 (6.1%). Out of 49 HIE cases; TCUS was positive in 46 cases. The overall sensitivity of the TCUS in comparison with MRI was 93.87% in the evaluation of HIE.

Conclusions: Hypoxic-ischemic encephalopathy (HIE) following birth asphyxia is the most common cause of neonatal encephalopathy (NE) that is associated with high mortality and morbidity. The main role of neuroimaging in the evaluation of HIE is to establish the time, severity, extent, location, and pattern of injury, and the probable neurological sequelae. TCUS is an ideal screening modality in the neonate, which can be performed at the bedside without sedation, and

suitable for follow-up. MRI is the most sensitive and specific imaging technique for examining infants with suspected HIE.

Keywords: Hypoxic-ischemic encephalopathy (HIE), Transcranial ultrasonography (TCUS), magnetic resonance imaging (MRI), germinal matrix hemorrhage (GMH), periventricular leukomalacia (PVL)..

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Introduction

HIE is the most common cause of Neonatal Encephalopathy (NE)[1]. Hypoxic-ischemic encephalopathy (HIE) is the condition that is diagnosed based on specific clinical findings of profound acidosis, poor Apgar score (0–3) at birth, seizure, coma, hypotonia, and multi-organ dysfunction and it is the most common cause of cerebral palsy[2]. Approximately 20% and 50% of newborn infants with HIE die during the newborn period. Among the survivors, as many as 25% exhibit permanent neurologic damage that is typically manifested as cerebral palsy, mental retardation, or seizures[3].

The pattern of injury depends on the maturity of the brain, period, and severity at the time of insult[4]. Early detection of cerebral injury in NE has a very important role in neuro-protective interventions, particularly induced hypothermia, and prognosis of the diseases. Therapeutic hypothermia, when initiated within 6 hours of perinatal asphyxia, increases infant survival and reduces the incidence of disability, cerebral palsy, and developmental delays[5,6].

The essential role of neuroimaging in the evaluation of the early cerebral injury in NE is to establish the time, severity, extent, location, and pattern of injury, and the probable neurological outcome[7].

Ultrasound is an ideal screening modality in the neonate because it is widely available, non-

ionizing, no pain, and no need for sedation or intravenous contrast. Transcranial ultrasound (TCUS) can be performed at the bedside, suitable for screening and follow-up[8]. Transcranial ultrasound (TCUS) is sensitive for the detection of hemorrhage, periventricular leukomalacia (PVL), and hydrocephalus. Doppler interrogation and the assessment of resistive index (RI) provide additional information on cerebral perfusion. Normally, the RI decreases with increasing gestational age, and thus correlation with gestational age is necessary for accurate interpretation of RI results[9].

However, TCUS is operator-dependent and less sensitive to structural abnormalities in the cerebral convexity and the brainstem[10]. Parenchymal abnormalities, such as PVL and cerebral edema, identified at TCUS are also often nonspecific[11].

Magnetic resonance imaging is the most sensitive and specific imaging technique for neonatal brain examination with HIE. The soft tissue contrast differentiation, the exact extent, and site of brain injury can be displayed by MRI[12]. Diffusion-weighted MR imaging (DWI) and MR spectroscopy (MRS) provide further insight into HIE and the potential for possible therapeutic intervention[11]. DWI performed with apparent diffusion coefficient (ADC) maps between 24 hours and 8 days of life is more sensitive for the detection of cytotoxic edema, as it reveals restricted

diffusion earlier than the signal intensity abnormalities evident on conventional T1- or T2-weighted image[12]. Magnetic resonance spectroscopy provides a gross biochemical analysis of the “compromised anaerobic” cerebral tissues, as it reveals changes in the concentrations of lactate, choline, creatine, N-acetylaspartate (NAA), and glutamine. Elevated lactate and diminished NAA concentrations are common findings in infants with late neurologic sequelae[13]. However, MRI cannot be used for screening purposes. MRI evaluation is not possible in hemodynamically unstable neonates due to prolonged examination time and the need for sedation.

The aim of the study was to establish a statistical breakdown of neonatal encephalopathy with respect to gestational age, sex, and etiology, to evaluate the diagnostic accuracy of the role of MRI and TCUS in the evaluation of HIE, to evaluate the advantages and disadvantages of each imaging modality for evaluating HIE.

Methods and materials:

It was an cross-sectional study carried out in the Department of Radiology, Silchar Medical College and Hospital, Silchar for one year from 1st of June 2019 to 30th of May 2020 consisting of 49 neonates with HIE. The sample size was calculated using sample size formula of $= [z^2 * p(1-p)] / e^2 / 1 + [z^2 * p(1-p)] / e^2 * N$. Approval from the ethical committee was taken for the study. In all the cases thorough history was taken and physical examination was done and informed consent was obtained from the parents before commencing the investigation. In all the cases trans-cranial ultrasound (TCUS) and MRI examinations were done.

Transcranial ultrasound study (TCUS) was performed using a **SAMSUNG RS80A PRESTIGE** in a warm environment to avoid hypothermia with a linear probe (3-12 MHz) transducer and a curvilinear array probe (1-7

MHz). The images were obtained through the anterior fontanelle (AF), posterior fontanelle (PF), temporosquamous fontanelle, and mastoid fontanelle.

Magnetic Resonance Imaging (MRI) evaluation was carried out on a **SIEMENS TIM AVANTO 1.5T SCANNER** using a head coils under supervision. Scanning was done in the axial, coronal, and sagittal planes. Sequences used were T1WI, T2WI, Fluid attenuation inversion recovery (FLAIR), GRE in all patients and Proton density (PD), Post Gadolinium T1WI, susceptibility-weighted imaging (SWI), Diffusion-weighted imaging (DWI), Apparent diffusion coefficient mapping (ADC Map), Multivoxel MR Proton Spectroscopy (MRS), 3D Spoiled Gradient Recalled (SPGR) sequence. The procedure and duration of the examination were explained in understandable terms to the parents and informed consent taken. Babies were checked for MR imaging contraindications, wrapped with a warm cloth, and positioning is done inappropriate supine position. The sedation was done with a slow intravenous bolus dose (2-5mg/kg) of Propofol. Atropine in a dose of 0.02 mg/kg was used to prevent oropharyngeal secretion.

Chi-square test and Fisher Exact test were done using statistical package for the Social Sciences (SPSS IBM) version 20. Microsoft Word and Excel were used to generate tables. The sensitivity and specificity calculations were done using MedCalc’s Diagnostic test evaluation calculator.

Inclusion criteria:

1. All cases of suspected perinatal cerebral injury.
2. All hemodynamically stable neonates with a clinical diagnosis of neonatal encephalopathy referred to the department of Radiodiagnosis for neuroimaging studies.
3. Neurologically abnormal in the first 48 hours of life, with abnormalities of tone

with or without convulsions and altered consciousness.

4. Fetal distress, diagnosed in the presence of cardiocotographic abnormalities of bradycardia (<100/minutes) with or without meconium stained liquor and with low Apgar scores and the necessity for resuscitation.

Exclusion criteria:

1. Hemodynamically unstable patients.
2. General contraindication of MRI examinations.
3. Parent's refusal.

Result:

Out of the 49 HIE cases 31(63.3%) were term and 18 (36.7%) were preterm, and 32 (65.3%) were male and 17 (34.7%) were female.

Central pattern of injury (basal ganglia-thalamus) was more common in term infant, 20 out 23 (87%) than preterm, 3 out of 23 (13%). Whereas peripheral pattern (cortex and subcortical white matter) was more common in preterm 8 out of 14 (57%). Germinal matrix hemorrhage (GMH) were more common in preterm than term, 3 out of 4 (75%).

Table 1: Patterns of HIE in term and preterm infants

Patterns	Term	Preterm	Total
Central pattern (basal ganglia-thalamus, brainstem)	20(87%)	3(13%)	23(46.9%)
Peripheral pattern (cortex and sub-cortical white matter)	6(42.9%)	8(57.1%)	14(28.6%)
GMH	1(25%)	3(75%)	4(8.2%)
White matter injury/PVL	2(40%)	3(60%)	5(10.2%)
Mixed pattern	2(67%)	1(33%)	3(6.1%)
Total cases	31(63.3%)	18(36.7%)	49(100%)



Figure 2: Coronal TCUS showing increased echogenicity involving the thalami and basal ganglia bilaterally in an 11 days old term (38 weeks 1 day) female neonate presents with a history of low

Apgar score, abnormal cord blood pH (6.4), and lethargy suggestive of central grey matter pattern of HIE

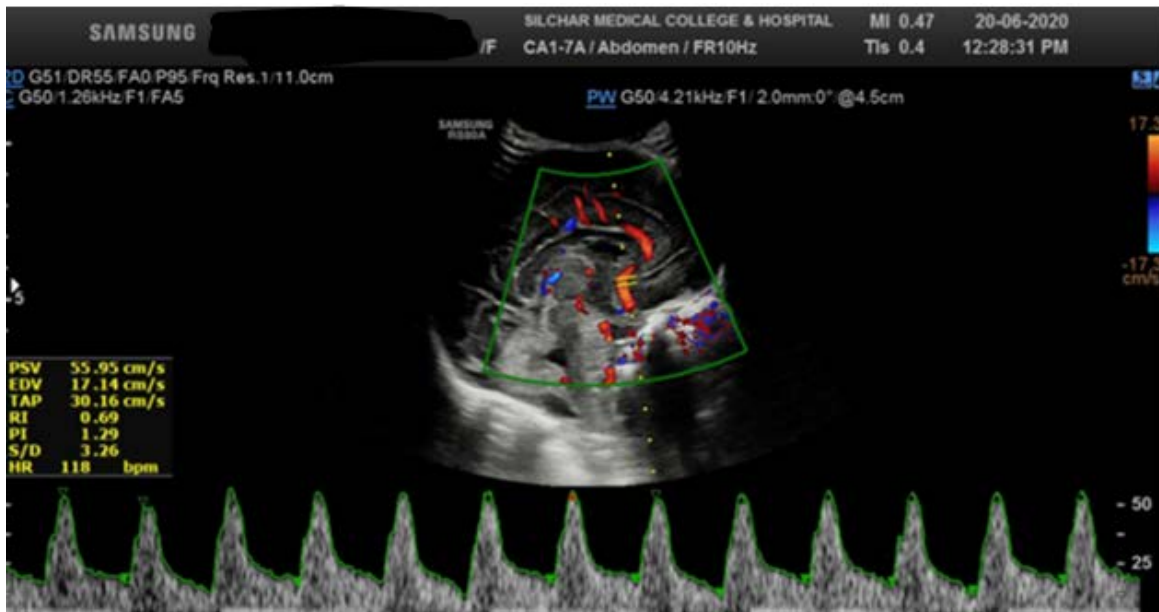


Figure 3: Duplex USG examination of the ACA of the same above patient shows decreased resistive index (RI=0.69) for an infant at this age (expected RI for age = 0.90).



Figure 4: TCUS showing increased periventricular echogenicity in a 5 day old female preterm baby with a history of birth asphyxia suggestive of periventricular leukomalacia.

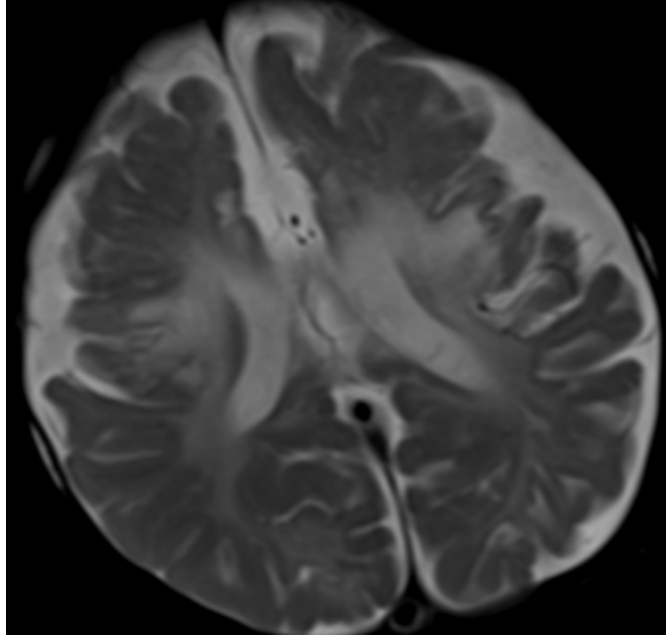


Figure 5: showing T2 hyperintensity involving the bilateral periventricular white matter in the same above-mentioned patients, suggestive of periventricular leukomalacia.

MRI detected involvement of basal ganglia in 40.8%, thalamus in 46.9%, brainstem in 16.3%, cortex in 22.4%, subcortical white matter in 28.6%, watershed zone in 8.2%, GMH in 8.2%, PVL in 10.2%, and mixed pattern in 6.1% out of the 49 HIE cases. The

sensitivity of TCUS in the detection of the site of involvement in HIE were as follows: basal ganglia 80%, thalamus 86.95%, cortex 63.6%, subcortical white matter 71.4%, watershed zone 50%, GMH 100%, and periventricular leukomalacia (PVL) 60%.

Table 2: Comparison of MRI and TCUS findings in HIE

Findings	MRI		TCUS		
	Positive	Negative	Positive	Negative	Sensitivity
Basal ganglia	20	29	16	33	80%
Thalamus	23	26	20	29	86.95%
Brainstem	8	41	3	46	37.5%
Cortex	11	38	7	42	63.6%
Sub-cortical white matter	14	35	10	39	71.4%
Watershed zone	4	45	2	47	50%
GMH	4	45	4	45	100%
PVL	5	44	4	46	60%
Mixed pattern	3	46	3	46	100%



Figure 6: A 25 days old male preterm (34 weeks) neonate presents with a history of birth asphyxia showing multi-cystic changes with volume loss noted in the bilateral parietal region on coronal TCUS image, suggestive of cystic encephalomalacic changes due to severe peripheral pattern of HIE.

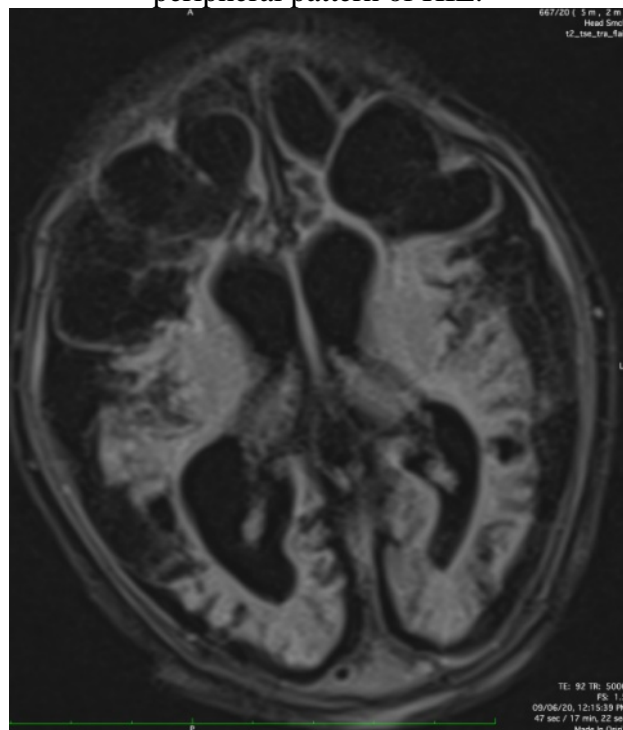


Figure 7: Axial FLAIR MR images showing cystic encephalomalacia involving the bilateral cerebral hemisphere with volume loss and compensatory ventriculomegaly of the same above mentioned patient.



Figure 8: Axial TCUS Images showing expansile hyperechoic focus involving the bilateral caudothalamic grooves (CTG) (right more than left) without intraventricular extension in a 4 days old preterm (34 weeks 5 days) female baby present with a history of birth asphyxia, suggestive of Grade I Germinal Matrix Hemorrhage (GMH).

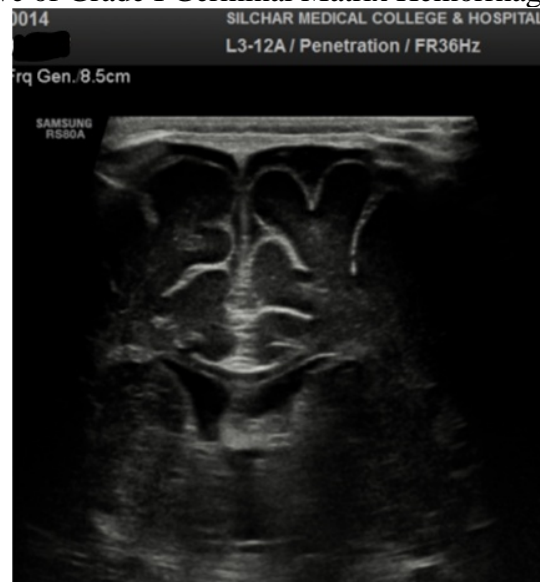


Figure 9: Axial TCUS showing left side GMH with intraventricular extension causing foramen of Monro obstruction resulting in mild dilatation of the bilateral frontal horns in 6 days old, preterm (35 weeks 5 days) infant presents with history of birth asphyxia, delayed cry at birth, unable to breastfeed, and decrease tone. This is a case of grade III Germinal Matrix Haemorrhage.

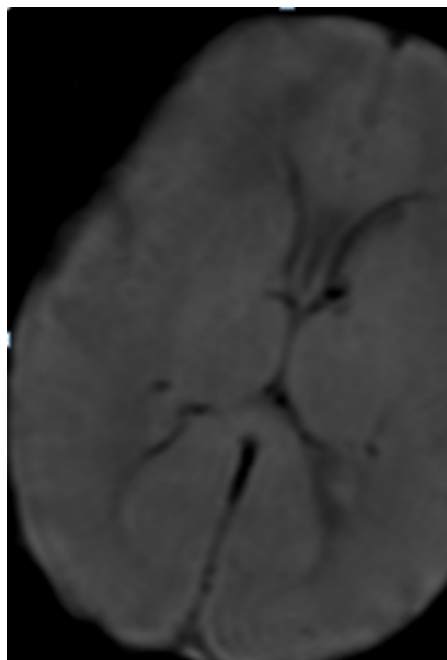


Figure 10: Axial SWI MR image showing blooming focus involving the left caudothalamic groove with ventricular extension, suggestive of GMH.

Out of the 49 HIE cases; the number of diffusion restricted cases was 34. TCUS was positive in 30 cases and negative in 19 cases. On the correlation with DWI, the overall

sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were 88.2%, 100%, 100%, 78.95%, and 91.84%, respectively.

Table 3: Comparison between DWI and TCUS findings

DWI	TCUS		Total
	Negative	Positive	
Negative	15	0	15
Positive	04	30	34
Total	19	30	49

Out of the 47 MRS positive cases, TCUS was positive in 42 and negative in 7 cases. The sensitivity and specificity of the TCUS on

correlation with MRS were 89.4% and 100%, respectively. PPV, NPV, and diagnostic accuracy were 100%, 28.6% and 89.8%, respectively.

Table 4: Comparison between MRS and TCUS findings

MRS	TCUS		Total
	Negative	Positive	
Negative	02	0	02
Positive	05	42	47
Total	07	42	49

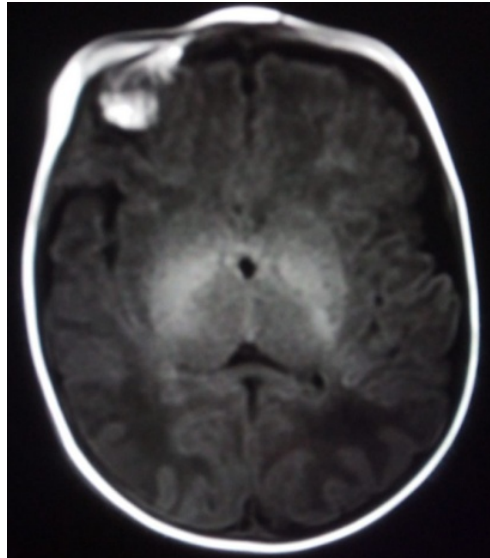


Figure 11: Showing T1 hyperintensity involving the bilateral basal ganglia in 6 days old preterm male baby, suggestive of central pattern of HIE.

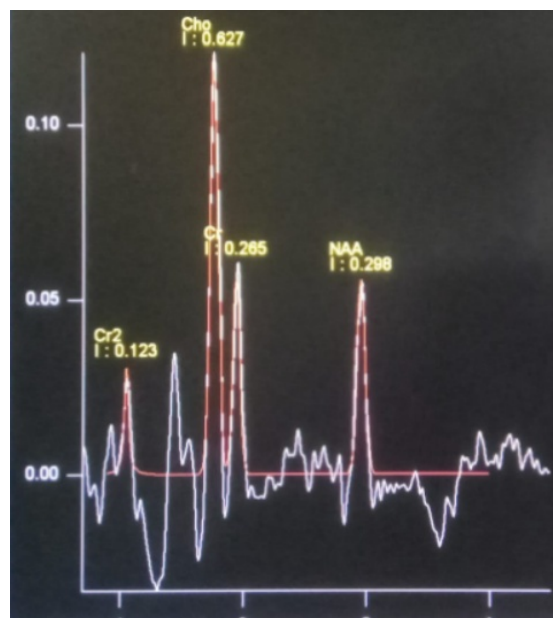


Figure 12: Magnetic resonance spectroscopy (MRS) image of the basal ganglia showing low levels of N-acetylaspartate (NAA) in the above-mentioned same patient.

Discussion:

Gestational age distribution

In the present study, out of 49 HIE cases, 31(63%) were term and 18 (37%) were preterm. Genedi et al[14] in a study of 38 neonatal encephalopathy cases, 25 (65.8%) were full-term and 13 (34.2%) were

preterm. The study conducted by Bhagat H et al[15] demonstrated out of 101 cases, 61.4% (62) were term and 38.6% (39) were preterm. The present study correlates with the previous studies mentioned above shown that the percentage of HIE is more in term than preterm.

Gender distribution

In the present study, out of 49 HIE cases, 32 (65.3%) were male and 17 (34.7%) were female. Bhagat H et al[15] in their study of 101 NE cases, 63 (62.4%) were males and 38 (37.6%) were females. Jose et al[16] in the study of 30 newborns with HIE, 19 (63.3%) were male and 11 (36.7%) were female. The present study and the other previous studies have shown that the frequency and percentage of HIE are more in males than females.

Pattern of HIE distribution

In the present study, out of 49 HIE cases, central pattern (basal ganglia-thalamus) injury was found in 23 (46.9%), peripheral pattern (cortex and subcortical white matter predominant) in 14 (28.6%), white matter injury in 5 (10.2%), GMH in 4 (8.2%), and mixed pattern in 2 (6.1%). The study conducted by Genedi et al[14], revealed out of 38 HIE cases the central pattern of injury was detected in 16 cases (42.5%) and white matter injury in 4 cases (10.5%), mixed pattern in one case (2.6%) and the other 2 cases (5.2%) elicited GMH. The present study is in conformity to that of Genedi et al[14] with respect to pattern of distribution of HIE

Comparison of pattern of HIE in term and preterm

The current study shows, in term infants central pattern of injury is 87% (20/23), peripheral pattern 42.9% (6/14), white matter injury 40% (2/5), mixed pattern 67% (2/3) and GMH 25% (1/4) whereas in preterm infant's peripheral pattern 57.1% (8/14), GMH 75% (3/4), white matter injury 60% (3/5), and mixed pattern 33% (1/3). Jose et al[16] in the study of 30 HIE cases found central pattern of injury in 50% of term neonates and 87.5% of babies with periventricular leukomalacia are preterm. Intracranial hemorrhage was seen in 7.4% of the neonates and all of them were preterm. Bhagat H et al[15] in a study of 101 HIE cases, the term infants had predominant central pattern of injury and preterm infants had a peripheral pattern of involvement. So, the

present study, Bhagat H et al (2017)[15] and Jose et al (2017)[16] shown that the central pattern of injury is more common in term infants than the preterm, whereas the peripheral pattern and GMH are more common in preterm than term infants.

Comparison of MRI and TCUS findings in HIE

In the present study, in correlation with MRI, the sensitivity of TCUS for detecting thalamic, basal ganglia and periventricular white matter, brain stem, cerebral cortex, and subcortical white matter lesions, watershed zone, GMH, and Mixed pattern was as follows 86.95%, 80%, 60%, 37.5%, 63.6%, and 71.4%, 50%, 100%, and 100%, respectively. Genedi et al[14] in their study of 38 neonates with HIE, the sensitivity of TCUS for detecting thalamic, basal ganglia, and periventricular white matter lesions, the corpus callosum, brain stem, cerebellar white matter, cerebral cortex, and subcortical white matter was 88.2%, 81.2%, 80%, 37.5%, 33.3%, 33.3%, 28.6%, and 50%, respectively. The present study and Genedi et al.[14] suggest that TCUS had better sensitivity for detecting the central pattern of abnormalities in HIE rather than the peripheral pattern of lesions. In the present study and Genedi et al.[14] the sensitivity of TCUS in the detection of GMH was 100%.

Comparison between DWI and TCUS findings

In the current study on the correlation with DWI, the overall sensitivity, specificity, PPV, NPV, and diagnostic accuracy of the TCUS were 88.2%, 100%, 100%, 78.95%, and 91.84%, respectively. Aun AE et al[17] in their study of 36 NE cases, the sensitivity, specificity, PPV, NPV, and diagnostic accuracy in correlation with MRI Diffusion were as follows 80.65%, 80%, 96.15%, 40%, and 80.56%, respectively (P-value=0.015). So, the current study is not matching with study conducted by Aun AE et al[17].

Comparison between MRS and TCUS findings

Out of the 47 MRS positive cases, TCUS was positive in 42 and negative in 7 cases. The sensitivity and specificity of the TCUS on correlation with MRS were 89.4% and 100%, respectively. PPV, NPV, and diagnostic accuracy were 100%, 28.6% and 89.8%, respectively. Aun AE et al[17] in their study of 36 NE cases, the sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 81.3%, 100%, 100%, 40%, and 83.33%, respectively (P-value=0.004). The present study conforms with that of Aun AE et al[17].

Conclusion:

TCUS is an ideal screening modality in the neonate. It can be performed at the bedside without sedation, and suitable for follow-up. It has good sensitivity for the detection of hemorrhage, and periventricular leukomalacia (PVL). The Duplex ultrasound provides additional information on cerebral perfusion. However, TCUS is operator dependent and less sensitive to abnormalities located in the cerebral convexity and the brainstem. MRI is the most sensitive and specific imaging technique for examining infants with suspected HI due to its better soft-tissue contrast differentiation and it can demonstrate the exact extent, and the site of brain injury. Diffusion-weighted (DWI) MR imaging and MR spectroscopy (MRS) provide additional information in HIE and the potential for possible therapeutic intervention.

Acknowledgements: The authors would like to thank the Department of Paediatrics, Silchar Medical College & Hospital, Assam, India for referring cases of HIE from indoor and outdoor services.

Funding: No funding source

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