Magnetic Resonance Imaging versus Trans-Cranial Sonography in Detection of Cerebral Injuries in Neonatal Hypoxic-Ischemic Encephalopathy

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Abstract
Background: Hypoxic ischemic encephalopathy in neonates is one of the common causes of morbidity and mortality. The clinical presentation and imaging findings are the corner stone in the diagnosis and determination of the severity of NE.
Objectives: Our study was planned to test the function of MRI and TCUS in the early recognition of neonatal HIE cerebral injuries.
Patients and methods: Our study registered 50 newborns presented with HIE manifestations. Brain MRI and TCUS were performed for each case and the results were compared.
Results: MRI findings were positive in 37 cases. The diagnostic accuracy of TCUS was 72 % while of MRI was 88%. The sensitivity of MRI was 78.9% and specificity was 81.8%. The sensitivity of TCUS was 70 % and the specificity was 60%.
Conclusion: TCUS is an efficient screening method in early detection of the etiology of NE in suspected cases; in seriously ill neonates it is sometimes important; however, early MRI is obligatory as it can detect precisely the degree of brain injury compared with TCUS alone.
Keywords: Neonatal encephalopathy (NE) ; Transcranial ultrasound; MRI Brain; Neonatal asphyxia; HIE

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Introduction

Neonatal hypoxic-ischemic encephalopathy (HIE) exists in 2/1100 live births, 15%–20% of the impacted neonates will die during early the postnatal period, also about 25% will reveal marked and long term neuropsychological defects, including mental retardation, visual dysfunction, hyperactivity, cerebral palsy, and epilepsy (**Lai et al.,2011).**

HIE is an acquired syndrome characterized by clinical and laboratory criteria of neuro-dysfunctiondue to ischemia (i.e., hypoxia, acidosis) **(Chao et al.,2006).**

About 15-28% of children with cerebral palsy are attributed to HIE. HIE is a brain injury results from insufficient brain blood flow during the intrauterine, intrapartum or postpartum periods **(Allen et al.,2011).**

About 60% of HIE infants will die or have serious disabilities by the age of 2 years. Even with improvements in intrauterine monitoring, the incidence of HIE has not diminished; so, much of the new neonatal studies on HIE focus on reducing the extent of the resulting brain damage **(Allen et al.,2011).**

There are three patterns of brain injury, mild and moderate injuries reveal PVL and germinal matrix hemorrhage in preterm neonates, but in full-term infants result in watershed zones infarction. However severe brain injuries involve deep gray matter in both term and preterm infants. The extent of brain HIE depends on the severity, duration of hypoxia and degree of brain maturation **(Shahina et al., 2017).**

This work aims at discussing and elaborating the role of Trans-cranialultrasound and conventional MRI in the workup of neonatal HIE.

Patients and methods

A prospective analytic study of 50 neonates with birth asphyxia were referred from NIC unit to Diagnostic Radiology Department of Qena University Hospitals, Egypt.

Inclusion criteria: Full term (≥37 weeks of gestational age), pre-term (≤37 weeks of gestational age) , neonates born with birth asphyxia and APGAR score at 5 minutes after birth is <7.

Exclusion criteria: Term or preterm neonates with infection and suspected metabolic diseases, neonates born with congenital anomalies.

All targeted neonates underwent history taking and clinical provisional examination then were subjected to high resolution Transcranial ultrasonography and MRI Brain.

Trans cranial US

(GE, LOGIQ P6) with an 11–MHz Probe and a low-value high-pass filter. Transcranialultrasound was done in all preterm infants, from the 3rdday of the birth mainly through the anterior fontanel in both coronal and sagittal planes. All three convex (3-5-5 MHz), cardiac (3.5- 5MHz), and linear (7-11MHz) transducers.

MRI of the Brain

MRI was done on Philips Achieva 1.5 Tesla MRI system. The neonate was sedated using chloral syrup and placed in the supine position and the following protocol taken place: T1-weighted spin-echo (TR/ TE, 400/12-300), T2-FLAIR (TR/TE, 9400/120), Axial T2 FSE TR/TE (4000/100) Echo train length 24, DWI (TR/TE 8000/100). The section thickness 3-4 millimeter. DWI and MRS are more sensitive than Conventional MRI in diagnosing acute brain injury. (FLAIR) sequence is useful for demonstrating cystic leukomalacia and gliosis. Gradient recalled echo-T2*-weighted sequence or susceptibility weighted imaging is sensitive for distinguishing hemorrhage from astrogliosis.

Statistical analysis

- Revision of data and coding of variables in the questionnaire was done and was entered in the computer
- Analysis of data was performed by Statistical Package for Social Sciences (SPSS) as follows:

1- Description of mean and range quantitative data.

2- Description of number and percentage (%) of qualitative data.

3- Qualitative parameters were compared by means of Chi-Square test.

4- R-test (correlation co-efficient) is used to rank different parameters against each other either direct or indirect. P value > 0.05 is considered non-significant (NS) and P value <0.05 is considered significant (S) while P value <0.01 is considered highly significant (HS).

Results

We presented the findings of our research, which was conducted in 50 cases.

MRI or TCUS in our case series was considered positive if at least one lesion was detected and was considered negative if no lesions were detected.

TCUS has not detected as many lesions as MRI in many cases, so TCUS was assumed to be true positive if at least one MRI finding was found in the same case.

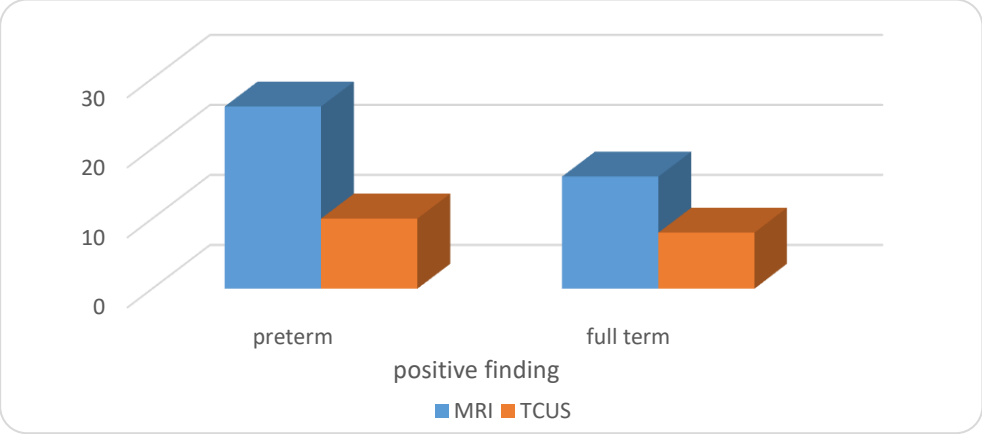

Fig.1. Positive findings detected by MRI and TCUS in preterm and full term infants.

Table 1. Correlation of TCUS findings with brain MRI findings

Variables		MRI		Total
		Positive	Negative	
TCUS findings	Positive	18	0	18
	Negative	24	8	32
Total		42	8	50

Total positive cases by TCUS were 18 and total negative cases were 32 while total positive cases by MRI were 42 and total negative cases 8. True positive cases were 18 and true negative cases were 8 (**Table.1 & Fig.1**).

Table 2. Positive findings of Transcranial ultrasound in different brain regions

Variables		TCUS		χ^2	P value
		+ve finding	-ve finding		
Cortex involvement	Yes	4(22.2%)	0	7.7	.005*
	No	14(77.8%)	32(100%)		
White matter involvement	Yes	6(33.3%)	16(50%)	1.29	.254
	No	12(66.7%)	16(50%)		
Brainstem involvement	Yes	2(11.1%)	0	3.7	.05*
	No	16(88.9%)	32(100%)		
Thalamic &basal gan. involvement	Yes	0	4(12.5%)	2.4	.11
	No	18(100%)	28(87.5%)		

IC hemorrhage	**Yes**	8(44.4%)	0	16.9	.000*
	No	10(55.6%)	32(100%)		
PVL	**Yes**	4(22.2%)	10(31.3%)	.46	.49
	No	14(77.8%)	22(68.8%)		
Loss of white grey matter differentiation	**Yes**	4(22.2%)	11(34.4%)	.81	.36
	No	14(77.8%)	21(65.6%)		
Cystic change	**Yes**	8(44.4%)	0	16.9	.000*
	No	10(55.6%)	32(100%0		
Ischemic changes	**Yes**	4(22.2%)	4(12.5%)	.81	.36
	No	14(77.8%)	28(87.5%)		

Positive finding was detected in 55.6% of preterm and in 44.4% of full term cases. Regarding cortical involvement 4 cases were true positive, 32 cases were true negative and 14 cases were false positive with statistical significant difference between two groups. According to white matter involvement true positive cases were 6, 12 cases were false positive, 16 cases were true negative and 16 cases were false negative with no statistical significant difference between 2 groups. According to brain stem involvement 2 cases were true positive, 16 cases were false positive and 32 cases were true negative with statistical significant difference between two groups. According to Thalamic &basal ganglia involvement no true positive cases, 18 false positive cases, 28 true negative cases and 4 false negative cases with no statistical significant difference between 2 groups. According to IC hemorrhage 8 true positive cases, 10 false positive cases, 32 true negative cases and no false negative cases with statistical significant difference between two groups. We resulted in overall sensitivity and specificity of TCUS in identification of brain changes compared to MRI were 81.8% and 60% respectively, and diagnostic accuracy of 78.9% (**Table.2**).

Ischemic changes in 4 cases were true positive and 14 cases false positive, however false negative cases were 4 and true negative cases were 28 with no statistical significant difference between 2 groups. According to PVL 4 cases were true positive, 14 cases were false positive, 10 cases were false negative and 22 cases were true negative with no statistical significant difference between 2 groups. According to Loss of white grey matter differentiation 4 cases were true positive, 14 cases were false positive, 11 cases were false negative and 21 cases were true negative with no statistical significant difference between 2 groups. According to Cystic change 8 were true positive cases, 10 cases were false positive and 32 cases were true positive with statistical significant difference between two groups (**Table.2**).

Table 3. Sensitivity and timing of different MR sequences

MR sequence	Sensitivity and Timing
DWI	Most sensitive within the first 1-5 days
T1WI	Sensitive during first 2-3 days
T2WI	Best sensitive within 7 days of life

DW imaging is best at the first 1–5 days of life, while T1 and T2 weighted imaging are sensitive after 2–3 days but best after 7 days (**Table.3**).

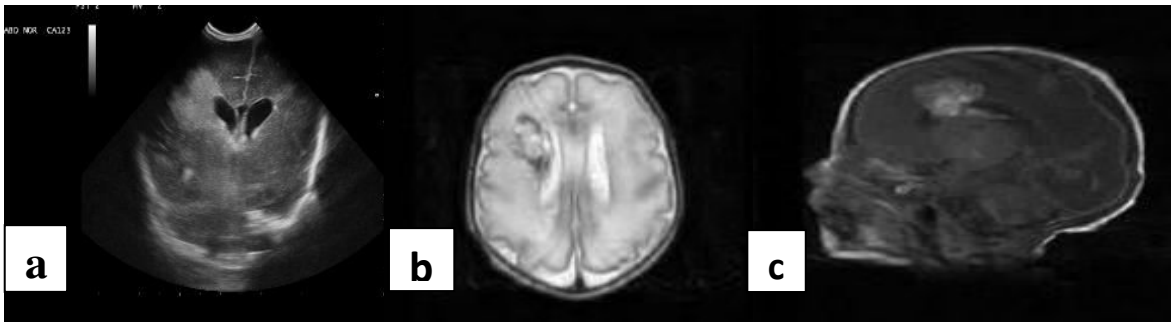

Fig 2. Coronal TCUS image showing right peri-ventricular and caudo-thalamic groove hyper-echogenicity area (hematoma) (a), T2WI showing iso to hyper-intense SI lesion(b), T1WI sagittal view hyper-intense SI lesion(c).

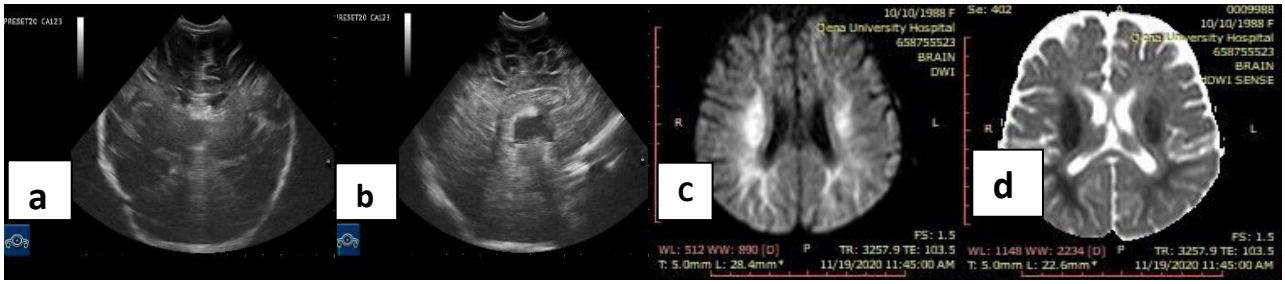

Fig .3. Sagittal and coronal TCUS images showing bilateral periventricular increased echogenicity (a) and (b). Correlated with axial DWI and ADC map images that show bilateral peri-ventricular areas of restricted diffusion (c) and (d).

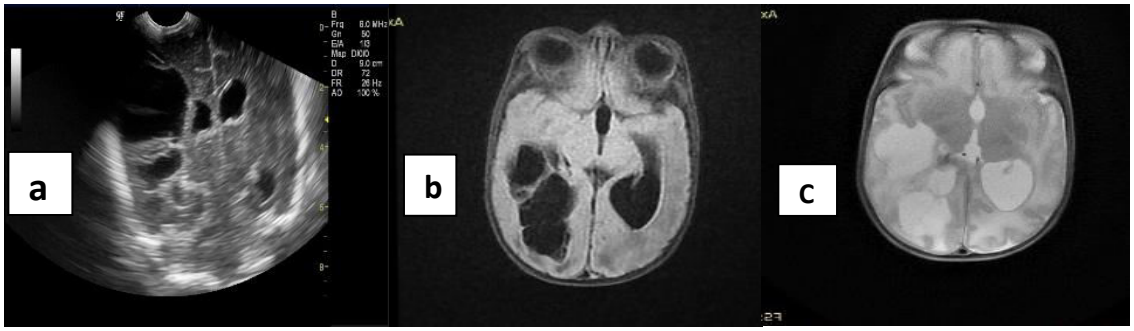

Fig 4. Post HIE right periventricular cystic changes shown in coronal TCUS (a), FLAIR and T2WI (b) and (c).

Discussion

Neonatal Encephalopathy is one of the most severe cause of neurological dysfunction in infancy.

Trans-cranial NE ultrasound is a ready-to-use, cheap and fast operator NE imaging tool. MR imaging is a well-known instrument for identifying neonatal brain injury in terms of timing, severity and magnitude and plays a major role in predicting neurologic outcomes.

The goal of our research was to study the significance of TCUS vs. MRI in recognizing brain injuries in newborns, with TCUS's global sensitivity in our study being consistent with previous studies comparing the TCUS and MRI of the same age group. **Epelman et al. (2006)** registered 100 percent TCUS sensitiveness in their analysis, with a specificity 33.3% and accuracy 95.7%.

In correlation with MRI, TCUS had better sensitivity for detecting thalamic, basal ganglia and peri-ventricular white matter lesions (88.2%, 81.2% and 80% respectively) rather than lesions in the corpus callosum, brain stem, cerebellar white matter, cerebral cortex and subcortical white matter (37.5%, 33.3%,

33.3%, 28.6% and 50% respectively), **(Table 2)**. However, TCUS revealed high specificity in most of the lesions reaching 100% sparingly lesions at the peri-ventricular and subcortical white matter and cortical lesions which had lower specificity (94%, 94.4% and 96.8% respectively) **. Epelman et al. (2006)** revealed in their study that TCUS had relatively higher sensitivities in lesions at the peri-ventricular white matter (79.5%), subcortical white matter (71.9%) and deep gray matter (71.1%) rather than lesions at the cortex (58.8%), corpus callosum (50%) and the brainstem (26.7%). Our results agreed with those of **Steggerda et al. (2009)** who depicted that TCUS can detect central abnormalities better than peripheral ones. **Blankenberg et al. (2002)** also stated in their study that TCUS is less sensitive to structural abnormalities in the cerebral cortex and brain stem. However, **Epelman et al. (2006)** concluded in their study that both peripheral and central brain findings were equally detected by Ultrasound.

The overall sensitivity of TCUS in our study agreed with other records from previous study **Miller (2003)** that compared TCUS and MRI in this age group and concluded that sonography remains a valuable modality for evaluation; however, early MRI will provide important information on the presence and extent of brain injuries.

Diffusion-weighted imaging (DWI) often reveals ischemic brain injury at an earlier stage than conventional MR imaging. **Forbes et al (2000)**. In our study, DWI was the only positive sequence that detected mild to moderate HIE pattern in a full term, while other conventional MR sequences and TCUS were negative.

MRI is the reference standard for infant brain imaging. **Childs et al (2001).** It is needed in most neonates with suspected parenchymal brain injury or neurological manifestations, However TCUS does not detect as many injuries as MRI. Thus, TCUS could significantly underestimate the degree of injury.

In our analysis, DWI was the only positive sequence that detected a full term mild to moderate HIE injury, whereas other traditional MR sequences and TCUS were negative**.** In addition, the GRE (T2WI) Sequences are highly susceptible to hemorrhage.

The neurological effects of brain trauma in encephalopathic neonates can be studied using MRI. We therefore suggest that the ultimate radiodiagnostic procedure for NE cases be using both TCUS and MR imaging.

Throughout this study, we encountered some limitations. First, working with critically ill neonates, especially in terms of transport from the NICU to the MRI unit, as well as qualified staff to provide continuous clinical treatment during MR scanning. Second, because of the inability to collect parallel MRI and TCUS studies for many patients, the relative limited number of patients in our study. This was due to their rapid death or the existence of barriers to their transfer into MRI scanner due to their critically unhealthy medical circumstances or technical factors affecting the transport equipment.

Conclusion

In conclusion, in suspicious cases, TCUS is an important screening method for detection of NE etiology; in critically ill neonates, it is often crucial; however, early MRI is mandatory as it can precisely diagnose the degree of brain damage compared to TCUS alone.

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