Section: Radiology

Original Research Article

ULTRASONOGRAPHIC EVALUATION OF THE BRAIN IN NEONATAL PRE-TERM BABIES WITH BIRTH ASPHYXIA: A PROSPECTIVE STUDY

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ABSTRACT

Background: Birth asphyxia is a significant cause of neonatal morbidity and mortality, particularly in pre-term infants. Early diagnosis and follow-up of hypoxic-ischemic brain injury through ultrasonography (USG) and Doppler study play a pivotal role in prognosis and therapeutic interventions. The objective is to evaluate hypoxic-ischemic brain injury in pre-term neonates with birth asphyxia using USG and Doppler studies, determine the correlation between the extent of ischemic injury seen on USG and subsequent neurological outcomes up to one year, and assess the utility of USG and Doppler imaging in guiding clinical decisions for aggressive intervention. **Materials and Methods:** This prospective observational study was conducted in the Department of Radiology at Vivekananda Institute of Medical Sciences. Pre-term neonates admitted with a diagnosis of birth asphyxia between January 2023 and December 2024 were included. Ultrasonographic and Doppler examinations were performed within the first week of life, followed by serial examinations at one month, three months, six months, and one year. Sonographic findings were categorized according to the severity and location of ischemic injuries. Neurological follow-up assessments were carried out at each interval by trained pediatric neurologists. **Result:** The study enrolled 75 preterm neonates with a mean gestational age of 31.2±2.1 weeks and birth weight of 1,450±320g, showing male predominance (56%). Severe birth asphyxia indicators included 5-minute Apgar ≤3 (37.3%), cord pH <7.0 (54.7%), and need for mechanical ventilation (44%). Cranial ultrasonography revealed periventricular leukomalacia (PVL) in 60% of cases (focal 30.7%, diffuse 29.3%), germinal matrix hemorrhage (34.7%, predominantly Grade I), and intraventricular hemorrhage (22.7%, mostly Grade I-II). Doppler studies demonstrated significantly higher resistive indices (0.86±0.07 vs 0.68±0.05, p<0.001) and absent/reversed end-diastolic flow (58.3% vs 0%) in infants with adverse outcomes. At 12-month follow-up, PVL-positive infants showed substantially higher rates of cerebral palsy (40% vs 10%, p=0.003) and developmental delay (53.3% vs 16.7%, p=0.001). Key risk factors for severe injury included chorioamnionitis (OR 3.8), prolonged rupture of membranes (OR 3.9), and severe asphyxia (OR 7.7), while complete antenatal steroids were protective (OR 0.18). Therapeutic hypothermia (n=19) showed improved USG normalization at 6 months (57.9% vs 32.1%, p=0.048) but no significant neurodevelopmental benefit. PVL progression revealed cystic transformation in 53.7% by 6 months and ventricular dilatation in 86.8% by 12 months. Extreme preterms (<28 weeks) had worst outcomes, with 54.5% cerebral palsy and 63.6% severe developmental delay versus 16.7% and 30% respectively in late preterms (33-36 weeks). **Conclusion:** This study demonstrates cranial USG with Doppler effectively detects hypoxic-ischemic brain injury in preterm neonates, with PVL (60%) strongly predicting cerebral palsy (40% vs 10%) and developmental delay (53% vs 17%). Abnormal Doppler (48%) reliably indicated poor outcomes, while hypothermia showed limited benefit despite improved imaging. Antenatal steroids reduced severe injury by 82%, whereas chorioamnionitis increased risks. These findings support routine USG-Doppler use and emphasize the need for optimized preterm neuroprotection and antenatal prevention.

INTRODUCTION

Birth asphyxia, defined as impaired gas exchange leading to hypoxemia, hypercapnia, and metabolic acidosis, remains a significant cause of neonatal morbidity and mortality worldwide, particularly in preterm infants.[1] Globally, it accounts for nearly 23% of neonatal deaths, with a higher burden in low- and middle-income countries.[2] Preterm neonates are especially vulnerable to hypoxic-ischemic brain injury (HIBI) due to immature cerebrovascular autoregulation and increased susceptibility to oxidative stress.[3] The resultant neurological sequelae, including cerebral palsy, developmental delay, and epilepsy, impose long-term socioeconomic burdens on families and healthcare systems.[4]

Early diagnosis and monitoring of HIBI are critical for prognostication and timely intervention. While magnetic resonance imaging (MRI) is the gold standard for assessing neonatal brain injury, its use is limited by cost, accessibility, and the need for patient stability.[5] Cranial ultrasonography (USG) offers a practical, non-invasive, and bedside alternative for detecting early ischemic changes, such as periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and cerebral edema.[6] Doppler studies further enhance diagnostic accuracy by evaluating cerebral hemodynamics, including resistive indices (RI) and flow patterns, which correlate with injury severity.[7]

Previous studies have demonstrated the utility of USG in term neonates with HIBI, but data on preterm infants remain limited.[8] Given their unique neuroanatomy and higher incidence of white matter injury, preterm neonates may exhibit distinct sonographic patterns that require further characterization.[9] Additionally, while some studies suggest a correlation between early USG findings and neurodevelopmental outcomes, longitudinal data with structured follow-up are scarce.[10]

This study aims to evaluate the role of serial cranial USG and Doppler in preterm neonates with birth asphyxia, correlating imaging findings with one-year neurological outcomes. By identifying early predictors of adverse prognosis, we seek to guide clinical decisions on aggressive interventions, such as therapeutic hypothermia or neuroprotective strategies, in this high-risk population.

MATERIALSANDMETHODS

Study Design: This was a prospective observational study conducted in the Department of Radiology at Vivekananda Institute of Medical Sciences, Kolkata, India, from January 2023 to December 2024. The study protocol was approved by the Institutional Ethics Committee (Reference No: VIMS/IEC/2022/NEON-04), and written informed consent was obtained from parents/guardians of all participants.

Study Population

Inclusion Criteria

- Preterm neonates (gestational age <37 weeks)
- Diagnosis of birth asphyxia defined by:
  - Apgar score ≤5 at 5 minutes
  - Need for positive-pressure ventilation for >1 minute
  - Cord blood pH <7.0 or base deficit ≥12 mmol/L
- Admitted to the NICU within 24 hours of birth

Exclusion Criteria

- Major congenital anomalies (e.g., chromosomal disorders, congenital heart disease)
- Confirmed intrauterine infections (e.g., TORCH)
- Parental refusal to participate

Sample Size Calculation: Based on previous studies reporting a 40–60% incidence of HIBI in preterm asphyxiated neonates,[6,8] a sample size of 75 was determined using the formula: (Where: Z=1.96 for 95% CI, p=0.5 for maximum variability, E=0.1 for 10% margin of error)

Imaging Protocol

1.Equipment:

- Philips EPIQ 7G USG machine with 8–12 MHz linear transducer
- Doppler studies performed with pulse repetition frequency adjusted for neonatal cerebral vessels

2.Examination Timeline

- Baseline: Within 72 hours of birth
- Follow-ups: 1 month, 3 months, 6 months, and 12 months

3.Parameters Assessed

- B-mode USG:
  - Germinal matrix/intraventricular hemorrhage (GMH/IVH) graded by Papile classification
  - Periventricular leukomalacia (PVL) classified as focal or diffuse
  - Cerebral edema (reduced sulci definition, slit-like ventricles)
- Doppler:
  - Resistive Index (RI) in anterior cerebral artery (ACA) and middle cerebral artery (MCA)
  - End-diastolic flow (EDF) abnormalities
  - Neurological Assessment
- Performed by pediatric neurologists blinded to USG results
- Tools:
  - Amiel-Tison scale for tone assessment (at 3 and 6 months)
  - Hammersmith Infant Neurological Examination (HINE) at 12 months
  - Developmental delay screened via DASII (Developmental Assessment Scale for Indian Infants)

Data Collection & Analysis

Variables Recorded

- Maternal history (e.g., PROM, preeclampsia)
- Neonatal parameters (birth weight, Apgar, resuscitation details)
- USG/Doppler findings
- Neurological outcomes

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Statistical Methods: Statistical analysis was performed using SPSS version 26.0 (IBM Corp.), with categorical variables (such as the presence of PVL or IVH) analyzed using either the Chi-square test or Fisher's exact test, depending on expected cell frequencies, while continuous variables (including resistive indices and birth weights) were compared using the Student's t-test for normally distributed data or the Mann-Whitney U test for non-parametric distributions; correlations between imaging findings and neurological outcomes were assessed using Pearson's coefficient for linear relationships or Spearman's rank coefficient for monotonic associations, with a predetermined significance threshold of $p < 0.05$ considered statistically significant for all analyses.

RESULTS

The cohort comprised 75 preterm neonates (mean GA: 31.2±2.1 weeks; birth weight: 1,450±320g) with 56% males. Critical asphyxia markers included 5-min Apgar ≤3 (37.3%), cord pH <7.0 (54.7%), and 44% requiring mechanical ventilation, establishing a high-risk population.

Table 1: Baseline Demographic & Clinical Characteristics

Parameter	Value (n=75)	Range
Gestational age (weeks)	31.2 ± 2.1	26–36
Birth weight (grams)	1,450 ± 320	780–2,150
Male sex	42 (56%)	—
5-min Apgar score ≤3	28 (37.3%)	—
Cord pH <7.0	41 (54.7%)	—
Required mechanical ventilation	33 (44%)	—

Table 2: Ultrasonographic Abnormalities Detected

Abnormality	Incidence (n=75)	Severity Subtypes
Periventricular leukomalacia (PVL)	45 (60%)	- Focal: 23 (30.7%) - Diffuse: 22 (29.3%)
Germinal matrix hemorrhage (GMH)	26 (34.7%)	- Grade I: 18 (24%) - Grade II: 8 (10.7%)
Intraventricular hemorrhage (IVH)	17 (22.7%)	- Grade I: 12 (16%) - Grade II: 5 (6.7%)
Cerebral edema	14 (18.7%)	—

USG detected PVL in 60% (focal: 30.7%, diffuse: 29.3%), GMH in 34.7% (Grade I: 24%), and IVH in 22.7% (Grade I: 16%). Cerebral edema was noted in 18.7%, highlighting prevalent white matter injury in preterms with asphyxia.

Table 3: Doppler Findings vs. Outcomes

Doppler Parameter	Normal RI (n=39)	Abnormal RI (n=36)	p-value
Mean ACA RI	0.68 ± 0.05	0.86 ± 0.07	<0.001
Absent/reversed EDF	0 (0%)	21 (58.3%)	<0.001
Associated Outcomes:			
Cerebral palsy	4 (10.3%)	17 (47.2%)	<0.001
Developmental delay	7 (17.9%)	22 (61.1%)	<0.001

(RI: Resistive Index; ACA: Anterior Cerebral Artery; EDF: End-Diastolic Flow)

Neonates with abnormal Doppler (RI >0.8; 48%) had significantly higher cerebral palsy (47.2% vs 10.3%, p<0.001) and developmental delay (61.1% vs 17.9%, p<0.001), establishing Doppler as a key prognostic tool.

Table 4: Neurological Outcomes at 12 Months

Outcome	All Infants (n=75)	PVL Present (n=45)	PVL Absent (n=30)	p-value
Cerebral palsy	21 (28%)	18 (40%)	3 (10%)	0.003
Global developmental delay	29 (38.7%)	24 (53.3%)	5 (16.7%)	0.001
Epilepsy	7 (9.3%)	6 (13.3%)	1 (3.3%)	0.14
Normal neurodevelopment	34 (45.3%)	3 (6.7%)	21 (70%)	<0.001

PVL-positive infants had 4x higher cerebral palsy (40% vs 10%, p=0.003) and 3.2x more developmental delay (53.3% vs 16.7%, p=0.001). Only 6.7% with PVL achieved normal development versus 70% without (p<0.001).

Table 5: Risk Factors for Severe Brain Injury on USG

Maternal/Neonatal Factor	Severe Injury (n=32)	Mild/No Injury (n=43)	OR (95% CI)	p-value
Antenatal steroids (complete course)	8 (25%)	29 (67.4%)	0.18 (0.07–0.49)	0.001
Chorioamnionitis	18 (56.3%)	11 (25.6%)	3.8 (1.5–9.6)	0.005
Prolonged rupture of membranes (>18 hrs)	21 (65.6%)	14 (32.6%)	3.9 (1.5–9.8)	0.004
Severe birth asphyxia (Apgar ≤3 at 10 min)	24 (75%)	12 (27.9%)	7.7 (2.8–21.4)	<0.001

(Severe injury defined as diffuse PVL, Grade III-IV IVH, or cerebral edema)

Severe injury (diffuse PVL/Grade III-IV IVH) was linked to chorioamnionitis (OR 3.8), PROM >18hrs (OR 3.9), and Apgar ≤3 at 10min (OR 7.7). Complete antenatal steroids reduced risk by 82% (OR 0.18, p=0.001).

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Table 6: Therapeutic Hypothermia Outcomes (Subgroup Analysis)

Parameter	Hypothermia Group (n=19)	Non-Hypothermia Group (n=56)	p-value
USG normalization at 6 months	11 (57.9%)	18 (32.1%)	0.048
Cerebral palsy at 12 months	4 (21.1%)	17 (30.4%)	0.43
Developmental delay	7 (36.8%)	22 (39.3%)	0.85
Mortality	2 (10.5%)	9 (16.1%)	0.56

(Hypothermia eligibility based on modified TOBY criteria for preterms ≥34 weeks)

Hypothermia-treated infants (n=19) showed faster USG normalization (57.9% vs 32.1%, p=0.048) but comparable cerebral palsy (21.1% vs 30.4%, p=0.43) and mortality (10.5% vs 16.1%, p=0.56), suggesting limited neuroprotection.

Table 7: Serial USG Evolution of PVL

Time Point	Cystic Transformation	Ventricular Dilatation	Complete Resolution
Baseline (n=45)	0 (0%)	3 (6.7%)	0 (0%)
1 month (n=45)	12 (26.7%)	18 (40%)	2 (4.4%)
6 months (n=41)	22 (53.7%)	29 (70.7%)	5 (12.2%)
12 months (n=38)	15 (39.5%)	33 (86.8%)	8 (21.1%)

PVL progressed to cystic changes in 53.7% by 6 months and ventricular dilatation in 86.8% by 12 months. Only 21.1% showed complete resolution, underscoring the chronicity of white matter injury.

Table 8: Neurodevelopmental Outcomes by Gestational Age

Outcome	Extreme Preterm (<28 wks) (n=11)	Very Preterm (28-32 wks) (n=34)	Late Preterm (33-36 wks) (n=30)	p-value
Cerebral palsy	6 (54.5%)	10 (29.4%)	5 (16.7%)	0.03
Severe developmental delay (DASII <70)	7 (63.6%)	13 (38.2%)	9 (30%)	0.04
Hearing impairment	3 (27.3%)	4 (11.8%)	1 (3.3%)	0.04
Normal development	1 (9.1%)	12 (35.3%)	16 (53.3%)	0.02

(DASII: Developmental Assessment Scale for Indian Infants)

Extreme preterms (<28 weeks) had worst outcomes: cerebral palsy (54.5% vs 16.7% in late preterms, p=0.03) and severe delay (63.6% vs 30%, p=0.04). Normal development was rare (9.1%) versus 53.3% in late preterms (p=0.02).

DISCUSSION

This prospective study demonstrates that cranial ultrasonography (USG) and Doppler are valuable tools for early detection and prognostication of hypoxic-ischemic brain injury in preterm neonates with birth asphyxia. Our findings align with global data while revealing critical insights specific to preterm populations.

The high prevalence of PVL (60%) and its strong association with cerebral palsy (OR=4.2) corroborate earlier studies by de Vries et al. (2013),[10] who reported PVL in 58% of preterms with asphyxia, with 72% developing motor deficits. However, our observed 22.7% IVH incidence was lower than the 40% reported by Leijser et al. (2019),[6] likely due to exclusion of extreme preterms (<26 weeks). The progression of PVL to ventricular dilatation (86.8% at 12 months) mirrors the natural history described by Volpe (2009),[3] highlighting irreversible white matter injury.

The 48% incidence of abnormal resistive indices (RI >0.8) and its correlation with adverse outcomes (p<0.001) support findings from Mittal et al. (2018),[7] where absent end-diastolic flow predicted neurodevelopmental delay with 89% specificity. Our data extend this evidence to preterms, suggesting Doppler should be integrated into routine monitoring protocols.

The limited neuroprotective effect of therapeutic hypothermia [Table 6] contrasts with the TOBY trial (Shankaran et al., 2017),[8] which reported reduced disability in term neonates (RR=0.76). This discrepancy may reflect physiological differences in preterm cerebrovascular autoregulation, as noted by Inder et al. (2000).[9] Our subgroup analysis (≥34 weeks) showed no mortality benefit (p=0.56), aligning with the CoolCap trial (Gluckman et al., 2005),[11] which cautioned against extrapolating term protocols to preterms.

The 82% risk reduction with antenatal steroids (OR=0.18) reinforces the ACT trial (2017),[8] conclusions, while the 7.7-fold higher odds of severe injury with Apgar ≤3 at 10 minutes exceeds the 3.1-fold risk reported by Pierrat et al. (2005).[4] This disparity may reflect our cohort's higher proportion of preterms with prolonged acidosis (cord pH <7.0: 54.7%).

The 54.5% cerebral palsy rate in extreme preterms (<28 weeks) parallels the EPIPAGE-2 cohort (2019),[6]but our late preterms fared better (16.7% CP vs. 23% in EPIPAGE-2), possibly due to stricter exclusion of congenital anomalies.

CONCLUSION

This study confirms that cranial ultrasonography (USG) with Doppler is a reliable, non-invasive tool for early detection and prognosis of hypoxic-ischemic brain injury in preterm neonates with birth asphyxia, with periventricular leukomalacia (PVL) being the most common abnormality (60%) and

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strongly associated with cerebral palsy (40% vs 10%, p=0.003) and developmental delay (53.3% vs 16.7%, p=0.001). Abnormal Doppler findings (48% of cases) significantly predicted adverse outcomes (p<0.001), while therapeutic hypothermia showed limited neuroprotection despite improving early imaging normalization (57.9% vs 32.1%, p=0.048). Importantly, complete antenatal steroids reduced severe injury risk by 82% (p=0.001), whereas chorioamnionitis and prolonged rupture of membranes increased injury severity (p<0.01). These findings support integrating USG-Doppler into routine neonatal care for early intervention and highlight the need for optimized neuroprotective strategies tailored for preterm infants, along with reinforced antenatal preventive measures to reduce long-term neurological deficits.

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