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Original Research Article

ACCURACY OF CRANIAL SONOGRAPHY IN IDENTIFYING HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN PRETERM INFANTS COMPARED WITH MRI

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ABSTRACT

Background: Hypoxic-ischemic encephalopathy (HIE) is a significant neonatal cause of morbidity and mortality, especially in premature babies. Magnetic resonance imaging (MRI) is the gold standard for diagnosis of HIE, but because of limited availability, cost and logistical issues, other imaging modalities may be required. Although cranial sonography is a portable, easily available and cost-effective modality, some studies report that it is not as accurate as others. **Objective:** To compare the diagnostic value of sonography in the head with MRI as the standard for the diagnosis of HIE in infants suspected of having HIE. **Duration and Place of study:** This study was conducted at Fatima Jinnah Institute of Chest Disease Quetta from June 2025 to June 2026. **Data collection Method:** Cross-sectional study.

Materials and Methods: A cross-sectional validation study of 150 premature neonates who were clinically suspected of having HIE. Cranial ultrasonography was performed on all infants followed by MRI. The results of the cranial sonography were correlated with those of MRI and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated.

Results: 150 neonates were studied by cranial sonography and MRI. 98 were diagnosed with HIE by cranial ultrasound, whereas, 104 were diagnosed on MRI. Cranial ultrasound was found to be 84.6% sensitive, 78.0% specific, 89.8% PPV, 68.4% NPV and 82.0% overall diagnostic accuracy when compared to MRI. The results suggest high agreement between cranial sonography and MRI, especially when HIE is considered to be moderate or severe.

Conclusions: Cranial sonography was effective in the diagnosis of HIE in premature infants and can be used as an effective imaging modality where MRI is not available or suitable. There are, however, some limitations in the detection of subtle or deep brain lesions that emphasizes the need for additional studies that include long term neurodevelopmental outcomes and MRI correlation to further strengthen evidence for its diagnostic usefulness.

Keyword: Hypoxic-ischemic encephalopathy, MRI, Cranial sonography, Imaging, Diagnostic accuracy, Premature infeants.

INTRODUCTION

Hypoxic-ischemic encephalopathy (HIE) is one of the most severe neurological emergencies in neonatology and an important cause of long-term neurodevelopmental impairment, morbidity and mortality in premature babies. Prompt and accurate diagnosis is crucial as early neuroprotective interventions such as therapeutic hypothermia have a significant impact when started early.[1] Magnetic resonance imaging (MRI) has been considered the gold standard for diagnosis of HIE because of its exquisite soft-tissue contrast, its ability to detect deep-brain lesions, and its ability to detect early ischemic changes.[2] In reality, however, MRI is not readily available, may require sedation, is associated with some transport risk, and may be limited in availability in resource limited environments, which is why alternative imaging modalities are of interest.[3]

Cranial sonography (cranial ultrasound, CUS) is a common imaging technique used at the bedside in neonatal intensive care units. It is portable, inexpensive, radiation-free, and can be repeated without risk, thus it is ideal for premature infants, who are clinically unstable or have the need for serial monitoring.[4] It has been assessed in a few studies for its diagnostic accuracy in HIE, with differing levels of accuracy reported by different time of use, the severity of the injury, and the operator's experience. A recent validation study showed that cranial ultrasound had a sensitivity of 84.75% and specificity of 88.10% in comparison to MRI, and was therefore found to be an effective screening modality as a first choice.[5] The results indicated that CUS is a promising diagnostic tool if MRI cannot be used.

The mechanisms that underlie HIE are a series of metabolic and vascular processes that result from inadequate cerebral blood flow and oxygenation. Premature infants are especially susceptible because of their immaturity of autoregulation, weak germinal matrix vasculature and sensitivity to fluctuations in perfusion.[6] This means that imaging is of very important value in early detection of structural and perfusion abnormalities. Results from transcranial ultrasound have been encouraging to identify critical sonographic characteristics of HIE, such as intraventricular hemorrhage, ventriculomegaly, multicystic leukomalacia and abnormal Doppler indices.[7] Transcranial ultrasound in a cross-sectional study of 168 preterm neonates was shown to have good sensitivity (85.7%) and specificity (82.4%) for HIE diagnosis, and therefore, has a strong diagnostic potential.[8]

In addition to structural abnormalities, sonographic markers including thalamic hyperechogenicity, basal ganglia changes, and changes in the appearance of the posterior limb of the internal capsule (PLIC) are known to be associated with acute and subacute hypoxic injury.[9] A more recent study noted that low RI values of ≤0.55 in the cerebral Doppler early in the first 72 hours of life were associated with poor outcome and higher mortality rates.[10] These results highlight the importance of cranial ultrasound as a means of diagnosis and follow-up of the disease as well as for clinical management.[11]

Quantitative neurosonography has also further enhanced the ultrasound diagnosis. A recent study from 2022, which looked at the echogenicity ratios in various brain regions, revealed that neonates with HIE had significantly higher echogenicity ratios than healthy neonates, especially in the perirolandic white matter (AUC 0.980).[12,13] The findings indicate that quantitative tools might be useful in improving early identification and may be able to discriminate between levels of severity.

Although great progress has been made, the use of cranial ultrasound has its drawbacks. May not be sensitive to subtle cortical injuries, deep-brain lesions, or early diffuse ischemic changes that can be seen on MRI.[14,15] Other factors that contribute to inconsistent diagnostic performance are operator dependency, inconsistent equipment quality, and interpretation difficulties with complex sonographic patterns. Thus, CUS is useful as a initial imaging modality, but MRI is still the modality of choice for detailed evaluation, prognosis and long-term follow-up.[16,17]

As the clinical importance of early detection of HIE and the limitations of MRI are known, it is important to assess the accuracy of cranial sonography in premature infants. Knowing its advantages and disadvantages, and its compatibility with MRI, will help the clinician decide on the type of imaging strategy to use, particularly when MRI is not available. The purpose of this study is to evaluate the value of cranial sonography for the diagnosis of HIE in clinically suspected premature infants with MRI as the gold standard. This study may help make informed imaging decisions and help improve neonatal care by offering fresh evidence of the study's performance.

MATERIALS AND METHODS

The cross-sectional validation study aimed to assess the accuracy of cranial sonography in diagnosing HIE in premature neonates who were clinically suspected of HIE, and who underwent magnetic resonance imaging (MRI) as the gold standard test.

150 premature neonates were included who clinically had HIE. All infants had cranial ultrasonography, then MRI. Neonates were included if they were premature and had clinical signs suggestive of HIE including abnormal tone, poor sucking, seizures, respiratory difficulty or low APGAR scores. Infants who had congenital brain malformations or intracranial infections, chromosomal abnormalities, or were not fully assessed using imaging were excluded.

A non-probability type of consecutive sampling technique was employed. The sample size of 150 neonates was determined to provide sufficient power to evaluate significant differences in diagnostic accuracy between cranial sonography and MRI, based on the reported sensitivity and specificity of previous literature.

A high-resolution linear-array transducer (5–8 MHz) appropriate for neonatal cranial imaging was used to perform cranial ultrasonography. Surgical examination was performed with anterior fontanelle and additional views through temporal, occipital, and posterior windows (when possible) and in the coronal and sagittal planes. The sonographic features suggestive of HIE were noted, including diffuse cerebral edema (sulci and fissures were lost), hemispheric asymmetry and increased echogenicity of subcortical white matter. Experienced radiologists blinded to MRI were used to interpret all ultrasound examinations.

MRI was conducted on a 1.5-Tesla machine with a neonatal head coil. When necessary, chloral hydrate (10%) was used to sedate the animals under pediatric supervision. Typical neonatal MRI sequences were acquired, such as T1-weighted and T2-weighted images. Increased signal intensity of basal ganglia and thalami and loss of normal T1 hyperintensity of the posterior limb of the internal capsule is a characteristic finding on MRI in HIE. Two senior blind to the cranial sonography results radiologists independently reviewed all MRI scans.

The main result was the diagnostic accuracy of cranial sonography for the diagnosis of HIE, when compared to MRI as the gold standard. Secondary outcomes included sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

IBM SPSS Statistics 26 was used to analyze the data. Continuous variables (gestational age, birth weight) were presented as mean and SD. Categorical variables such as sex, mode of delivery and imaging findings were expressed as frequencies and percentages.

The diagnostic accuracy parameters were determined using a 2×2 contingency table with cranial sonography and MRI results. Calculations of sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy were performed. Stratified analyses were undertaken for the potential effect modifiers of gender and gestational age. The association between categorical variables was evaluated by Chi-square test or Fisher's exact test as needed. A p-value <0.05 was considered statistically significant.

RESULTS

150 preterm neonates with clinical HIE were included. The mean age at birth was 33.1 ± 2.0 weeks, the mean birth weight was 1820 ± 395 grams. Of these, 86 (57.3%) were males and 64 (42.7%) were females. 55.3% of the women delivered by cesarean section and 61.3% of mothers lived in rural areas.

Cranial Sonography showed suggestive findings for diagnosis of HIE in 98 (65.3%) neonates while MRI confirmed the diagnosis of HIE in 104 (69.3%) neonates. A 2x2 diagnostic table was created to assess the sensitivity, specificity, positive and negative predictive values and the overall diagnostic accuracy of cranial sonography compared with MRI as the gold standard.

Table 1: Baseline demographic and clinical characteristics (N = 150)

Characteristic	Value (n or Mean ± SD)
Gestational Age (weeks)	33.1 ± 2.0
Birth Weight (grams)	1820 ± 395
Gender	Male: 86 (57.3%); Female: 64 (42.7%)
Mode of Delivery	Caesarean: 83 (55.3%); Vaginal: 67 (44.7%)
Maternal Education	Illiterate: 76 (50.7%); Literate: 74 (49.3%)
Maternal Booking Status	Booked: 58 (38.7%); Unbooked: 92 (61.3%)
Residence	Urban: 58 (38.7%); Rural: 92 (61.3%)

Among the 104 MRI-confirmed cases of HIE, 88 were also positive on cranial sonography (true positives), while 16 were missed (false negatives). Of the 46 neonates without HIE on MRI, 10 were incorrectly labelled as having HIE by sonography (false positives), leaving 36 true negatives.

Table 2: Diagnostic accuracy of cranial sonography for HIE (N = 150)

Cranial Sonography	HIE on MRI (Yes)	HIE on MRI (No)	Total
HIE Detected	88 (True Positives)	10 (False Positives)	98
HIE Not Detected	16 (False Negatives)	36 (True Negatives)	52
Total	**104**	**46**	**150**

Diagnostic Performance Metrics

Metric	Formula	Value (%)
Sensitivity	88 / (88 + 16)	**84.6**
Specificity	36 / (36 + 10)	**78.3**
PPV	88 / (88 + 10)	**89.8**
NPV	36 / (36 + 16)	**69.2**
Accuracy	(88 + 36) / 150	**82.7**

The sonography of the head proved to be very sensitive (84.6%) and had a good positive predictive value (89.8%), making it a reliable tool for detecting premature neonates that present with HIE. Specificity and NPV were satisfactory (78.3% and 69.2%, respectively) and represented moderate power to rule out disease. The overall diagnostic accuracy of 82.7% confirms the good performance of a cranial ultrasound in a setting in which the availability of MRI is limited.

The results affirm the usefulness of cranial sonography as a practical, readily available and reasonably accurate tool to help evaluate HIE in the premature infant, especially in resource limited neonatal care settings.

DISCUSSION

Cranial sonography had the following characteristics in detecting HIE in premature neonates: the sensitivity was 84.6%, the specificity was 78.3%, the positive predictive value was 89.8%, the negative predictive value was 69.2%, and the overall diagnostic accuracy was 82.7%. This is confirmation of the utility of cranial ultrasound in the neonatal unit where MRI is less readily available.

The diagnostic accuracy obtained in the present study agrees with that reported by Shah Zaib et al. who reported a sensitivity of 84.75% and a specificity of 88.10% for cranial ultrasound compared to MRI.[17] They found that their sensitivities were comparable with what we observed in our group, but specificity was slightly higher, which may relate to differences in operator experience and/or selection criteria. In the same way, another study found that cranial sonography was 85.7% sensitive and 82.4% specific for preterm neonates.[18] which is quite similar to our findings and indicates the validity of cranial sonography for early diagnosis of HIE.

Our results are consistent with those of Kumar et al, who emphasized the value of point-of-care ultrasound for the detection of hypoxic-ischemic brain injury in the resource-poor setting.[19] They emphasized the value of bedside imaging for unstable neonates and our findings support that of this study in that domain. One study showed quantitative neurosonography was able to distinguish HIE from normal neonatal brain patterns with a high accuracy.[20] We did not use quantitative PPV in our study, but the high PPV we have seen indicates that even the traditional sonographic measurement can be a reliable indicator of HIE in premature infants.

In addition, the diagnostic capability seen in our study was similar to that of previous studies by Rehman et al. who reported that cranial ultrasound was very useful in identifying deep brain abnormalities and white matter changes in neonates.[21] Their results corroborate the powerful PPV that we found in our sample, showing that if cranial sonography suggests HIE, the probability of actual disease is indeed high. They did, however, point out that there are limitations in detecting subtle cortical injuries, which could account for the false-negative rate in our study.

A further study identified specific brain injury patterns in NED and found that the MRI is superior in detecting lesions of the basal ganglia and the cortex.[22] This is consistent with the false negative cases in our study, in which cranial sonography did not pick up HIE that was subsequently identified on MRI. The results highlight the role of MRI in full assessment where sonographic evaluation is not definitive or there is a high clinical suspicion.

In addition, Gupta et al. have shown that MRI biomarkers are strongly associated with long term neurodevelopmental outcomes.[23] This further emphasizes the need for MRI in all neonates with HIE, even when sonography of the head is normal. This is supported by our study, which shows that although cranial ultrasound is helpful as a first line screening tool, it should not be used as a substitute for MRI in prognosis or detailed evaluation of severity of injuries.

Last but not least, Ibrahim et al. found that cranial ultrasound detected major intracranial abnormalities, but failed to detect subtle lesions.[24] This echoes our specificity and NPV which suggest that although cranial sonography is good at detecting HIE, it is not as powerful in ruling out disease. In our study, an apparent false-positive rate may have been due to the difficulty of interpreting sonograms, especially in premature infants who had features such as edema or increased echoogenicity, which made it difficult to diagnosis the condition.

In general, the present study helps add to the rising body of evidence indicating cranial sonography as a useful imaging modality that can be obtained as an initial assessment tool in premature neonates with suspected HIE. In resource-limited areas it is very useful due to its portability, accessibility, and its relatively high diagnostic accuracy. As in the previous studies, however, it should be recognized that cranial sonography should not replace MRI but be used as a complement to it. However, MRI is still of critical importance in the definitive diagnosis, assessment of the pattern of injuries and long-term prognosis.

CONCLUSION

This study showed that the sonography of the cranium has a good diagnostic performance in the detection of HIE in premature neonates, when compared with MRI as the gold standard. Cranial ultrasound was highly sensitive and had a positive predictive value for the diagnosis of HIE and was a useful imaging modality as a first line test at the bedside. Its specificity and negative predictive value were both less, however the overall diagnostic

efficacy was good, lending weight to its utility in early clinical decision making.

The advantages of cranial sonography are numerous and include its portability, accessibility and the fact that it can be conducted quickly at the bedside, without transport or sedation. These properties render it especially useful in neonatal wards where there is a scarcity of MRI or when the baby is clinically unstable. But cranial ultrasound is not enough to make a full evaluation; subtle injuries to the cortex or deep brain may be missed.

The results of this study support the use of cranial sonography as a first-line screening test for premature infants with suspected HIE overall. The reasonable diagnostic accuracy and feasibility in limited resource settings demonstrate its potential to enhance early detection and management of HIBI. Future studies with longer-term neurodevelopmental outcomes and more sophisticated sonographic techniques could improve diagnostic accuracy and further support the value of sonography in neonatal neuroimaging.

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