Original Article

Resistive Index as an Early Prognostic Marker in Term Neonates with Perinatal Asphyxia: Correlation with Hypoxic-Ischemic Encephalopathy Staging

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Abstract

Background: Perinatal asphyxia and hypoxic-ischemic encephalopathy (HIE) are serious neonatal morbidity and mortality conditions. Early prognostic markers are necessary for intervention and for predicting outcome. The Resistive Index (RI), assessed by cranial Doppler ultrasound, has emerged as a possible non-invasive bedside device for measuring cerebral hemodynamics. This is study to determine the estimation of RI in term infants with perinatal asphyxia and its correlations with HIE staging and short-term conditions of the neurological outcomes. **Material and Methods:** The study was a prospective observational study that involved 130 term neonates (37 weeks) with perinatal asphyxia who were hospitalized after delivery at less than 24 hours. Doppler ultrasound was used to measure RI of the first 24 hours in life. HIE was assessed based on the Sarnat and Sarnat standards. The Short Hammersmith Neonatal Neurological Examination (HNNE) was used to determine neurological outcomes at 40 days. Chi-square tests and ROC curve analysis were used in the statistical analysis. **Results:** In 130 neonates, 56.9% had normal RI; 6.2%, 19.2%, and 17.7% showed mild, moderate, and severe RI exemptions, respectively. The need for TM: there was a significant relationship between RI and HIE grade (P=0.001), with 85.7% of HIE Grade 1 neonates demonstrating normal RI, compared with 51.3% of Grade 3 neonates demonstrating severe RI. Severe RI was equated with a mortality incidence of 60.9 (P=0.001). Analysis of the ROC curve indicated that RI had an AUC of 0.949, predicting mortality with an optimal cutoff of 0.55 (sensitivity = 100, specificity = 92.24). The failure rates of HNNE were dependent on the severity of the HIE (30.6% in Grade 1, 87.0% in Grade 3, P=0.001) and significantly associated with abnormal RI (P=0.001). **Conclusion:** The evidence-based practice RI is a valid, non-invasive early prognostic in neonates with perinatal asphyxia. An RI of less than 0.55 is a good prognosticator of mortality and adverse neurological prognosis. Longitudinal RI measurements should be assessed in conjunction with clinical evaluation to inform early therapeutic interventions, especially in resource-constrained environments.

Keywords: Resistive Index, Perinatal Asphyxia, Hypoxic-Ischemic Encephalopathy, Doppler Ultrasound, Neonatal Outcomes, Hammersmith Examination.

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Introduction

One of the most urgent issues in the field of neonatal medicine is perinatal asphyxia, which is defined by the insufficient provision of oxygen to important organs during the perinatal period. The neurological outcome of perinatal asphyxia is called hypoxic-ischemic encephalopathy (HIE); it has a high incidence of 2 per 1,000 live births in resource-rich environments, but is ten to twenty times more common in areas with limited resources, representing disparities in access to maternal and neonatal care.[1] Hypoxic-ischemic encephalopathy (HIE) has a high rate of 1520 per 1,000 live births in the resource-rich environment [1]

HIE has a bi-phasic pattern of pathophysiology. The immediate consequence following the hypoxic-ischemic insult is known as primary energy failure, which is accompanied by impairment of oxidative metabolism and cellular depletion of energy. This is succeeded by a latent period and later secondary energy failure that transpires 6-48 hours later and is caused by excitotoxicity, oxidative stress, and inflammation; understanding such a time course of evolution is essential in applying neuroprotective therapy, as is the case with therapeutic hypothermia that has become the standard of care in moderate to severe HIE of term infants.[2,3]

Though useful, traditional clinical assessment methods, such as the Apgar score, cord blood pH, and base deficit, are limited in their ability to predict long-term neurodevelopmental outcomes and may delay assessment due to the need for specialized

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equipment, expertise, and patient stability. The gap has led to the search for bedside diagnostic instruments that can provide high-quality early prognostic information.[4]

Cranial Doppler ultrasound has become a potential method for real-time evaluation of cerebral hemodynamics, thereby increasing the number of non-invasive techniques. The resistive index (RI) (Peak Systolic Velocity/End Diastolic Velocity)/Peak Systolic Velocity) is a derivation that indicates the downstream vascular resistance and cerebral perfusion.[5] In neonates with HIE, the values of the resistive index (RI) are characteristic due to changes in cerebral autoregulation. Recent research has established that abnormal RI is associated with the severity of HIE and predicts unfavorable outcomes, suggesting its potential as an early prognostic factor.[6]

Although evidence is increasing, standardized guidelines on the optimal timing of RI measurement, the cutoff levels for outcomes to predict, and the combination of other clinical measurements are still needed. Besides, the available literature has primarily investigated short-term mortality or long-term neurodevelopmental outcomes, with scant information on intermediate neurological tests, including the Hammersmith Neonatal Neurological Examination.

The study aimed to determine RI as a powerful early prognostic issue in term babies with perinatal asphyxia. We sought to determine the clinical utility of this bedside tool by comparing RI measurements with HIE staging and short-term neurological outcomes measured with the HNNE method, and by selecting the optimal threshold values for prognostic stratification.

Materials and Methods

Study Design and Setting: The proposed cross-sectional study was a prospective study conducted at the Neonatal Intensive Care Unit (NICU) of M.Y. Hospital, Department of Paediatrics, M.G.M. Medical College, Indore, Madhya Pradesh, over 12 months (August 2023 to August 2024). The Institutional Ethics Committee approved this research plan before it was conducted.

Study Population: We also included term neonates (a gestational age of at least 37 weeks) with perinatal asphyxia and HIE, and who were admitted within the first 24 hours of birth. The sample size was determined using the prevalence formula based on an HIE prevalence of 3, yielding a sample size of 128 subjects; 130 neonates were recruited to account for potential dropouts.

Inclusion Criteria:

1. All naturally born neonates who died of asphyxia in utero, older than the study period.
2. Outborn babies admitted in the last 24 hours with perinatal asphyxia.
3. Gestational age ≥37 weeks

Exclusion Criteria:

1. Major congenital, developmental, or chromosomal abnormalities
2. Suspected metabolic disorders
3. Significant antenatal risk factors leading to early-onset sepsis or CNS depression unrelated to asphyxia
4. Preterm neonates (<37 weeks)
5. Parental refusal of consent

Clinical Assessment: Perinatal asphyxia was diagnosed using the conventional criteria, such as low Apgar scores, cord blood acidosis (where it was present), and clinical dysfunction of multiple organs. HIE severity was determined by the Staging scales of Sarnat and Sarnat into three grades as determined by level of consciousness, tone, reflexes, seizures, and autonomic dysfunction.

Doppler ultrasound Technique: Colour Doppler measurements of the resistive Index were done within the first 24 hours of life. The qualified radiologists, using standardized tests, examined those. Measurement of RI was done in the anterior cerebral artery (ACA) of the anterior fontanelle with a 7.5 MHz transducer. The equation was: RI = (Peak Systolic Velocity -End Diastolic Velocity)/Peak Systolic Velocity.

RI values were categorized as:

- Normal: 0.68–0.72
- Mild asphyxia: 0.63–0.67
- Moderate asphyxia: 0.58–0.62
- Severe asphyxia: ≤0.57

Neurological Assessment: The Short Hammersmith Neonatal Neurological Examination (HNNE) was used to determine the short-term neurological outcomes at 40 days. It is a standardized test that assesses cranial nerve function, posture, movements, tone, and reflexes. The results were considered as a pass or a fail according to the set criteria.

Data Collection: Complete maternal and neonatal history was received, such as maternal age, gravidity, mode of delivery, antepartum and perinatal risk factors, birth weight, Apgar scores, resuscitation, demand of ventilatory support, the use of inotropes, length of stay, and outcome (discharge, death, left against medical advice).

Statistical Analysis: The data were entered into MS Excel 2016 and analyzed using IBM SPSS Version 22. Frequencies and percentages were used to illustrate the descriptive statistics. The Pearson chi-square test was used to measure associations between categorical variables. Receiver Operating Characteristic (ROC) curves were analyzed to assess the predictive value of RI for mortality. The goal of statistical significance was P 0.05.

Results

Baseline Characteristics

The sample that was studied consisted of 130 term infants who had perinatal asphyxia. The frequency of male babies was higher (67.7%) than that of females (32.3%). The majority of the mothers were 2130 years of age (89.2%), and 55.4% were primigravida. The birth weight distribution was 61.5% in the normal range (2.0–3.0 kg), 33.1% >3.0 kg, and 5.4% <2.0 kg.

Delivery characteristics revealed vaginal delivery in 49.2%, assisted vaginal delivery in 30.8%, and lower segment cesarean section in 20.0%. While 54.5% had uneventful labor, complications included obstructed labor (20.7%), prolonged second stage (11.5%), and protracted first stage (13.1%).

Antenatal risk factors were documented in a subset of cases and are summarized in [Table 1]. Uteroplacental insufficiency and eclampsia & preeclampsia were the most common, each affecting 7 (5.4%) neonates. Gestational hypertension was observed in 6 (4.6%) cases, followed by oligohydramnios and gestational diabetes mellitus (GDM) in 5 (3.8%) cases each. Less frequent conditions included short maternal stature (4 cases, 3.1%), type 2 diabetes mellitus and hypothyroidism (3 cases each, 2.3%), and polyhydramnios, chorioamnionitis, severe anemia, and HBsAg positivity (2 cases each, 1.5%).

Table 1: Distribution According to Antenatal Risk Factors

Antenatal Risk Factors	Number (n)	Percentage (%)
Polyhydramnios	2	1.5
Chorioamnionitis	2	1.5
Oligohydramnios	5	3.8
Eclampsia & Preeclampsia	7	5.4
Gestational hypertension	6	4.6
Uteroplacental insufficiency	7	5.4
Gestational diabetes mellitus (GDM)	5	3.8
Short maternal stature	4	3.1
Diabetes mellitus type-2	3	2.3
Hypothyroidism	3	2.3
Severe anemia	2	1.5
HBsAg positive	2	1.5

Clinical Presentation and Severity

Apgar scores at 1 minute were severely depressed (0–3) in 56.2% of neonates, with 18.5% scoring 4–7, and 25.4% unassessed due to immediate resuscitation needs. By 5 minutes, improvement was evident with only 2.3% scoring 0–3, 72.3% scoring 4–7, and 25.4% remaining unassessed.

Resuscitation requirements included bag-and-mask ventilation (52.3%), intubation (36.9%), and tactile stimulation (10.8%). Ventilatory support was needed in 62.3% of cases (42.3% non-invasive, 20.0% invasive), and 46.2% required inotropic support within the first 24 hours.

HIE grading showed 43.1% with Grade 1, 26.9% with Grade 2, and 30.0% with Grade 3 severity. The distribution is presented in [Table 2]. Hospital stay ranged from 8–14 days (47.7%), 2–7 days (40.0%), >14 days (10.8%), and ≤1 day (1.5%).

Table 2: Distribution of Hypoxic-Ischemic Encephalopathy Grading

HIE Grade	Number (n)	Percentage (%)
Grade 1	56	43.1
Grade 2	35	26.9
Grade 3	39	30.0
Total	130	100.0

Resistive Index Distribution and Correlation with HIE

RI distribution obtained 56.9% normal values, 6.2% mild, 19.2% moderate, and 17.7% severe abnormalities. The relationship between RI and HIE grade was very substantial (P=0.001). [Table 3] describes this relationship. In HIE Grade 1 neonates, 85.7% had normal RI, and among Grade 3, only 12.8% had normal RI, with 35.9% having moderate and 51.3% having severe RI abnormalities.

Table 3: Association Between HIE Grade and Resistive Index

HIE Grade	Normal RI n (%)	Mild RI n (%)	Moderate RI n (%)	Severe RI n (%)	Total n (%)
Grade 1	48 (85.7)	5 (8.9)	0 (0.0)	3 (5.4)	56 (100.0)
Grade 2	21 (60.0)	3 (8.6)	11 (31.4)	0 (0.0)	35 (100.0)
Grade 3	5 (12.8)	0 (0.0)	14 (35.9)	20 (51.3)	39 (100.0)
Total	74 (56.9)	8 (6.2)	25 (19.2)	23 (17.7)	130 (100.0)

Pearson Chi-square test: χ^2=79.962, df=6, P=0.001 (Significant)

Outcome Analysis

General results indicated that the discharge rate was 78.5%, the mortality rate was 10.8%, and the left-against-medical-advice rate was 10.8%. Grade 3 of Mortality was only seen in HIE Grade 3 (35.9%, P=0.001). RI presented a great prognostic value, and severe RI meant 60.9 percent mortality in comparison to 0 percent in normal, mild, and moderate groups of RI (P=0.001). [Table 4] demonstrates the correlation between the outcome and RI.

Table 4: Association Between Resistive Index and Outcome

Resistive Index	Discharge n (%)	LAMA n (%)	Death n (%)	Total n (%)
Normal	60 (81.1)	14 (18.9)	0 (0.0)	74 (100.0)
Mild	8 (100.0)	0 (0.0)	0 (0.0)	8 (100.0)
Moderate	25 (100.0)	0 (0.0)	0 (0.0)	25 (100.0)
Severe	9 (39.1)	0 (0.0)	14 (60.9)	23 (100.0)
Total	102 (78.5)	14 (10.8)	14 (10.8)	130 (100.0)

Pearson Chi-square test: χ^2=82.276, df=6, P=0.001 (Significant)

Predictive Value of Resistive Index

ROC curve analysis demonstrated exceptional predictive accuracy of RI for mortality. The results are illustrated in [Figure 1]. The Area Under the Curve was 0.949 (95% CI: 0.895–0.980, P<0.0001). An optimal cutoff of ≤0.55 yielded 100% sensitivity and 92.24% specificity, with a positive predictive value of 75% and a negative predictive value of 90%.

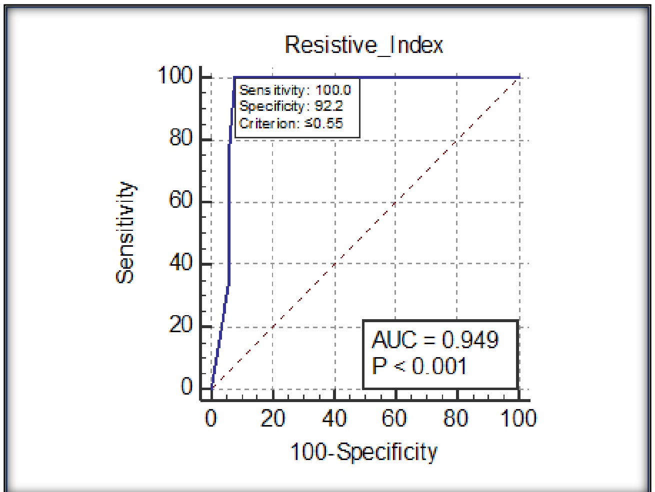

Figure 1: ROC Curve Analysis of Resistive Index for Prediction of Mortality

Area Under Curve (AUC): 0.949 (95% CI: 0.895–0.980)
Optimal cutoff: ≤0.55
Sensitivity: 100%
Specificity: 92.24%
P<0.0001

The ROC curve demonstrates the exceptional discriminatory ability of the Resistive Index in predicting neonatal mortality in perinatal asphyxia cases.

Neurological Assessment

HNNE screening was completed in 102 neonates (28 excluded due to early death or discharge against medical advice). Failure rates were 58.8% overall, with significant correlation to HIE severity: 30.6% in Grade 1, 83.3% in Grade 2, and 87.0% in Grade 3 (P=0.001). HNNE failure also correlated significantly with abnormal RI, with failure rates of 38.3% for normal RI, 87.5% for mild RI, 92.0% for moderate RI, and 77.8% for severe RI (P=0.001). This association is presented in [Table 5].

Table 5: Association Between Resistive Index and HNNE Screening Results (n=102)

Resistive Index	HNNE Fail n (%)	HNNE Pass n (%)	Total n (%)
Normal	23 (38.3)	37 (61.7)	60 (100.0)
Mild	7 (87.5)	1 (12.5)	8 (100.0)
Moderate	23 (92.0)	2 (8.0)	25 (100.0)
Severe	7 (77.8)	2 (22.2)	9 (100.0)
Total	60 (58.8)	42 (41.2)	102 (100.0)

Pearson Chi-square test: χ^2=25.812, df=3, P=0.001 (Significant)

28 neonates excluded (14 deaths, 14 LAMA before 40-day assessment).

Discussion

This multi-centre analysis of 130 term neonates with perinatal asphyxia reveals that the Resistive Index, as measured by Doppler ultrasound, is a strong early prognostic factor, which is significantly associated with the severity of HIE and predetermines short-term outcomes. Our results are consistent with prior studies and provide new insights into the incorporation of RI into standardized neurological tests.[7,8]

The noted male preponderance (67.7) of our own cohort is comparable to other reports, both the primigravida mothers (55.4) and Kudreviciene et al., indicating an inherent vulnerability of males to perinatal complications causing asphyxia.[9,10] The high rate of primigravida mothers (55.4) also serves to reinforce the fact that primigravida mothers are generally more vulnerable to labor complications, as indicated by asphyxia.[11]

The study population is further characterized by the inclusion of data on risk factors in the prenatal stage [Table 1]. The prevalence of uteroplacental insufficiency (5.4-6.4) and hypertensive disorders (eclampsia/preeclampsia: 5.4, gestational hypertension: 4.6) are in accordance with the established pathophysiological associations with perinatal asphyxia, especially, compromised fetal blood circulation caused by poor placental perfusion. This supports the need for specific antenatal observation in high-risk pregnancies.[12,13]

The main conclusion of our study, the high level of correlation between the variables RI and the severity of HIE (P=0.001), supports the claims and results of various researchers. The gradual decline of RI, proportional to the severity of HIE, indicates the pathophysiology of dysfunctional cerebral autoregulation. Among mild HIE (Grade 1), 85.7% of neonates had normal RI, suggesting preservation of autoregulatory responses and a better prognosis. On the other hand, normal RI was observed in only 12.8% (Grade 3), and 51.3% presented with severe RI abnormalities, indicating hemodynamic derangement and poor cerebral perfusion.[14,15]

These data are in line with Ilves et al., who reported that decreased RI in cerebral arteries in 12120 hours of asphyxia was found in severe cases of HIE and was a predictor of outcome at 1 year in terms of neuromotor status.[16,17]

The outstanding prognostic capability demonstrated in our ROC analysis (AUC=0.949) for predicting mortality is better than most reported results. A 100 percent sensitivity and 92.24 percent specificity at a cutoff ≤0.55, with an optimal RI value reported by Kumar et al., provide a very definite cutoff point for clinical decision-making. This is a very stable, moderately close consistency with the results of Natique et al. and Pishdad et al., with similar cutoffs (≤0.55 and ≤0.62, respectively) and identical diagnostic accuracy.= Look= □
|human|>This is a very stable, moderately close consistency with the results of Natique et al. and Pishdad et al., with similar cutoffs (≤0.55 and ≤0.62, respectively), with a similar diagnostic accuracy.[18,19]

The high mortality trend observed in our study, evident only in the severe RI group (60.9%), but not in the normal, mild, or moderate groups, provides strong evidence that RI is a prognostic tool. This dichotomous differentiation offers clinicians a clear framework for risk classification and resource allocation. The same result was found by Ahmad and other researchers with much higher levels of mortality (28.6 percent) in the case of abnormal RI. Still, our study found more powerful discriminatory power.[9]

There is significant additional prognostic information from integrating 40-day HNNE screening. The gradually rising failure rates of HNNE by HIE severity (30.6% in Grade 1 to 87.0% in Grade 3) and the high level of correlation with abnormal RI confirm the value of combining functional hemodynamic examination with systematic neurological examination. This two-sided method provides instant prognostic data (RI) and early neurological trend evaluation (HNNE), providing a full picture for predicting outcomes.

The strength of our study lies in its holistic approach, including standardized HIE staging, standardized RI measurement procedures, structured neurological assessment, and strong statistical validation. The sample size is quite large, and both mortality and morbidity outcomes have been included in the study, thus offering a complete picture of the prognostic utility of RI. Moreover, our results are particularly applicable in resource-constrained environments where state-of-the-art neuroimaging devices may not be readily accessible.

It has several limitations that should be discussed. The single-center method can introduce referral bias and other issues, thereby restricting generalizability. The temporal development of cerebral hemodynamics could not be evaluated because RI was measured at a single time point (within 24 hours). Serial measurements, as suggested by Natique et al., could have provided further prognostic information by ensuring that the dynamics of cerebral injury were captured, but failed to establish an anatomical-functional correlation due to the absence of MRI correlation. But cranial ultrasound provided some structural data, including Grade 1 and Grade 2 IVH (70.8 percent normal, 24.6 percent Grade 1 IVH, 4.6 percent Grade 2 IVH).[20]

The short-term follow-up (40 days) of those who used HNNE, though basic at the clinical level, fails to reflect on long-term neurodevelopmental outcomes, which are usually realized after infancy. Prognostic validity would be enhanced with long-term follow-up with comprehensive follow-up developmental analyses at 12, 18, and 24 months. The 28 neonates excluded from the HNNE assessment (14 deaths, 14 LAMA) are also a major limitation, as it introduces the possibility of survivorship bias.

Our results have great clinical implications. Any RI reading less than 0.55 warrants intensive monitoring, whether therapeutic intervention is already in place, and early counseling regarding prognosis. RI may be used in resource-limited environments that lack access to an MRI or in environments with long latency, so that the most effective neuroprotective treatments can be delivered during the initial hours of acute stroke. Normal RI has a high negative predictive value (90%), indicating it is reassuring, whereas abnormal values require increased vigilance.[21]

Several areas in future research should be addressed. Larger, more diverse multicenter studies would improve generalizability and enable subgroup analyses. Hemodynamic evolution would be described by the serial RI measurements at predefined intervals (ex, 6, 12, 24, and 48 hours), and this method may enhance the accuracy of prognostication. Coupling with MRI scoring systems would provide anatomical-functional correlation and serve as a gold standard for RI. Neurodevelopmental follow-up with longitudinal approaches to 1824 months, using comprehensive measures (e.g., Bayley Scales, Gross Motor Function Classification System), would determine the predictive capabilities of RI for long-term outcomes. Last but not least, interventional research comparing RI-guided management skills with usual management techniques would demonstrate clinical usefulness in addition to prognostic value.

Conclusion

The present research confirms that the Resistive Index measured using cranial Doppler ultrasound is a very effective non-invasive and early prognostic outcome of perinatal asphyxia and HIE in term infants. The strong correlation between RI and HIE severity, and its unparalleled ability to predict mortality (AUC = 0.949), make RI an attractive clinical instrument for risk stratification at an early stage. A minimum RI of 0.55 or less showed the most accurate interpretation of the most at-risk population of neonates, with 100 percent sensitivity and 92.24 percent specificity in predicting death. [6]

Combining RI measurement with Short HNNE screening provides a single, focused assessment of cerebral hemodynamics and neurological function. The combination of this method will help in the early detection of vulnerable neonates, administer precise treatment, and direct parental counseling. Doppler ultrasound can be easily accessed, repeated, and made available at the bedside; hence, RI measurement is especially useful in resource-restricted practices that lack advanced neuroimaging or are delayed.

The context of the present study helps us to conclude that RI assessment should be integrated into standard neonatal care policies in relation to infants with perinatal asphyxia. Short-term results are encouraging, but long-term neurodevelopmental follow-up and multicenter validation studies would be needed to provide convincing evidence on RI's predictive value for long-term outcomes and to inform the optimization of neuroprotective approaches. However, RI represents a major step forward in early prognostic evaluation, providing clinicians with a quantifiable tool that complements clinical judgment and supports evidence-based practice in this high-risk group.

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Conflicts of interest

There are no conflicts of interest.

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