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Predictive Value of Transcranial Doppler Parameters for Intracerebral Hemorrhage in Preterm Neonates.

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Abstract

Background: Preterm neonates (≤ 32 weeks gestational age) are highly vulnerable to intracerebral hemorrhage (ICH) and intraventricular hemorrhage (IVH) due to anatomical fragility of the subependymal germinal matrix and immature cerebral pressure-passive autoregulation. Identifying early hemodynamic fluctuations that precede hemorrhagic injury is critical for implementing timely neuroprotective interventions. ***Methods:*** A prospective observational cohort study was conducted over a 6-month period in the ESIC Medical College and PGIMSR, Kalaburagi. A total of N = 60 preterm neonates (≤ 32 weeks gestational age) were enrolled. Serial bedside transcranial Doppler (TCD) ultrasonography of the anterior cerebral artery (ACA) was performed on Days 1, 3, and 7 of life. Key hemodynamic variables analyzed included Resistive Index (RI), Pulsatility Index (PI), Peak Systolic Velocity (PSV), End-Diastolic Velocity (EDV), and Mean Flow Velocity (Vm). Cranial ultrasonography was performed concurrently to detect and grade ICH. ***Results:*** Among the enrolled cohort, 18 neonates (30%) developed ICH. Neonates who developed ICH exhibited significantly higher vascular resistance and lower diastolic perfusion early after birth. On Day 1 of life, mean RI was significantly elevated in the ICH group compared to the non-ICH group (0.76 ± 0.05 vs. 0.66 ± 0.04, $p < 0.001$), accompanied by an elevated PI (1.68 ± 0.22 vs. 1.32 ± 0.18, $p < 0.001$) and reduced EDV (4.1 ± 1.1 cm/s vs. 6.2 ± 1.4 cm/s, $p < 0.001$). Receiver operating characteristic (ROC) analysis demonstrated that a Day 1 RI ≥ 0.72 predicted ICH with a sensitivity of 83.3% and a specificity of 85.7% (AUC = 0.89). ***Conclusion:*** Serial bedside TCD assessment of cerebral hemodynamics during the first week of life provides valuable predictive indicators for ICH in preterm neonates. Elevated early vascular resistance indices (RI and PI) serve as robust, non-invasive biomarkers for early risk stratification.

Keywords: Transcranial Doppler; Resistive Index; Preterm Neonates; Intracerebral Hemorrhage; Cerebral Hemodynamics.

INTRODUCTION

Intracerebral hemorrhage (ICH) and intraventricular hemorrhage (IVH) are amongst the leading causes of neonatal mortality and long-term neurodevelopmental morbidity in survivors. These include cerebral palsy, post hemorrhagic hydrocephalus and cognitive impairment in surviving premature infants. [1,2] According to a few studies, the pathogenesis of hemorrhagic brain injury in preterm infants born at ≤ 32 weeks of gestation is multifactorial. Primarily originated from the anatomical fragility of the subependymal germinal matrix which is a highly vascularized brain area containing immature endothelial vessels. Nevertheless, they lack structural connective tissue support. [1,3]

The immaturity of cerebral autoregulation also contributes to this microvascular vulnerability. While healthy full-term neonates and adults are able to maintain constant cerebral blood flow (CBF) across a wide physiological range of systemic arterial blood pressures, premature infant are often believed to demonstrate pressure-passive cerebral circulation [2,5]. During this phase, systemic hypotension, reperfusion surges or blood gas changes manages to transmit directly into the brain microvasculature, causing damage to the fragile germinal matrix capillaries resulting in shear stress next rupture.The standard two-dimensional cranial ultrasonography (CUS) remains the bedside modality of choice for the detection of structural brain lesions once bleeding has occurred. However, it cannot realize the temporal detection of hemodynamic disturbances until anatomical tissue failure takes place [4, 6].

Transcranial Doppler (TCD) ultrasonography using the anterior fontanelle allows for real time assessment of cerebral vascular event and quantification of flow velocity in the major cranial arteries as well as estimation of the vascular impedance parameters such as Resistive Index (RI) and Pulsatility Index (PI) [4,6].Although isolated Doppler indices have been studied in various neonatal disorders, formal evaluation of continuous or serial hemodynamic tracking in the transitional first week of life in extreme prematurity is still needed [5,6]. The aim of the study was to assess the predictive

capacity of serial TCD hemodynamic parameters on Days 1, 3 and 7 of life for the development of intracerebral hemorrhage (ICH) in premature neonates admitted to ESIC Medical College and PGIMSR , Kalaburagi.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational cohort study was conducted over a continuous 6-month period in the ESIC Medical College and PGIMSR , Kalaburagi. The institutional ethics review board approved the study protocol, and written informed consent was obtained from the parents or legal guardians of all participating neonates prior to enrollment.

Patient Demographics and Eligibility Criteria

A total of N = 60 preterm neonates delivered at or below 32 weeks of gestational age (≤ 32 weeks) were enrolled sequentially upon admission to the NICU.

Inclusion Criteria: Inborn preterm neonates with gestational age ≤ 32 weeks, admitted to the NICU within 6 hours of birth, whose parents provided consent.
Exclusion Criteria: Neonates with major congenital chromosomal anomalies, complex congenital heart disease (excluding patent ductus arteriosus), severe perinatal asphyxia (5-minute Apgar score < 3), or absence of an adequate transfontanelle acoustic window.

Study Protocol and Serial Doppler Measurements

Bedside cerebral hemodynamic assessments were conducted using a high-resolution color Doppler ultrasound system equipped with a 5–8 MHz phased-array pediatric transducer. To capture critical hemodynamic shifts during the immediate neonatal transition, serial scans were scheduled at three standardized timepoints: Day 1 of life (12–24 hours post-birth), Day 3 of life (60–72 hours post-birth), and Day 7 of life (156–168 hours post-birth). All examinations were performed with the infant in a quiet, resting supine position inside the incubator, avoiding sedation or environmental disturbance. The transducer was placed gently over the anterior fontanelle in the sagittal and coronal planes to identify the anterior cerebral artery (ACA) around the corpus callosum. The Doppler angle of incidence was maintained below 30° to ensure measurement accuracy.

Variables Analyzed

At each timepoint, three consecutive arterial pulse waveforms were recorded, and quantitative parameters were averaged including Peak Systolic Velocity (PSV, cm/s), End-Diastolic Velocity (EDV, cm/s), and Mean Flow Velocity (Vm, cm/s).
Resistive Index (RI): Calculated according to Pourcelot's formula: RI = (PSV − EDV) / PSV.
Pulsatility Index (PI): Calculated using the formula: PI = (PSV − EDV) / Vm.

Outcome Determination

Standard two-dimensional cranial ultrasonography was performed concurrently with TCD evaluations on Days 1, 3, and 7, and repeated at 14 days of life or clinically indicated intervals by radiologist. Intracerebral and intraventricular hemorrhages were classified according to the Papile grading system [2]. Patients were stratified into two groups: the ICH Group (neonates developing any grade of ICH/IVH during the study period) and the Non-ICH Group (neonates with normal serial cranial neuroimaging).

Statistical Analysis

Continuous variables were assessed for normality using the Shapiro-Wilk test and presented as mean ± standard deviation (SD). Intergroup comparisons between the ICH and Non-ICH groups were conducted using Student's independent t-test or the Mann-Whitney U test for continuous data, and Pearson's χ^2 test or Fisher's exact test for categorical data. Receiver operating characteristic (ROC) curves were constructed to determine the area under the curve (AUC), optimal predictive cutoffs, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for TCD parameters. A two-tailed p-value < 0.05 was considered statistically significant.

RESULTS

During the 6-month study period, 60 preterm neonates meeting the inclusion criteria completed the serial monitoring protocol. Among them, 18 neonates (30.0%) developed intracerebral/intraventricular hemorrhage (ICH Group), while 42 neonates (70.0%) remained free of hemorrhage (Non-ICH Group). The majority of hemorrhages (14/18, 77.8%) were diagnosed within the first 72 hours of life. Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences in gestational age, birth weight, sex distribution, Apgar scores, or antenatal steroid exposure (Table 1).

Table 1: Baseline Demographic and Clinical Characteristics of the Study Cohort

Clinical Variable	Total Cohort (N=60)	ICH Group (n=18)	Non-ICH Group (n=42)	p-value
Gestational Age (weeks), Mean ± SD	29.8 ± 1.6	29.3 ± 1.7	30.0 ± 1.5	0.12
Birth Weight (grams), Mean ± SD	1240 ± 215	1180 ± 230	1265 ± 205	0.16
Male Sex, n (%)	32 (53.3%)	10 (55.6%)	22 (52.4%)	0.82
Antenatal Steroid Coverage, n (%)	48 (80.0%)	13 (72.2%)	35 (83.3%)	0.32
5-minute Apgar Score < 7, n (%)	15 (25.0%)	6 (33.3%)	9 (21.4%)	0.33
Respiratory Distress Syndrome, n (%)	38 (63.3%)	13 (72.2%)	25 (59.5%)	0.35
Mechanical Ventilation Required, n (%)	26 (43.3%)	10 (55.6%)	16 (38.1%)	0.21
Patent Ductus Arteriosus (PDA), n (%)	14 (23.3%)	6 (33.3%)	8 (19.0%)	0.24

Serial evaluation of the anterior cerebral artery demonstrated distinct hemodynamic trajectories between neonates who developed ICH and those who did not (Table 2). On Day 1 of life, neonates in the ICH Group exhibited a marked increase in vascular resistance, reflected by a significantly elevated RI (0.76 ± 0.05 vs. 0.66 ± 0.04, $p < 0.001$) and PI (1.68 ± 0.22 vs. 1.32 ± 0.18, $p < 0.001$). This elevated impedance was driven primarily by a reduction in diastolic perfusion, with EDV significantly lower in the ICH group (4.1 ± 1.1 cm/s vs. 6.2 ± 1.4 cm/s, $p < 0.001$).

By Day 3 of life, while overall flow velocities increased physiologically across the entire cohort, vascular impedance remained significantly higher in the ICH Group (RI: 0.74 ± 0.06 vs. 0.64 ± 0.04, $p < 0.001$). By Day 7 of life, hemodynamic parameters began to normalize between surviving neonates, showing no statistically significant differences in RI or PI, though mean flow velocities remained slightly lower in neonates recovering from hemorrhagic injury.

Table 2: Serial Anterior Cerebral Artery Doppler Parameters by Group and Timepoint

TCD Parameter / Timepoint	ICH Group (n=18)	Non-ICH Group (n=42)	Difference (95% CI)	p-value
Day 1 of Life				
Resistive Index (RI)	0.76 ± 0.05	0.66 ± 0.04	0.07 to 0.13	< **0.001**
Pulsatility Index (PI)	1.68 ± 0.22	1.32 ± 0.18	0.25 to 0.47	< **0.001**
Peak Systolic Velocity (PSV, cm/s)	24.8 ± 3.5	26.1 ± 3.2	-3.2 to 0.6	0.17
End-Diastolic Velocity (EDV, cm/s)	4.1 ± 1.1	6.2 ± 1.4	-2.9 to -1.3	< **0.001**
Mean Flow Velocity (Vm, cm/s)	11.8 ± 2.1	13.5 ± 2.0	-2.8 to -0.6	**0.004**
Day 3 of Life				
Resistive Index (RI)	0.74 ± 0.06	0.64 ± 0.04	0.07 to 0.13	< **0.001**
Pulsatility Index (PI)	1.59 ± 0.24	1.28 ± 0.16	0.20 to 0.42	< **0.001**
Peak Systolic Velocity (PSV, cm/s)	28.4 ± 4.1	30.2 ± 3.8	-4.0 to 0.4	0.11
End-Diastolic Velocity (EDV, cm/s)	5.2 ± 1.3	7.5 ± 1.5	-3.1 to -1.5	< **0.001**
Mean Flow Velocity (Vm, cm/s)	13.6 ± 2.4	15.8 ± 2.2	-3.5 to -0.9	**0.002**
Day 7 of Life				
Resistive Index (RI)	0.68 ± 0.05	0.65 ± 0.04	0.00 to 0.06	0.06
Pulsatility Index (PI)	1.42 ± 0.20	1.34 ± 0.17	-0.02 to 0.18	0.12
Mean Flow Velocity (Vm, cm/s)	15.4 ± 2.6	17.2 ± 2.3	-3.2 to -0.4	**0.01**

Receiver operating characteristic (ROC) curve analyses were conducted to evaluate the diagnostic accuracy of early TCD indices in predicting ICH (Table 3). On Day 1 of life, the Resistive Index demonstrated excellent discriminatory power with an AUC of 0.89 (95% CI: 0.80–0.98). An optimal threshold of RI ≥ 0.72 yielded a sensitivity of 83.3%, a specificity of 85.7%, a positive predictive value (PPV) of 71.4%, and a negative predictive value (NPV) of 92.3%. Similarly, Day 1 Pulsatility Index (PI ≥ 1.50) demonstrated robust predictive capacity (AUC = 0.88), correctly identifying 83.3% of infants who subsequently suffered hemorrhage.

Day 3 measurements maintained strong prognostic value, confirming that persistent cerebrovascular constriction and elevated impedance serve as reliable indicators of impending or evolving intracranial hemorrhage.

Table 3: Diagnostic Accuracy of Day 1 and Day 3 Doppler Indices for Predicting Intracranial Hemorrhage

Predictor Variable	Cutoff Value	AUC (95% CI)	Sens (%)	Spec (%)	PPV (%)	NPV (%)
Day 1 RI	≥ 0.72	0.89 (0.80–0.98)	83.3	85.7	71.4	92.3
Day 1 PI	≥ 1.50	0.88 (0.78–0.97)	83.3	80.9	65.2	91.9
Day 1 EDV	≤ 4.8 cm/s	0.85 (0.74–0.96)	77.8	83.3	66.7	89.7
Day 3 RI	≥ 0.70	0.87 (0.77–0.96)	77.8	88.1	73.7	90.2
Day 3 PI	≥ 1.45	0.86 (0.75–0.96)	77.8	85.7	70.0	90.0

DISCUSSION

According to a prospective cohort study, transcranial Doppler ultrasonography (TCD) performed at the bedside within the first week of life is clinically useful in predicting the occurrence of intracerebral hemorrhage in preterm neonates of ≤ 32 weeks gestation at birth. Most babies with ICH have early increase in anterior cerebral vessel impedance with severely increased RI and PI and decreased end-diastolic velocity by 12-24 hours of post-natal life. An early RI threshold of ≥ 0.72 on Day 1 has high sensitivity (83.3%) and negative predictive value (92.3%) to predict ICH, reaffirming spectral Doppler as an early biomarker of cerebrovascular distress [4, 6].Our results are consistent with and contribute to the modern neonatal neurovascular literature. The early history by Perlman and Volpe suggested that anterior cerebral artery velocity fluctuations may not reliably predict the timing of IVH.

However, subsequent advances in high-resolution Doppler instrumentation have clarified the diagnostic significance of microvascular impedance. The data presented here are consistent with the most recent prospective cohort data from Kaushal et al., who have shown that Doppler-derived resistive indices of the anterior cerebral artery better diagnose and detect intracranial pathology in high-risk preterm babies. Our longitudinal tracking data supports the computational hemodynamic models of Sidorenko et al., who demonstrated that elevated anterior cerebral artery resistive index (ACA-RI) is associated with cerebral perfusion disturbances that precede microvascular rupture in the periventricular germinal matrix [5].The mechanisms causing the increase in early vascular resistance are thought to related to the particular vulnerability of the preterm brain [2,3].

In extremely low birth weight infants, an acute increase in intracranial vascular tone occurs following various perinatal stresses like hypoxia, hypothermia, or respiratory distress. When the cerebral autoregulation is not functioning properly, the vasoconstrictive response will reduce end-diastolic perfusion (EDV), leading to an increase in calculated RI and PI [4,6]. Moreover, upon the onset of subclinical germinal matrix bleeding, extravasated blood and breakdown products, particularly free heme, induce interleukin-1 (IL-1) release through inflammasome activation and local depletion of nitric oxide, which trigger secondary microvascular vasospasm [2]. This chain of vasospasm events, according to [2, 3], causes further ischemia in the brain as well as a higher resistance of the blood vessels. Similarly, Liu et al. have mentioned that hemodynamic changes characterized by a reduction in diastolic flow and changes in impedance indices are important predictors of neonatal brain injury and systemic inflammatory injury [3].

The findings have important clinical implications for practicing in neonatal intensive care. At present, routine cranial ultrasonography screening protocols mainly focus on anatomical imaging at late intervals (e.g., Days 7 to 10 of life) that usually identifies hemorrhage only after irreversible tissue injury has happened [4, 6]. The transfontanelle Doppler monitoring [6] at the point of care would provide a quantitative assessment of risk to clinicians on Day 1 and Day 3 of life which can be incorporated into the routine admission assessment. Detection of an RI ≥ 0.72 within the first 24 hours will permit institution of hemodynamically directed neuroprotective measures to maximize systemic blood pressure (afterload), avoid rapid fluid boluses, avoid sudden surges in endotracheal suctioning, and maintain exact blood gas balance without hyperoxia. These measures will stabilize cerebral perfusion and avoid bleeding evolution [4,5].

CONCLUSION

This study aims to assess the predictive capacity of serial bedside transcranial Doppler ultrasonography for intracerebral hemorrhage in preterm neonates (≤32 weeks of gestation). An increased Resistive Index on Day 1 of life ≥0.72 and Pulsatility index are early and non-invasive markers of higher cerebrovascular impedance and lower diastolic perfusion before clinical hemorrhage. The implementation of spectral Doppler parameters into early neonatal brain screening protocols may provide significant risk stratification allowing appropriate neuroprotective measures for very ill neonates.

REFERENCES

1. Perlman JM, Volpe JJ. Cerebral blood flow velocity in relation to intraventricular hemorrhage in the premature newborn infant. The Journal of Pediatrics. 1982;100:956–959. doi:10.1016/s0022-3476(82)80527-1

2. Eisenhut M, Choudhury S. In Premature Newborns Intraventricular Hemorrhage Causes Cerebral Vasospasm and Associated Neurodisability via Heme-Induced Inflammasome-Mediated Interleukin-1 Production and Nitric Oxide Depletion. Frontiers in Neurology. 2017;8. doi:10.3389/fneur.2017.00423
3. Liu C, Fang C, Shang Y, Yao B, He Q. Transcranial ultrasound diagnostic value of hemodynamic cerebral changes in preterm infants for early-onset sepsis. Translational Pediatrics. 2022;11:1149–1155. doi:10.21037/tp-22-269
4. Kaushal M, Sahu N, Pattanaik R, Das S. Role of Transcranial Ultrasound and Doppler Studies to Evaluate Intracranial Pathologies in Preterm and High-risk Term Neonates. Journal of Medical Ultrasound. 2024. doi:10.4103/jmu.jmu_72_23
5. Sidorenko I, Brodkorb S, Felderhoff-Müser U, Rieger-Fackeldey E, Krüger M, Feddahi N, Kovtanyuk A, Lück E, Lampe R. Assessment of intraventricular hemorrhage risk in preterm infants using mathematically simulated cerebral blood flow. Frontiers in Neurology. 2024;15. doi:10.3389/fneur.2024.1465440
6. Kim EH, Park JB, Kim JT. Intraoperative transfontanelle ultrasonography for pediatric patients. Anesthesia and Pain Medicine. 2024;19:S25–S35. doi:10.17085/apm.24106.