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Transcranial Ultrasound and Cerebral Doppler for Early Detection of Neonatal Hypoxic-Ischemic Encephalopathy

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Abstract

Background:

Neonatal hypoxic–ischemic encephalopathy (HIE) remains a major cause of neonatal mortality and long-term neurodevelopmental disability worldwide. Early diagnosis is crucial because timely intervention, including therapeutic hypothermia and intensive supportive care, may reduce neurological injury and improve outcomes. Transcranial ultrasonography (TCUS) combined with Doppler assessment offers a bedside, non-invasive, and cost-effective method for evaluating both cerebral morphology and cerebral hemodynamics in critically ill neonates.

Materials And Methods:

A prospective case–control study was conducted in the Department of Radio-Diagnosis, J.J.M. Medical College, Davangere, over a period of 18 months. Thirty neonates with clinically diagnosed HIE and gestational age greater than 34 weeks were included as cases, while forty healthy neonates served as controls. All neonates underwent neurosonography and Doppler evaluation of the anterior cerebral artery (ACA) and middle cerebral artery (MCA). Clinical profile, APGAR scores, fetal distress, cranial ultrasound findings, Doppler resistive indices, and neonatal outcomes were analyzed.

Results:

A total of 70 neonates were evaluated, including 30 HIE cases and 40 controls. Clinical abnormalities, fetal distress, and cranial ultrasound abnormalities were significantly associated with HIE ($p<0.001$). Mean ACA resistive index was significantly higher in cases (0.766 ± 0.03) than controls (0.659 ± 0.036), while mean MCA resistive index was 0.765 ± 0.037 in cases and 0.660 ± 0.03 in controls ($p<0.001$). APGAR scores at 1, 5, and 10 minutes were significantly lower among HIE neonates. Doppler resistive indices demonstrated a progressive increase with disease severity. ACA RI increased from 0.7358 ± 0.0100 in Stage I to 0.8120 ± 0.0084 in Stage III, while MCA RI increased from 0.7317 ± 0.0111 to 0.8300 ± 0.0200. Mortality occurred exclusively among HIE cases (13.33%).

Conclusion:

Transcranial ultrasound combined with cerebral Doppler assessment is a reliable bedside imaging tool for the diagnosis and severity assessment of neonatal HIE. Elevated ACA and MCA resistive indices correlate significantly with disease severity and adverse outcomes, making Doppler evaluation a valuable prognostic marker. Early identification of Doppler abnormalities may facilitate timely intervention and improve neonatal outcomes.

Keywords: Hypoxic–ischemic encephalopathy, Transcranial ultrasound, Cerebral Doppler, Resistive index, Neurosonography, Neonatal brain injury

Introduction

Neonatal hypoxic–ischemic encephalopathy (HIE) is one of the most serious neurological emergencies encountered during the neonatal period and remains a major cause of neonatal mortality and long-term neurodevelopmental disability worldwide. It results from impaired cerebral blood flow and oxygen delivery to the fetal or neonatal brain during the perinatal period, leading to varying degrees of neuronal injury and cerebral dysfunction. Despite significant advances in obstetric and neonatal intensive care, HIE continues to contribute substantially to neonatal morbidity and mortality, particularly in low- and middle-income countries.[1,2]

The incidence of HIE is estimated to be approximately 1–3 per 1000 live births in developed countries and considerably higher in developing nations, where the burden of perinatal asphyxia remains significant.[3] Approximately 15–25% of neonates with moderate-to-severe HIE die during the neonatal period, while many survivors develop long-term neurological sequelae including cerebral palsy, epilepsy, cognitive impairment, hearing loss, visual deficits, and developmental delay.[4–6] These adverse outcomes impose substantial emotional, social, and economic burdens on affected families and healthcare systems.

The pathophysiology of HIE is complex and involves a cascade of biochemical, metabolic, and hemodynamic events. The initial hypoxic–ischemic insult leads to reduced cerebral perfusion, depletion of cellular energy stores, metabolic acidosis, and failure of neuronal ion pumps, resulting in primary energy failure. Subsequent excitotoxicity, intracellular calcium accumulation, oxidative stress, mitochondrial dysfunction, inflammation, and apoptosis contribute to secondary energy failure and progressive neuronal injury.[7,8] The extent and distribution of brain injury depend on the severity and duration of hypoxia, gestational age, and the effectiveness of cerebral autoregulatory mechanisms.

Early diagnosis and accurate assessment of disease severity are critical because timely therapeutic interventions may significantly improve neurological outcomes. Therapeutic hypothermia has emerged as the standard neuroprotective therapy for moderate and severe HIE and is most effective when initiated within the first six hours after birth.[9] Consequently, reliable bedside diagnostic tools capable of detecting cerebral injury during the early neonatal period are essential for prompt identification and management of affected neonates.

Neuroimaging plays a pivotal role in the diagnosis and prognostication of neonatal HIE. Magnetic resonance imaging (MRI) is widely regarded as the reference standard for evaluating hypoxic–ischemic brain injury because of its high sensitivity in detecting cortical, deep gray matter, and white matter abnormalities.[10,11] However, MRI may not always be feasible in critically ill neonates because of limited availability, high cost, prolonged examination time, transport-related risks, and the need for monitoring during image acquisition. These limitations highlight the importance of alternative imaging modalities that are readily available, safe, and repeatable.

Transcranial ultrasonography (TCUS) has become an indispensable imaging tool in neonatal intensive care units because it provides a rapid, portable, and non-invasive method for assessing the neonatal brain. The open fontanelles serve as natural acoustic windows, enabling detailed visualization of cerebral structures without radiation exposure. Conventional gray-scale neurosonography can demonstrate cerebral edema, increased parenchymal echogenicity, ventricular compression, basal ganglia and thalamic involvement, periventricular leukomalacia, and intracranial hemorrhage associated with hypoxic–ischemic injury.[12,13] In addition, serial examinations can be performed safely at the bedside, making TCUS particularly useful for monitoring disease progression.

The incorporation of Doppler ultrasonography significantly enhances the diagnostic capability of transcranial ultrasound by providing functional information regarding cerebral blood flow and vascular resistance. Color and spectral Doppler imaging allow assessment of major intracranial

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vessels including the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA). Parameters such as peak systolic velocity, end-diastolic velocity, pulsatility index, and resistive index (RI) provide valuable insight into cerebral hemodynamics and autoregulatory status.[14,15]

Among these parameters, the resistive index has attracted considerable attention as a potential marker of disease severity and prognosis. Alterations in RI reflect changes in cerebrovascular resistance and cerebral autoregulation following hypoxic–ischemic injury. Elevated RI values may indicate increased vascular resistance and impaired cerebral perfusion, whereas abnormal reductions may occur during reperfusion and hyperemic phases. Several investigators have reported significant correlations between abnormal cerebral Doppler indices and adverse neurological outcomes, including mortality, cerebral palsy, and developmental delay.[16–18]

The anterior cerebral artery and middle cerebral artery are particularly suitable for Doppler assessment because they are readily accessible through the anterior fontanelle and represent major components of the cerebral circulation. Previous studies have demonstrated significant differences in ACA and MCA Doppler parameters between healthy neonates and those affected by HIE. Furthermore, Doppler abnormalities have been shown to correlate with clinical staging systems such as the Sarnat classification, suggesting that cerebral Doppler evaluation may provide an objective measure of disease severity.[19–21]

In resource-limited settings where access to advanced neuroimaging may be restricted, transcranial ultrasonography combined with Doppler assessment offers a practical and cost-effective alternative for early diagnosis and prognostication. Identification of reliable Doppler markers may facilitate prompt therapeutic intervention, optimize neonatal intensive care management, and improve parental counseling regarding expected outcomes.

Therefore, the present study was undertaken to evaluate the role of transcranial ultrasonography and cerebral Doppler imaging in neonates with hypoxic–ischemic encephalopathy. The study aimed to assess neurosonographic findings, compare cerebral Doppler resistive indices between HIE cases and healthy controls, determine the association between Doppler parameters and disease severity, and evaluate the prognostic value of cerebral Doppler assessment in neonatal HIE.

MATERIALS AND METHODS

Study Design and Setting

This prospective case–control study was conducted in the Department of Radio-Diagnosis, Jagadguru Jayadeva Murugarajendra (J.J.M.) Medical College and associated teaching hospitals, Davangere, Karnataka, India, over a period of 18 months. The study was designed to evaluate neurosonographic findings and cerebral Doppler parameters in neonates with hypoxic–ischemic encephalopathy (HIE) and compare them with healthy neonates. Ethical clearance for the study was obtained from the Institutional Ethics Committee prior to commencement of the study. Written informed consent was obtained from the parents or legal guardians of all participating neonates.

Study Population

A total of 70 neonates were included in the study. The study population was divided into two groups:

1. **Cases:** Thirty neonates clinically diagnosed with hypoxic–ischemic encephalopathy.
2. **Controls:** Forty healthy neonates without evidence of neurological abnormalities or perinatal asphyxia.

The diagnosis and staging of HIE were established by the attending neonatologist based on clinical findings and Sarnat and Sarnat staging criteria.[1]

Inclusion Criteria

Cases

Neonates were included in the HIE group if they fulfilled the following criteria:

1. Gestational age greater than 34 weeks.
2. Clinical diagnosis of hypoxic–ischemic encephalopathy.
3. History suggestive of perinatal asphyxia, including fetal distress, delayed cry at birth, need for resuscitation, or low APGAR scores.
4. Availability for cranial ultrasonography and Doppler examination.
5. Informed parental consent.

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Controls

Neonates were included in the control group if they met the following criteria:

1. Gestational age greater than 34 weeks.
2. Absence of neurological symptoms or signs.
3. No history of perinatal asphyxia or fetal distress.
4. Normal clinical examination.
5. Informed parental consent.

Exclusion Criteria

The following neonates were excluded from the study:

1. Premature neonates with gestational age less than 34 weeks.
2. Neonates with congenital central nervous system anomalies.
3. Neonates with chromosomal abnormalities or genetic syndromes.
4. Neonates with intracranial infections.
5. Neonates with significant congenital cardiac disease affecting cerebral hemodynamics.
6. Neonates whose parents declined consent.

Clinical Assessment

Detailed maternal, antenatal, intrapartum, and neonatal histories were obtained from hospital records and parental interviews. The following variables were documented:

1. Gestational age
2. Birth weight
3. Gender
4. Mode of delivery
5. Presence of fetal distress
6. Antenatal risk factors
7. APGAR scores at 1, 5, and 10 minutes
8. Clinical manifestations including seizures, lethargy, poor feeding, hypotonia, and coma

All neonates underwent detailed clinical examination by the attending neonatologist.

Ultrasound Equipment and Imaging Technique

Neurosonographic evaluation was performed using a high-resolution ultrasound system equipped with grayscale, color Doppler, and spectral Doppler capabilities. A sector transducer with a frequency range of 5–8 MHz was utilized.

All examinations were performed while the neonates were calm or naturally sleeping. Sedation was not required.

The anterior fontanelle was used as the primary acoustic window because it provides excellent visualization of intracranial structures and cerebral vessels. Standard coronal and sagittal imaging planes were obtained according to established neonatal neurosonography guidelines.[2]

Gray-Scale Neurosonography

Gray-scale ultrasonography was performed to assess cerebral morphology and detect abnormalities associated with hypoxic–ischemic injury.

The following structures were systematically evaluated:

1. Cerebral hemispheres
2. Basal ganglia and thalami
3. Periventricular white matter
4. Ventricular system
5. Corpus callosum
6. Cerebellum (when visualized)
7. Intracranial extra-axial spaces

The presence or absence of the following abnormalities was recorded:

1. Diffuse cerebral edema
2. Germinal matrix hemorrhage
3. Loss of gray-white matter differentiation
4. Ventricular compression
5. Intraventricular hemorrhage
6. Periventricular leukomalacia
7. Other focal parenchymal abnormalities

Doppler Ultrasonography

Color Doppler and spectral Doppler examinations were subsequently performed to evaluate cerebral blood flow patterns and vascular resistance.

The intracranial vessels evaluated included:

1. Anterior cerebral artery (ACA)
2. Middle cerebral artery (MCA)

These vessels were selected because they are readily accessible through the anterior fontanelle and are commonly used for assessment of neonatal cerebral hemodynamics.[3]

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Color Doppler imaging was initially used to identify the arteries, followed by spectral Doppler waveform acquisition.

Care was taken to:

1. Maintain an angle of insonation below 30°
2. Avoid excessive transducer pressure on the fontanelle
3. Obtain at least three consecutive uniform waveforms
4. Minimize motion artifacts

Doppler Parameters

The following Doppler measurements were obtained:

1. Peak systolic velocity (PSV)
2. End-diastolic velocity (EDV)
3. Resistive Index (RI)

Resistive Index was calculated using the formula:

RI = (PSV – EDV) / PSV

RI values from both ACA and MCA were recorded for analysis because RI is considered a reliable indicator of cerebrovascular resistance and cerebral perfusion.[4]

Outcome Assessment

Immediate neonatal outcomes were documented and categorized as:

1. Recovery
2. Death

Clinical outcome data were obtained from neonatal intensive care unit records and discharge summaries.

Case Series

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 25.0.

Quantitative variables were expressed as mean ± standard deviation (SD), while qualitative variables were expressed as frequency and percentage.

The following statistical tests were applied:

1. Independent Student's t-test for comparison of continuous variables between cases and controls.
2. Chi-square test for comparison of categorical variables.
3. One-way Analysis of Variance (ANOVA) for comparison of Doppler resistive indices across different stages of HIE.
4. p-value <0.05 was considered statistically significant.

Results were presented using tables, graphs, and descriptive statistics.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of J.J.M. Medical College, Davangere. All procedures were performed in accordance with the ethical principles outlined in the Declaration of Helsinki. Confidentiality of patient information was maintained throughout the study, and participation in the study did not interfere with standard neonatal management protocols.

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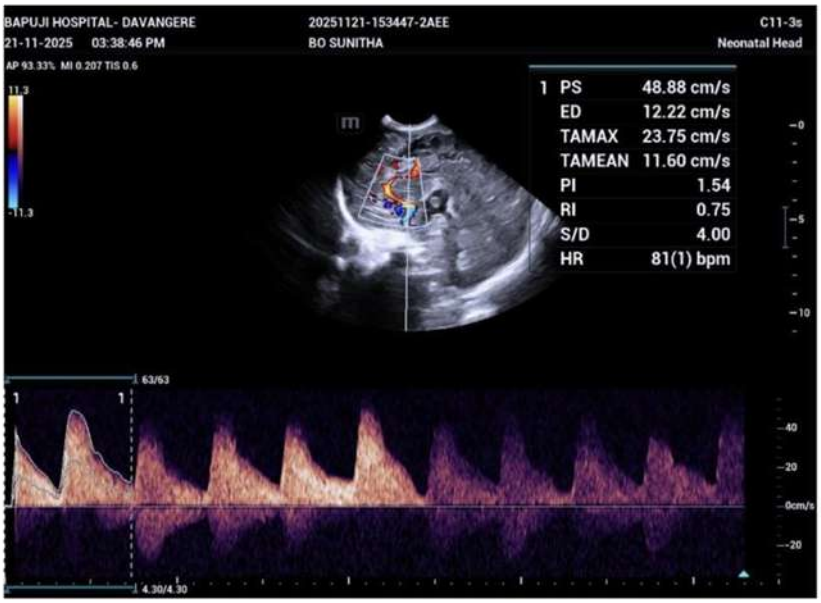
PATIENTS LABORATORY REPORT

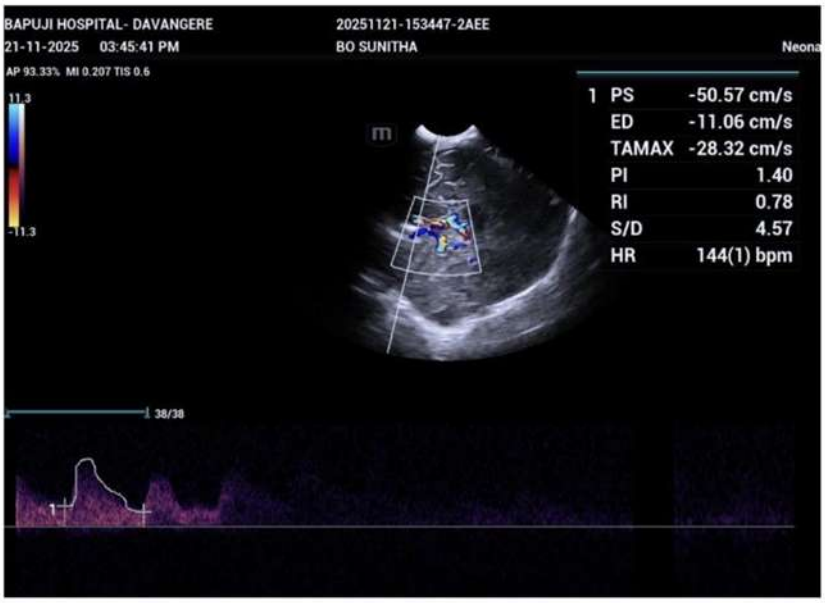
CASES

CASE-1: NSG in a 20 day old baby with HIE II stage mean resistance index (RI) of ACA was 0.75 and of MCA was 0.78.

RI of ACA:



RI of MCA:



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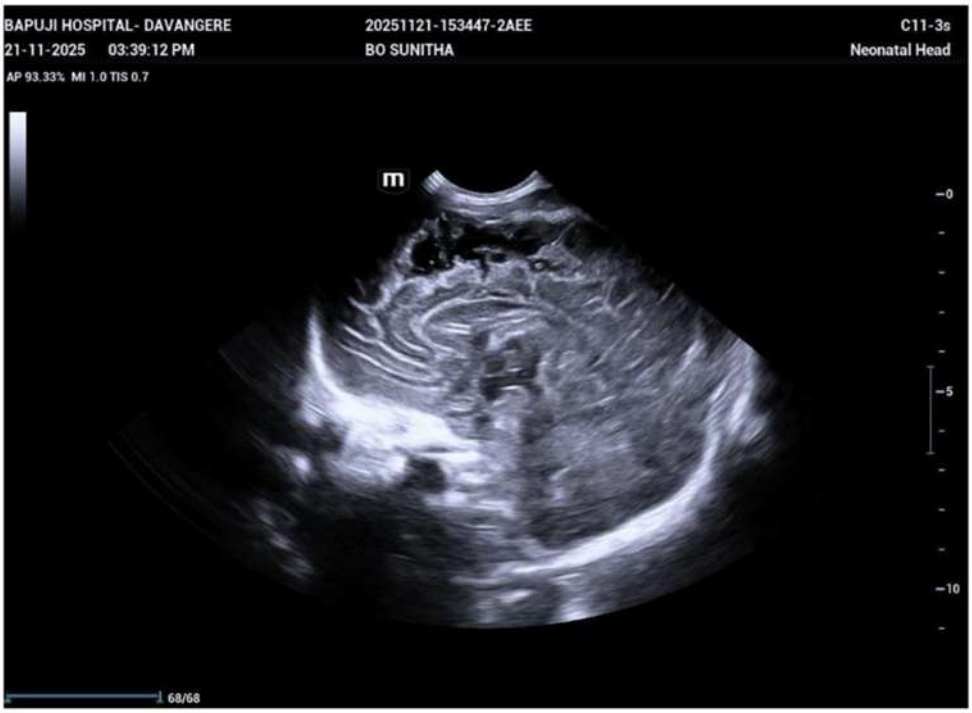
Thinning of corpus callosum along with cerebral vein thrombosis involving superior Sagittal sinus - s/o perinatal hypoxic ischemic injury.



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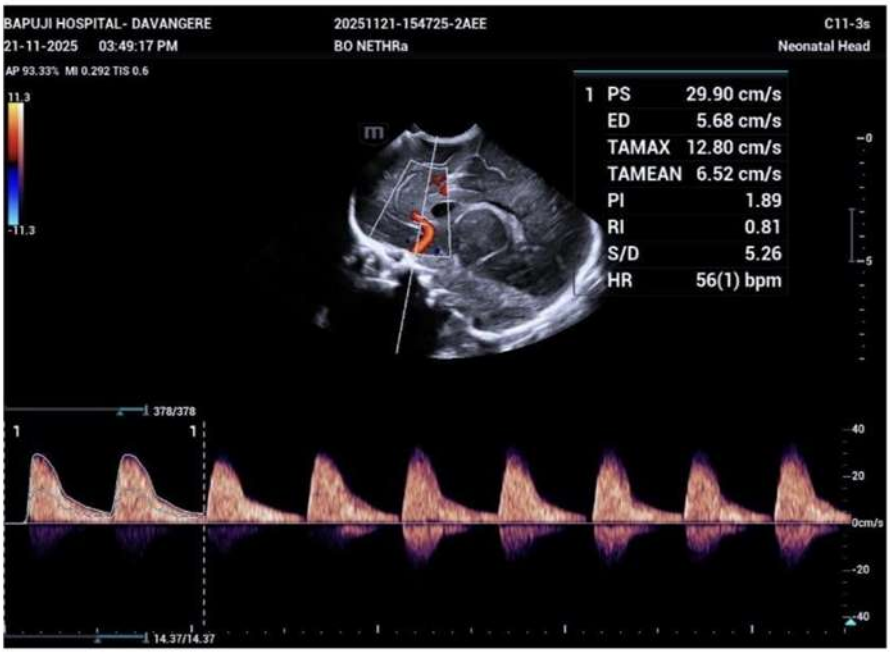
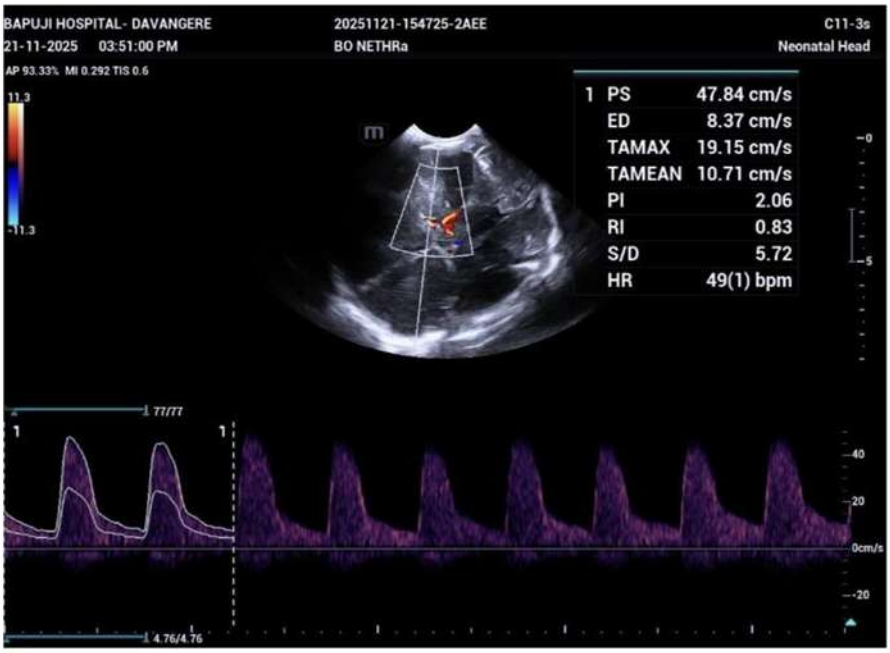
CASE-2: NSG in a 7 day old baby with HIE III stage mean resistance index (RI) of ACA was 0.81 and of MCA was 0.83.

RI of ACA:



RI of MCA:



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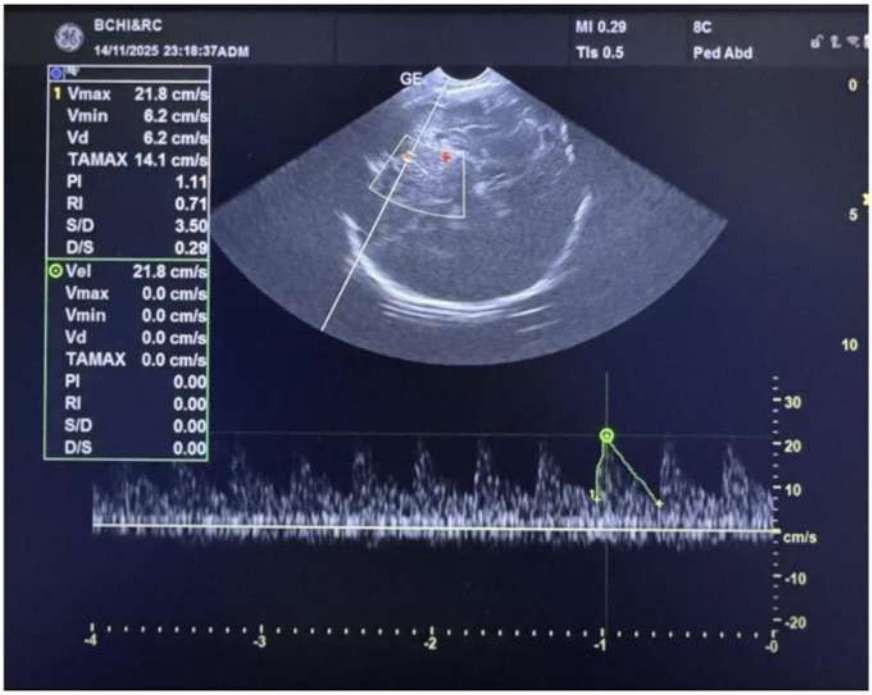
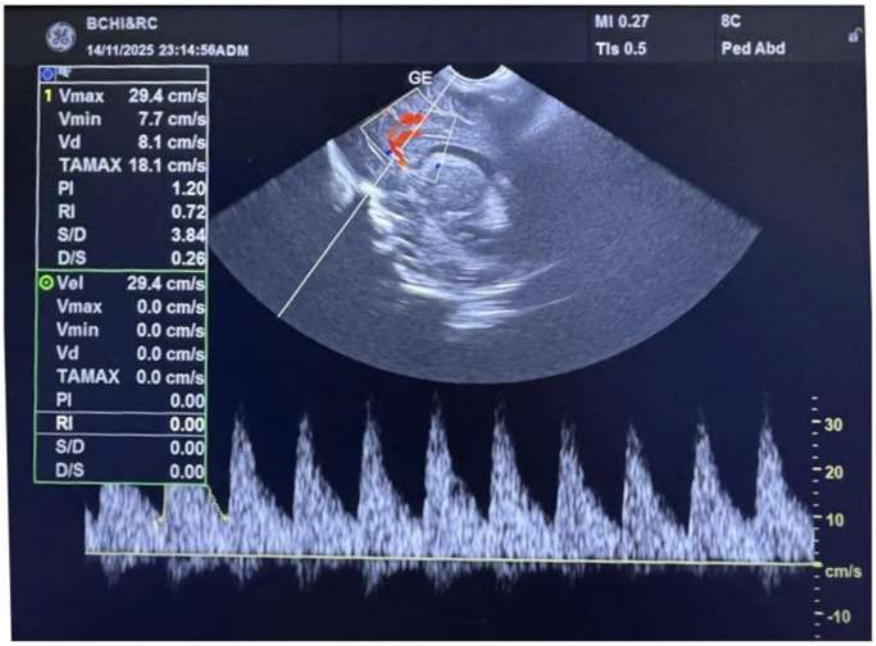
CONTROL

CASE-3: NSG in control that is normal neonates mean resistance index (RI) of ACA was in range of 0.68 ± 0.05 and of MCA was in range of 0.66 ± 0.05.

RI of MCA



RI of ACA



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Summary Of Case Series

The presented cases demonstrate progressive neurosonographic and Doppler abnormalities with increasing severity of hypoxic–ischemic encephalopathy. Mild HIE showed only subtle increases in cerebral echogenicity and Doppler resistive indices, whereas severe HIE was characterized by diffuse cerebral edema, loss of gray-white differentiation, marked elevation of ACA and MCA resistive indices, and poor clinical outcome.

These representative cases illustrate the ability of transcranial ultrasonography and Doppler evaluation to identify structural brain injury, assess cerebral hemodynamics, stratify disease severity, and provide valuable prognostic information in neonates with hypoxic–ischemic encephalopathy.

Results

Table 1: Comparison of cranial ultrasonography (USG) findings between case and control groups

Cranial USG Findings	Groups		Total	Chi-Square Tests	p-value
	Case	Control			
Cerebral edema	6	0	6	33.409	< 0.001*
Diffuse echogenicity	3	0	3		
Germinal matrix hemorrhage (Grade I)	1	0	1		
Germinal matrix hemorrhage (Grade II)	2	0	2		
Germinal matrix hemorrhage (Grade III)	3	0	3		
Normal	11	40	51		
PVL	4	0	4		
Total	30	40	70		

*Statistical significance p-value < 0.05, Chi-square test

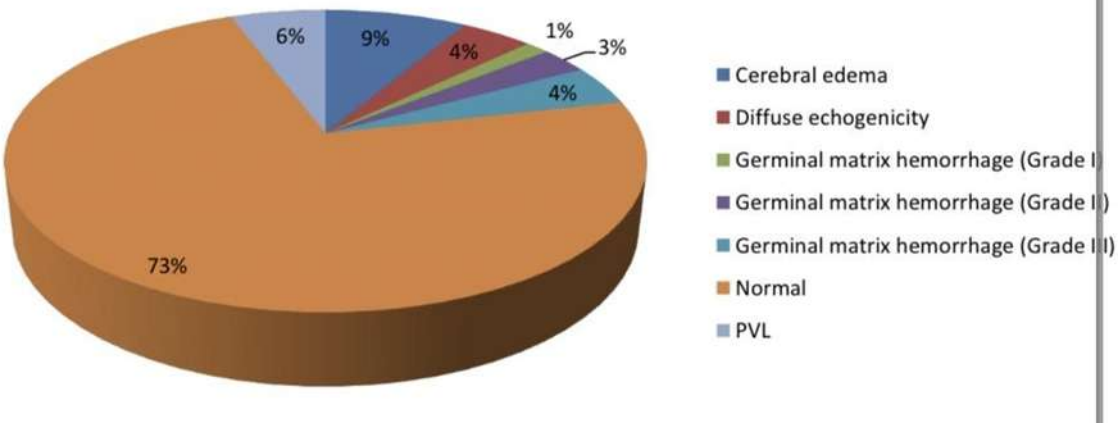

Figure 1: Distribution of cranial USG findings among case and control groups

Table 1 and Figure 1 shows that the cranial ultrasonography findings showed a distinct difference between case and control groups. Among the cases, abnormal findings such as cerebral edema(20.00%), periventricular leukomalacia (13.33%), germinal matrix hemorrhage of varying grades(20.00%) and diffuse echogenicity (10.00%) were observed, whereas none of these abnormalities were present in the control group. In contrast, normal cranial USG findings were seen in 36.67% ofcases and 100% of controls. The association between cranial USG findings and case-control statuswas found to be highly statistically significant (Chi-square = 33.409, p <

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0.001). These results indicate that abnormal cranial USG findings are strongly associated with the case group and reflect underlying neurological injury.

Table 2: Comparison of APGAR scores at different time intervals between HIE cases and controls

APGAR time(min)	Cases (Mean ± SD)	Controls (Mean ± SD)	t-value	p-value
1 min	2.40 ± 0.93	7.98 ± 0.86	-25.861	< 0.001*
5 min	4.83 ± 0.87	9.13 ± 0.79	-21.478	0.005*
10 min	6.63 ± 0.85	10.00 ± 0.00	-25.103	<0.001*

*Statistical significance p-value < 0.05, Independent t-test

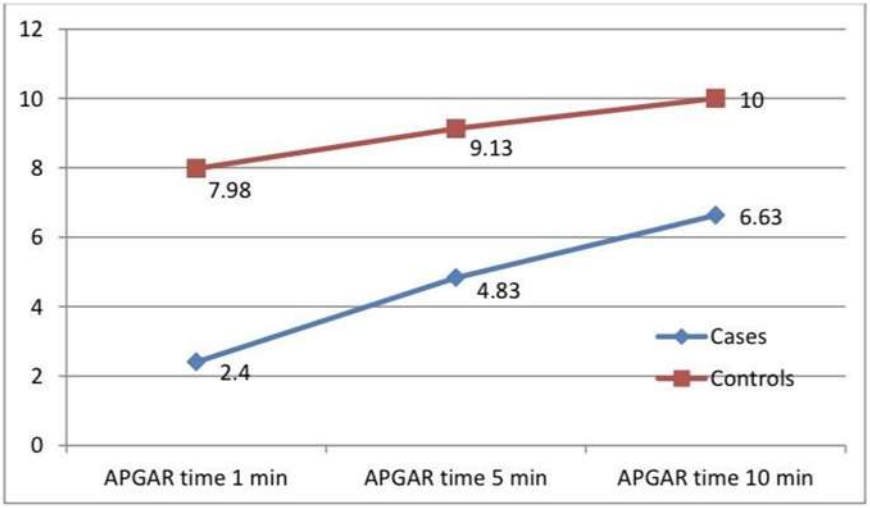

Figure 2: Line graph showing trend of mean APGAR scores at 1, 5, and 10 minutes in cases and controls

Table 2 and Figure 2 shows that the APGAR scores between HIE cases and controls at 1, 5, and 10 minutes revealed significantly lower scores in cases at all time intervals. At 1 minute, cases had a mean APGAR score of 2.40 ± 0.93 compared to 7.98 ± 0.86 in controls ($t = -25.861$, $p < 0.001$).Similarly, at 5 minutes, the mean score was 4.83 ± 0.87 in cases versus 9.13 ± 0.79 in controls ($t = -21.478$, $p = 0.005$), and at 10 minutes, it was 6.63 ± 0.85 in cases compared to 10.00 ± 0.00 in controls ($t = -25.103$, $p < 0.001$). These findings demonstrate a highly significant and persistent reduction in APGAR scores among neonates with HIE, indicating that low APGAR scores are strongly associated with hypoxic-ischemic encephalopathy and serve as an important early clinical predictor of disease severity and outcome.

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Table 3: Comparison of Doppler RI of ACA and MCA between HIE cases and controls

Doppler RI	Group	N	Mean	Median	SD	SE	t-test	p-value
RI (ACA)	Case	30	0.766	0.765	0.03	0.0054	13.2	< 0.001*
	Control	40	0.659	0.66	0.036	0.0057		
RI (MCA)	Case	30	0.765	0.76	0.037	0.0067	13.3	< 0.001*
	Control	40	0.66	0.66	0.03	0.0047		

*Statistical significance p-value < 0.05, Independent t-test

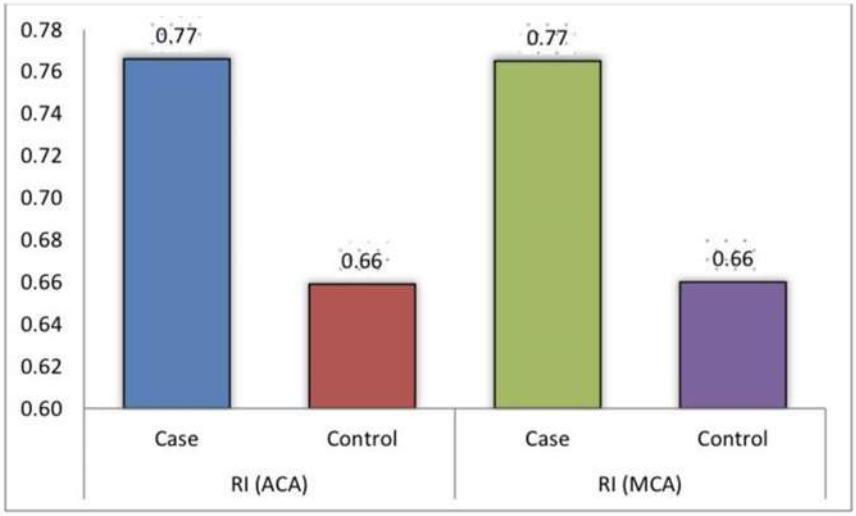

Figure 3: Bar diagram showing comparison of mean Doppler Resistive Index (ACA and MCA) between cases and controls

Table 3 and Figure 3 shows that the Doppler assessment of cerebral blood flow demonstrated significantly higher RI values in HIE cases compared to controls for both the ACA and MCA. The mean RI of ACA in cases was 0.766 ± 0.03 compared to 0.659 ± 0.036 in controls, with a highly significant difference ($t = 13.2$, $p < 0.001$). Similarly, the mean RI of MCA was 0.765 ± 0.037 in cases and 0.660 ± 0.03 in controls, which was also highly significant ($t = 13.3$, $p < 0.001$). The median values closely approximated the means in both groups, indicating a consistent distribution.These findings indicate markedly increased cerebral vascular resistance in neonates with hypoxic-ischemic encephalopathy, highlighting the crucial role of Doppler ultrasound in detecting altered cerebral hemodynamics and supporting its utility as a reliable diagnostic and prognostic tool in the evaluation and management of HIE.

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Table 4: Comparison of Doppler Resistive Index (ACA and MCA) across different stages of HIE

Variable	HIE Stage	Mean ± SD	Min–Max	F-test	p-value
ACA RI	Stage I	0.7358 ± 0.0100	0.72–0.75	105.59	< 0.001*
	Stage II	0.7754 ± 0.0113	0.76–0.79		
	Stage III	0.8120 ± 0.0084	0.80–0.82		
MCA RI	Stage I	0.7317 ± 0.0111	0.72–0.75	122.06	< 0.001*
	Stage II	0.7708 ± 0.0086	0.76–0.78		
	Stage III	0.8300 ± 0.0200	0.80–0.85		

*Statistical significance p-value < 0.05, ANOVA test

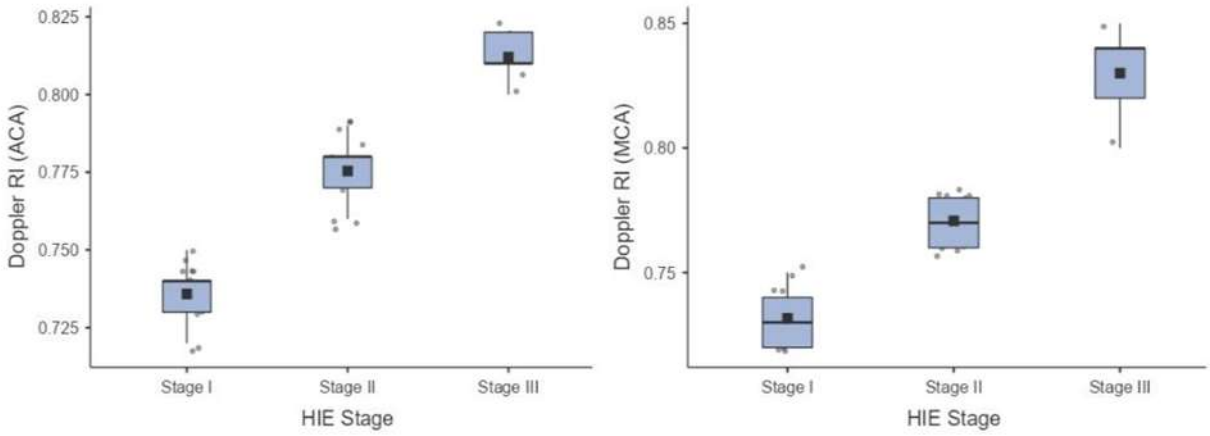

Figure 4: Distribution of ACA and MCA resistive index values across HIE stages

Table 4 and Figure 4 represent that the analysis of this study demonstrates a progressive increase in Doppler RI values of both the ACA and MCA with increasing severity of HIE. The mean ACA RI increased from 0.7358 ± 0.0100 in Stage I to 0.8120 ± 0.0084 in Stage III, while MCA RI showed a rise from 0.7317 ± 0.0111 to 0.8300 ± 0.0200 across the same stages. One-way ANOVA revealed these differences to be highly statistically significant for both ACA ($F = 105.59$, $p < 0.001$) and MCA ($F = 122.06$, $p < 0.001$). These findings indicate a strong association between increasing HIE severity and elevated cerebral Doppler indices. Thus, Doppler RI of ACA and MCA can serve as reliable, non-invasive markers for assessing the severity and progression of hypoxic ischemic encephalopathy in neonates.

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Table 5: Comparison of immediate outcome between HIE cases and controls

Outcome	Cases	%	Controls	%	Total	%	Chi-square tests	p-value
Death	4	13.33	0	0.00	4	5.71	5.657	0.017*
Recovered	26	86.67	40	100.00	66	94.29		
Total	30	100.00	40	100.00	70	100.00		

*Statistical significance p-value < 0.05, Chi-square test

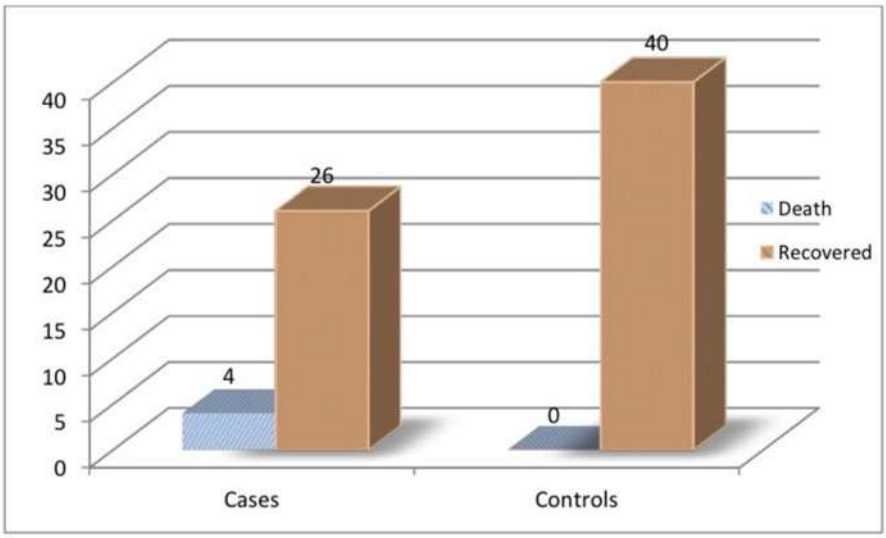

Figure 5: Bar diagram showing distribution of immediate outcomes (Death and Recovery) among cases and controls

Table 5 and Figure 5 shows that the comparison of immediate outcomes between HIE cases and controls revealed that all neonates in the control group recovered (100%), whereas among cases,13.33% resulted in death and 86.67% recovered. Overall, mortality was observed only in the HIE group, accounting for 5.71% of the total study population. The association between HIE status and immediate outcome was found to be statistically significant (χ^2 = 5.657, p = 0.017). These findings indicate that neonates with hypoxic-ischemic encephalopathy have a significantly higher risk of adverse outcomes, particularly mortality, highlighting the importance of early identification and timely intervention to improve prognosis.

Discussion

The present case–control study evaluated 70 neonates (30 cases and 40 controls) to analyze clinical profile, perinatal factors, cranial ultrasonography findings, and Doppler indices in HIE.The proportion of cases (42.86%) and controls (57.14%) in this study is comparable to similar observational neonatal studies, where slightly higher control groups are often included to improve statistical comparison.

In terms of gender distribution, females constituted 60% of cases while males accounted for 65% of controls . Although some studies suggest male neonates are more vulnerable to hypoxic injury due to hormonal and neuroprotective differences, other reports have shown inconsistent gender associations. Thus, the gender variation observed in this study may not independently influence HIE occurrence.

Antenatal risk factors such as pregnancy-induced hypertension (30%) and prolonged labor (30%) were more frequent in cases compared to controls (15% and 12.5%, respectively), although the association was not statistically significant (p = 0.102) .

The clinical presentation in this study showed a highly significant association with HIE (p <0.001), where

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coma (20%), lethargy (16.67%), poor feeding (23.33%), and seizures (13.33%) were observed exclusively in cases, while 100% of controls were clinically normal .

Cranial ultrasonography findings in this study revealed abnormalities such as cerebral edema(20%), germinal matrix hemorrhage (20% combined grades), periventricular leukomalacia(13.33%), and diffuse echogenicity (10%) among cases, while 100% of controls had normal scans ($p < 0.001$) . These findings are consistent with studies by Rutherford et al., which highlight that hypoxic injury commonly affects periventricular white matter and basal ganglia regions. Although MRI is more sensitive, cranial USG remains a valuable, accessible tool in early diagnosis, especially in low-resource settings.

Among perinatal characteristics, the mean birth weight was significantly lower in cases (3.02 ± 0.42 kg) compared to controls (3.23 ± 0.35 kg; $p = 0.014$), whereas gestational age was comparable ($p = 0.519$).

APGAR scores at 1, 5, and 10 minutes were significantly reduced in cases (2.40, 4.83, and 6.63 respectively) compared to controls (7.98, 9.13, and 10.00; $p < 0.001$). This persistent depression in APGAR scores reflects severe perinatal asphyxia.

A key finding of this study is the significantly elevated Doppler RI in both ACA (0.766 ± 0.03) and MCA (0.765 ± 0.037) in cases compared to controls (0.659 and 0.660, respectively; $p <0.001$). This indicates increased cerebral vascular resistance, likely due to impaired auto regulation following hypoxic injury.

Furthermore, a progressive increase in RI values was observed with increasing HIE severity, with ACA RI rising from 0.7358 in Stage I to 0.8120 in Stage III, and MCA RI from 0.7317 to 0.8300 ($p < 0.001$) . Thus, Doppler indices can serve as reliable non-invasive markers for staging and prognosis.

In terms of outcomes, mortality was observed in 13.33% of cases, while all controls survived($p = 0.017$). This finding is consistent with global data indicating that HIE remains a significant cause of neonatal mortality.

Early interventions such as therapeutic hypothermia have been shown to improve survival and neurological outcomes, emphasizing the need for early detection.

Overall, the present study findings strongly correlate with previously published literature and highlight that Doppler ultrasound, combined with clinical and imaging findings, plays a crucial role in early diagnosis, severity assessment, and prognostication of HIE.

Conclusion

The present study highlights the significant clinical and diagnostic differences between neonates with hypoxic-ischemic encephalopathy and healthy controls, emphasizing the importance of early identification and comprehensive evaluation. The findings demonstrate that fetal distress was present among all cases, establishing it as a major contributing factor for hypoxic-ischemic encephalopathy.

Clinical manifestations such as poor feeding, coma, lethargy, and seizures were observed exclusively in affected neonates, showing a strong association with disease severity.

Cranial ultrasonography revealed that abnormalities including cerebral edema, germinal matrix hemorrhage, and periventricular leukomalacia were confined to the case group, while all controls exhibited normal findings, reinforcing its role as an important bedside diagnostic tool. Furthermore,Doppler evaluation showed significantly elevated resistive index values in both anterior cerebral artery and middle cerebral artery among cases compared to controls, indicating altered cerebral hemodynamics. A progressive increase in resistive index values with advancing stages of hypoxic-ischemic encephalopathy further supports its utility in assessing disease severity.

Additionally, significantly lower APGAR scores at different time intervals and reduced birth weight among cases underline their prognostic importance. The presence of mortality only in affected neonates further emphasizes the seriousness of the condition. Overall, this study concludes that a combination of clinical assessment, cranial ultrasonography, and Doppler indices provides a reliable and non-invasive approach for early diagnosis, severity grading, and outcome prediction in neonates with hypoxic-ischemic encephalopathy.

In conclusion, transcranial ultrasonography and cerebral Doppler evaluation are valuable diagnostic and prognostic tools in neonatal hypoxic–ischemic encephalopathy. Measurement of ACA and MCA

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resistive indices provides objective assessment of cerebral hemodynamics and correlates strongly with disease severity. Incorporation of cerebral Doppler evaluation into routine neonatal assessment protocols may facilitate early diagnosis, appropriate risk stratification, therapeutic decision-making, and improved neonatal outcomes.

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