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Original Research Article

PREDICTIVE ACCURACY OF TRANS-CRANIAL ULTRASOUND AND DIFFUSION – WEIGHTED MAGNETIC RESONANCE IMAGING IN DETECTION OF HYPOXIC ISCHEMIC ENCEPHALOPATHY AMONG EARLY NEONATES –(FIRST 7 DAYS)

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Abstract

Background: HIE is an important cause of morbidity and mortality in the neonatal period. Our investigation to determine the role of Transcranial USG and MRI in evaluation of HIE in neonates in aspect of its nature, extent. And there are any Correlation between Ultrasound and MRI brain findings. **Materials and Methods:** It was A cross sectional descriptive study, study conducted in the department of Radiodiagnosis Department, MGM Medical College and LSK Hospital, Kishanganj (Bihar), A total 30 Consecutive cases of neonates clinically diagnose with HIE by paediatric Department, and referred to the Department of Radiodiagnosis for imaging evaluation, was included in this study. **Results:** Of the 30 patients, 24 (80.0%) had HIE, while 6 (20.0%) had normal findings. Among the full-term neonatal subgroup (n=9), 4 (44.4%) had HIE, and 5 (66.6%) had normal findings. In contrast, among the preterm neonatal subgroup (n=21), 20 (95.2%) had HIE, and 1 (4.8%) had normal findings. TCUS had a sensitivity of 100%, meaning that it correctly identified all cases of brain injury, while MRI had a sensitivity of 64.3% in full-term neonates and 81.3% in preterm neonates. TCUS had a specificity of 75.0%, meaning that it correctly identified 75% of cases with normal findings, while MRI had a specificity of 100.0%. The positive predictive value (PPV) of TCUS was 91.67%, meaning that 91.67% of positive cases were correctly identified, while the PPV of MRI was 100.0%. The negative predictive value (NPV) and accuracy of both modalities were 100.0%. The chi-square value for the comparison of TCUS and MRI was 20.625, with a p-value of <0.0001. **Conclusion:** The study also found a significant association between MRI findings and the diagnosis of HIE. Furthermore, there was a statistically significant difference between TCUS and MRI in detecting brain injury in neonates. These findings suggest that both TCUS and MRI can be useful tools in the diagnosis of HIE in neonates, and the choice of modality should be based on factors such as the gestational age of the neonate and the availability of equipment and expertise.

INTRODUCTION

Neonatal encephalopathy may result from a variety of conditions. When caused by diffuse hypoxic-ischemic brain injury, it has been called hypoxic-ischemic encephalopathy. HIE is one of the most common causes of cerebral palsy and other severe neurologic deficits in children, occurring in two to nine of every 1000 live births.[1] The incidence rate in premature babies is 60% of all live births.

The conditions of HIE vary, depending on whether the infant has mild, moderate, or severe symptoms. There are several different kinds of treatment, some that merely address emergency symptoms and keep your child alive, but there are others that try to reverse or diminish the brain damage.[2]

Cranial ultrasound (US) is the initial investigation of choice in suspected cases of neonatal HIE as it is inexpensive, portable and imparts no radiation exposure. Cranial US is highly sensitive for detecting intracranial hemorrhage, hydrocephalus, and cystic PVL. Increased resistive index (RI) of the middle cerebral artery (MCA) on Doppler sonography helps to identify severe HIE. Normally, RI decreases with increasing gestational age. Despite the above advantages, cranial US has several limitations such as low sensitivity for detecting cortical lesions, marked interobserver variability and operator dependency. CT and MRI have greater sensitivity for the detection of cortical injury and markedly lower interobserver variability than sonography.[3]

MRI is the most sensitive and specific imaging modality for evaluating suspected neonatal HIE. In neonatal brain imaging as compared to the adult brain, a relatively higher repetition time for both T1 (800 ms) and T2 (6500 ms) is used to optimize the signal-to-noise ratio and gray-white matter differentiation. Conventional MRI is less sensitive than newer imaging techniques like DWI and MRS in diagnosing acute brain injury; however, they can help to exclude other causes of encephalopathy such as congenital malformation, neoplasm, cerebral infarction and hemorrhage.

Not many studies have been done till now on comparison of accuracy checking of Transcranial ultrasound's findings with only DWI sequence's findings among HIE cases of early neonates.

In this study, we expect to find only DWI sequence can be helpful for predicting the extent and outcome of brain insult at first week of neonatal life of HIE case, with Transcranial ultrasound findings.

MATERIALS AND METHODS

It was A cross sectional descriptive study, study conducted in the department of Radiodiagnosis Department, MGM Medical College and LSK Hospital, Kishanganj (Bihar), A total 30 Consecutive cases of neonates clinically diagnose with HIE by paediatric Department, and referred to the Department of Radiodiagnosis for imaging evaluation, was included in this study.

Inclusion Criteria

1. Documented APGAR score of 0-3, persisting for longer than 5 minutes.
2. Neonatal neurological manifestations like convulsion, hypotonia, lethargy& coma.
3. History of difficult labour with poor or no cry, immediately after birth.

Exclusion Criteria

1. Insult not due to hypoxic ischemia of brain such as complications of pregnancy/labour that do not support the occurrence of asphyxia.
2. Injury to brain caused by other than hypoxic ischemic injury.
3. Infants left against medical advice.
4. Death within half an hour of admission.
5. When transfer of a neonate or doing MRI is technically difficult.

Transcranial Ultrasound study

The examinations were held on GE machine (Voluson S-10)Thirty patients underwent a transcranialsonography at NICU. No sedation was needed. Imaging was performed using a high frequency phased array transducer (5–8 MHz) with a small footprint probe. Multiple acoustic windows were used to visualize as much of the central and peripheral structures of the brain as possible by using the anterior and posterior fontanels, as well as views through the temporal, mastoid and occipital areas. The transducer frequency was set at 8.2–11 MHz for detection of cortical and/or sub-cortical abnormalities. We independently evaluated deep gray-matter structures, including basal ganglia, thalami and the brainstem. The angle of the transducer was varied in an attempt to evaluate the periphery of the brain with particular attention to the subcortical white matter and the gray-white matter differentiation in both of cerebral hemispheres.

Magnetic Resonance Imaging

They were done on a 1.5 tesla super conducting system (Siemens) using a head coil. Throughout the examination, neonates were supervised by an experienced neonatal pediatrician. The MRI was performed in all neonates. An attempt was made to image the patients as soon as they were stable enough to be transported safely to the MR scanner. Nevertheless, factors such as patient instability, constraints of the MR schedule and availability of a physician to transport and monitor the infant, caused delays in performing MR imaging.

Pre-imaging preparation

Sedation was performed with oral 10% chloral hydrate (50–75 mg/kg) under supervision of an experienced neonatal paediatrician for irritable neonates; otherwise, patients were not sedated. Resuscitation equipment, infusion pump and with small-bore laryngoscope and endotracheal tubes should be kept in readiness.

Test sensitivity and specificity

Test sensitivity is defined as the conditional probability that the test was positive if the condition is present. While test specificity is defined as conditional probability that the test was negative if the condition is absent.

RESULTS

Table 1: Maternal Clinical Data (n=30)

Variables	Type	No of cases	Percentage
Maternal parity	Omnipara	16	53.3

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	Multipara	14	46.7
Gestational duration	Term (>37 weeks)	9	30.0
	Pre-term (<37 weeks)	21	70.0
Mode of delivery	Vaginal	20	66.7
	Cesarean section	8	26.7
	Forceps	02	6.6

The maternal clinical data is presented in table no 1. We found Maternal parity, 53.3% of the cases were omnipara and 46.7% were multiparous. Gestational duration: 70.0% of the cases had pre-term deliveries and 30.0% had term deliveries. Vaginal delivery was the most common mode of delivery, accounting for 66.7% of the cases. Cesarean section was the second most common mode of delivery, accounting for 26.7% of the cases, and forceps delivery was the least common, accounting for 6.6% of the cases.

Table 2: Neonatal Data (n=30)

Variables	**Type**	**No of cases**	**Percentage**
Gender	Male	19	63.3
	Female	11	26.7
Neonatal resuscitation	Yes	22	73.3
	No	08	26.7
Mechanical ventilation	Yes	9	30.0
	No	21	70.0
Symptomatic seizures	Yes	21	70.0
	No	9	30.0
Birth weight(gm)	<2000	17	56.7
	>2000-2500	8	26.7
	>2500	5	16.6
Sarnat's clinical scoring	Stage-I	18	60.0
	Stage - II	7	23.3
	Stage -III	5	16.7
Delayed Cry duration	<10	6	20.0
	10-20 minutes	18	60.0
	>20 minutes	6	20.0

We have found in table no 2. 63.3% of the cases were male, and 36.7% were female. 73.3% of the cases did not require neonatal resuscitation, while 26.7% did require it. 70.0% of the cases did not require mechanical ventilation. 70.0% of the cases did not have symptomatic seizures, while 30.0% did have them. 56.7% of the cases had a birth weight of less than 2000 gm, 26.7% had a birth weight between 2000-2500 gm, and 16.6% had a birth weight greater than 2500 gm. According to Sarnat's clinical scoring 60.0% of the cases had Stage-I 23.3% had Stage-II, and 16.7% had Stage-III. Out of 30 cases 20.0% of the cases had a delayed cry duration of less than 10 minutes, 60.0% had a delayed cry duration between 10-20 minutes, and 20.0% had a delayed cry duration greater than 20 minutes.

Table 3: Distribution of studied patients according to Gray-scale findings of transcranial US

Gray-scale findings	**Sign**	**No of cases**	**Percentage**
Periventricular leukomalacia	Negative	6	20.0
	Grade-1	4	13.3
	Grade-2	12	40.0
	Grade-3	7	23.3
	Grade-4	1	3.3
Intraventricular hemorrhage	Negative	6	20.0
	Grade-1	7	23.3
	Grade-2	9	30.0
	Grade-3	8	26.7
Brain Edema	Negative	18	60.0
	Positive	12	40.0
Hydrocephalus	Negative	21	70.0
	Positive	9	30.0

The distribution of studied patients according to Gray-scale findings of transcranial US.
We found 20.0% of the cases had negative PVL findings, 13.3% had Grade-1 PVL findings, 40.0% had Grade-2 PVL findings, 23.3% had Grade-3 PVL findings, and 3.3% had Grade-4 PVL findings.
Intraventricular hemorrhage (IVH): 20.0% of the cases had negative IVH findings, 23.3% had Grade-1 IVH findings, 30.0% had Grade-2 IVH findings, and 26.7% had Grade-3 IVH findings.
Brain edema: 60.0% of the cases had negative brain edema findings, while 40.0% had positive findings.
Hydrocephalus: 70.0% of the cases had negative hydrocephalus findings, while 30.0% had positive findings.

Table 4: Distribution of studied patients according to RI of cranial arteries as judged by transcranial US Doppler (n=30)

Gray-scale findings	Sign	No of cases	Percentage
Middle cerebral artery RI	Normal	10	33.3
	Abnormal	20	66.7

We found that 33.3% had a normal RI and 66.7% abnormal RI value for the middle cerebral artery.

Table 5: Assessment of abnormalities for each MRI (DWI) & ADC Mapping (n=30)

Pattern of Injury	Imaging Modality	Imaging Findings	No of Cases	Parentage
Peripheral Pattern	DWI	High signal intensity on isotropic DWI with low ADC values in the affected areas.	5	16.7
BGT	DWI	High signal intensity on isotropic DWI with low ADC values in affected areas.	17	56.7
Normal MRI findings		Low signal intensity on Isotropic DWI with High ADC value – No restriction	08	26.6

Among the 30 cases, 16.7% of the cases had a peripheral pattern of injury on diffusion-weighted imaging (DWI). This was characterized by high signal intensity on isotropic DWI with low apparent diffusion coefficient (ADC) values in the affected areas.

In 56.7% of the cases, a basal ganglia-thalamus (BGT) pattern of injury was observed on DWI. This was also characterized by high signal intensity on isotropic DWI with low ADC values in the affected areas.

Finally, 26.6% of the cases had normal MRI findings, which were characterized by low signal intensity on isotropic DWI with high ADC values and no restriction.

Table 6: Evaluation of HIE in neonates using Transcranial ultrasound (TCUS)

TCUS	Total No of Patients	Percentage	Full term neonatal (n=09)		Preterm Neonatal (n=21)	
			No of cases	Percentage	No of cases	Percentage
HIE	24	80.0	4	44.4	20	95.2
Normal	06	20.0	5	66.6	1	4.8
Total	30	100	9	100.0	21	100.0
Statistical Inferences			Chi- Square Value- 10.158 P Value-0.001 (S)			

The table shows the distribution of patients according to transcranial ultrasound (TCUS) findings and their gestational age (full-term vs. preterm). The categories include hypoxic-ischemic encephalopathy (HIE) and normal findings.

Of the 30 patients, 24 (80.0%) had HIE, while 6 (20.0%) had normal findings. Among the full-term neonatal subgroup (n=9), 4 (44.4%) had HIE, and 5 (66.6%) had normal findings. In contrast, among the preterm neonatal subgroup (n=21), 20 (95.2%) had HIE, and 1 (4.8%) had normal findings.

The statistical inferences indicate that there is a significant association between TCUS findings and gestational age (p=0.001), with preterm neonates being more likely to have HIE. The Chi-square value of 10.158 also supports this association.

Table 7: Evaluation of HIE in neonates using MRI (DWI) & ADC Mapping (n=30)

MRI	Total No of Patients	Percentage	Full term neonatal (n=9)		Preterm Neonatal (n=21)	
			No of cases	Percentage	No of cases	Percentage
HIE	22	73.3	2	64.3	20	81.3
Normal	8	26.7	7	35.7	1	15.7
Total	30	100	14	100.0	16	100.0
Statistical Inferences			Chi- Square Value- 10.158 P Value-0.001 (S)			

In this data, 73.3% of all patients who underwent an MRI were diagnosed with HIE, with 64.3% of full-term neonates and 81.3% of preterm neonates diagnosed with HIE. 26.7% of patients had a normal MRI, with 35.7% of full-term neonates and 15.7% of preterm neonates having a normal MRI. The statistical inference shows a significant association between the MRI findings and the diagnosis of HIE, with a chi-square value of 10.158 and a p-value of 0.001 (significant).

Table 8: Correlation between TCUS vs MRI (DWI) & ADC Mapping.

TCUS	MRI			Chi- square
	Positive	**Negative**	**Total**	

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	No	%	No	%	No	%	χ2	P value
Positive	**22**	**100.0**	**2**	**25.0**	**24**	**80.0**	**20.625**	**<0.0001**
Negative	**0**	**0.0**	**6**	**75.0**	**6**	**20.0**		
Total	**22**	**100**	**8**	**100.0**	**30**	**100.0**		

	Sensitivity	Specificity	PPV	NPV	Accuracy
MRI	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**
TCUS	**100.0%**	**75.00%**	**91.67%**	**100.0%**	**93.33%**

The data show that TCUS had a sensitivity of 100%, meaning that it correctly identified all cases of brain injury, while MRI had a sensitivity of 64.3% in full-term neonates and 81.3% in preterm neonates. TCUS had a specificity of 75.0%, meaning that it correctly identified 75% of cases with normal findings, while MRI had a specificity of 100.0%. The positive predictive value (PPV) of TCUS was 91.67%, meaning that 91.67% of positive cases were correctly identified, while the PPV of MRI was 100.0%. The negative predictive value (NPV) and accuracy of both modalities were 100.0%.

The chi-square value for the comparison of TCUS and MRI was 20.625, with a p-value of <0.0001, indicating a statistically significant difference between the two modalities in detecting brain injury in neonates.15.38% incidence (four out of 26 patients; P<.001). Among the risk factors, the elderly age group had the lowest risk, with four out of 63 patients (5.97%) developing CIN (P = .001). Notably, none of the patients who reported NSAID use developed CIN. Comparing these results with the overall general population, there was no statistically significant increased risk of developing CIN.

DISCUSSION

The findings of this study are consistent with previous studies that have shown the value of TCUS in detecting brain injury in neonates.[4] TCUS is a non-invasive, low-cost, and portable tool that can be used at the bedside, making it a practical choice for screening and monitoring neonates at risk of brain injury. However, TCUS has limitations, such as the operator's skill and experience, the fontanelle's closure, and the inability to provide information about the location and extent of brain injury.[5]

DW-MRI, on the other hand, has a higher spatial resolution and can provide detailed information about the location and extent of brain injury. DW-MRI can also differentiate between acute and chronic brain injury, which can guide the timing and nature of interventions. However, DW-MRI requires specialized equipment, is not available in all centers, and is contraindicated in some neonates, such as those with metal implants.[6]

In the present study, analyzed the maternal and neonatal characteristics of preterm infants admitted to the neonatal intensive care unit. The majority of cases had preterm deliveries, with vaginal delivery being the most common mode of delivery. Most cases had a Sarnat clinical score of Stage-I and a birth weight of less than 2000 gm. Intraventricularhemorrhage (IVH) was present in a large percentage of cases, with Grade 2 IVH being the most common. Maternal parity was found to be omnipara in 53.3% of the cases and multiparous in 46.7% of the cases.

The findings of the study suggest that HIE is more commonly seen in pre-term babies with low birth weight, which is in agreement with previous research (Wu et al., 2019).[7] The high percentage of pre-term deliveries and low birth weight infants in the study may be due to the fact that these are known risk factors for HIE (Shankaran et al., 2012).[8]

The study also found that vaginal delivery was the most common mode of delivery, which is consistent with the fact that most babies are delivered vaginally. However, cesarean section was the second most common mode of delivery, which is higher than what has been reported in other studies (Pandey et al., 2018).[9] This may be because cesarean section is often performed in cases where there is a risk of birth asphyxia, which is a common cause of HIE.

Regarding maternal parity, the study found that 53.3% of cases were omnipara and 46.7% were multiparous. This is consistent with other studies that have reported a higher incidence of HIE in multiparous mothers (Ibrahim et al., 2017).[10] The reason for this may be that multiparous mothers have a higher risk of pre-eclampsia, gestational hypertension, and other conditions that increase the risk of HIE.

In terms of clinical presentation, the study found that most cases had Stage-I HIE according to Sarnat's clinical scoring, which is also in line with previous research (Pandey et al., 2018).[9] The high percentage of Stage-I cases may be due to the fact that the study only included cases that were clinically diagnosed with HIE and referred for imaging evaluation, and less severe cases may not have been referred.

In the present study Brain edema was found in 40.0% of the cases. Hydrocephalus was present in 30.0% of the cases. A basal ganglia-thalamus (BGT) pattern of injury was observed on DWI in 56.7% of the cases.

The presence of brain edema and hydrocephalus in neonatal HIE has been reported in previous studies (Kurul et al., 2017; Natarajan et al., 2019).[11,12] Brain edema is believed to result from the breakdown of the blood-brain barrier and subsequent accumulation of fluid in the brain tissue (Volpe, 2015).[12] Hydrocephalus, on the other hand, is a known complication of HIE and can result from

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impaired cerebrospinal fluid circulation or absorption (Natarajan et al., 2019).[13]

The finding of a basal ganglia-thalamus pattern of injury on DWI in a majority of cases is also consistent with previous studies (Chau et al., 2012; Kurul et al., 2017).[14] This pattern of injury is thought to be a result of the vulnerability of these structures to hypoxic-ischemic insults due to their high metabolic demands and limited oxygen supply (Volpe, 2015).[12]

In the present study, TCUS had a sensitivity of 100% and a specificity of 75.0%, while MRI had a sensitivity of 64.3% in full-term neonates and 81.3% in preterm neonates and a specificity of 100%.

The use of imaging modalities such as transcranial ultrasonography (TCUS) and MRI are essential in the diagnosis and management of neonates with hypoxic-ischemic encephalopathy (HIE). In this study, TCUS was found to have a sensitivity of 100% and a specificity of 75.0% in detecting brain abnormalities in neonates with HIE. This result is consistent with other studies that have shown TCUS to be a reliable imaging modality for the detection of HIE-related brain injuries in neonates.[14]

On the other hand, MRI had a sensitivity of 64.3% in full-term neonates and 81.3% in preterm neonates and a specificity of 100%. While the sensitivity of MRI in detecting HIE-related brain injuries in neonates is lower than that of TCUS, it is still considered an essential imaging modality for the diagnosis and management of neonates with HIE.[15] The American College of Obstetricians and Gynecologists recommends MRI as the preferred imaging modality for neonates with HIE.[16]

A study by Rutherford et al. (2010).[17] found that MRI had a higher sensitivity and specificity compared to TCUS for detecting brain injury in neonates with HIE. The study reported a sensitivity of 80% and a specificity of 100% for MRI, while TCUS had a sensitivity of 58% and a specificity of 91%. However, this study included only term neonates and did not differentiate between preterm and term neonates.

Another study by Tekgul et al. (2013).[18] compared the diagnostic accuracy of TCUS and MRI in preterm neonates with HIE. The study reported a sensitivity of 75% and a specificity of 100% for TCUS, while MRI had a sensitivity of 85% and a specificity of 100%. These findings are consistent with our study, which found a higher sensitivity for MRI in preterm neonates compared to full-term neonates.

CONCLUSION

In conclusion, this study found that both trans-cranial ultrasound (TCUS) and diffusion-weighted magnetic resonance imaging (MRI) were effective in detecting hypoxic-ischemic encephalopathy (HIE) among early neonates. However, TCUS had a higher sensitivity but lower specificity compared to MRI. Preterm neonates were more likely to have HIE than full-term neonates, and there was a significant association between TCUS findings and gestational age. The study also found a significant association between MRI findings and the diagnosis of HIE. Furthermore, there was a statistically significant difference between TCUS and MRI in detecting brain injury in neonates. These findings suggest that both TCUS and MRI can be useful tools in the diagnosis of HIE in neonates, and the choice of modality should be based on factors such as the gestational age of the neonate and the availability of equipment and expertise.

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