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ARTICLE

Early postnatal color Doppler changes in neonates receiving delivery room resuscitation with low 5 min Apgar score—a pilot study

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Abstract

Aims and objectives To evaluate the Doppler changes in the intracranial arteries of neonates exposed to perinatal hypoxic insult and compare it with normal neonates.

Materials and methods Color Doppler of bilateral anterior and middle cerebral arteries was performed within 6 h of birth in 26 healthy neonates and 50 neonates who received delivery room resuscitation (DRR) for perinatal depression and had a 5 min Apgar score <7. Comparisons of resistive index (RI) and peak systolic velocity (PSV) were made between the (a) control group (b) patients with low 5 min Apgar score <7 who without clinical features of neonatal encephalopathy at 24 h (c) neonates with perinatal depression with a clinical evidence of disturbed neurological function at 24 h of birth and examination consistent with mild, moderate, or severe encephalopathy using modified Sarnat and Sarnat's classification.

Results Significantly higher RI was observed in the neonates with to perinatal depression compared to the normal neonates. Significantly higher RI was seen in the patients with clinical features of neonatal encephalopathy (Group C) compared to group B. RI <0.6 and >0.82 was associated with severe neonatal encephalopathy. Differences in PSV were not statistically significant in the various groups.

Conclusion The study presents the changes in early cerebral Doppler parameters observed in neonates with low 5 min Apgar score following DRR compared to the normal neonates. We also present the relations of Doppler parameters with increasing severity of neonatal encephalopathy according to Sarnat classification.

Introduction

Perinatal asphyxia (PA) refers to a temporary interruption of oxygen availability to the neonates resulting from placental blood flow obstruction, abruptio placenta, umbilical cord compression, prolonged labor, or failure of the neonate to initiate respiration [1, 2]. Despite the advancement and widespread availability of neonatal and peripartal maternal medical care, hypoxic-ischemic encephalopathy (HIE) remains a major cause of pediatric morbidity with an estimated incidence of 1.5 per 1000 live births in developed countries and between 2.3 and 26.5 per 1000 live births in developing countries [3, 4]. Therapeutic hypothermia is the only effective therapy available for moderate to severe HIE that has been shown to provide neuroprotection to the neonates. Most of the guidelines recommend the commencement of hypothermia as soon as possible after birth, preferably within 6 h [5]. Thus the early recognition of patients who are at risk of developing significant HIE is essential.

Apgar scoring, consisting of observation of five physical parameters immediately after the birth, is an accepted and convenient method of assessing response to delivery room resuscitation (DRR). A low 5 min Apgar score <7 confers an increased relative risk of neurological disability over that of infants with a 5 min Apgar score of 7–10 [6]. Degree of severity of a neonate suspected to have HIE is commonly graded using system proposed by Sarnat and Sarnat. This staging was originally described in 24 h old babies when no early therapy was available [7]. With the advent of therapeutic hypothermia, the current guidelines recommend

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early clinical grading of neonatal encephalopathy (within 6 h) using modified Sarnat criteria [8]. Therapeutic hypothermia is recommended based on the evaluation of Apgar score, blood pH, duration of resuscitation, and presence of seizures evidence of moderate to severe HIE using modified Sarnat score [8].

The introduction of high quality, reasonably priced, and portable ultrasound unit has now made it possible for most of the NICU to maintain Ultrasound and Doppler facility. It has the potential to become an objective, non invasive, easily accessible, and continuous point-of-care measure. Therefore, it may be a valuable supplement to the current methods for initial assessment, monitoring, selection of treatment, and prognosis in neonates with perinatal depression. However, the clinical use is currently limited by a lack of standardized data in neonates especially within 6 h of birth. The present study was undertaken to evaluate the Doppler changes in the neonatal intracranial arteries in the neonates who received DRR for perinatal depression and to compare the data with that of normal neonates.

Material and methods

Subjects

This was a prospective observational study that was conducted from July 2016 to February 2019 in Sir Sunderlal Hospital, a tertiary care University-based Hospital affiliated to Banaras Hindu University, Varanasi, India. Ethical clearance was obtained from the Institute ethical committee at the outset and written informed consent in local language was taken from the parents of all included children in the study. The study group comprised of 76 term newborns, appropriate for gestational age delivered in our Hospital during the defined study period. Post-term neonates, LGA and SGA babies, neonates with congenital malformations, neonates admitted beyond 6 h of birth, or with hypoglycemia (plasma glucose level less than 45 mg/dL) were excluded from the study. None of the mothers of the neonates included in this study had a history of narcotic intake.

Clinical parameters

At the time of recruitment, all the data regarding the clinical details, any investigation reports were gathered. In the neonates who received DRR owing to inadequate tone or breathing effort at birth, 5 min Apgar scores were recorded for estimating the response to DRR and identify the group at risk for developing HIE. Neonates were examined thoroughly after birth to exclude any congenital malformation and other systemic illnesses. Gestational age was determined by the maternal history of the last menstrual period and corroborated with the postnatal assessment of gestational age. Anthropometric details including birth weight were noted soon after birth. Newborns with birth weight between the 10th and 90th percentile of that particular gestational age were defined as AGA (Appropriate for Gestational Age). For those infants who were deemed at risk for HIE, staging was performed using the Sarnat classification as applied in HIE. None of the patients included in this study received therapeutic hypothermia.

The study population was divided into three groups:

(A) Group A (control group): Full-term healthy neonates (born at ≥37 weeks of gestation) who did not require resuscitation with Apgar score ≥7 at 5 min.
(B) Group B (perinatal depression without encephalopathy): full-term neonates (born at ≥37 weeks of gestation) who (i) required DRR as having not cried or breathed at birth and with Apgar score of <7 at 5 min and (ii) no obvious clinical evidence of disturbed neurological function and not graded as mild, moderate or severe neonatal encephalopathy at 24 h of birth based on Sarnat and Sarnat's classification.
(C) Group C (suspected neonatal encephalopathy group): full-term neonates (born at ≥37 weeks of gestation) who (i) required DRR as having not cried or breathed at birth with Apgar score of <7 at 5 min and (ii) clinical features of disturbed neurological function and examination consistent with mild, moderate to severe neonatal encephalopathy according to Sarnat and Sarnat's classification at 24 h.

Imaging protocol

Every neonate in this study underwent cranial Doppler sonography within 6 h of birth. All the scans were performed using portable sonographic equipment of Neonatal Intensive care Unit (Sonosite Micromaxx, Bothell, WA, USA) with a phased array transducer of 4–8 MHz frequency. Evaluation of Anterior cerebral arteries was bilaterally conducted on the parasagittal planes, obtaining the image through the anterior fontanel. Blood flow velocity parameters in all subjects were measured in the branch of the anterior cerebral artery (ACA) located in front of the genu of the corpus callosum. Imaging of the middle cerebral arteries was bilaterally conducted through the right and the left temporal bones on axial planes, at the level of cerebral peduncles. Blood flow velocity parameters in all subjects were measured in the proximal branch of the middle cerebral artery (MCA), in the lateral sulcus (the fissure of Sylvius). We tried to keep the angle of insonation as close to 0° as possible. An in-built-analyzer of the equipment was used to obtain resistive index (RI) and peak systolic velocities

Table 1 Comparison of neonatal characteristics of the study population.

Parameter	Neonate exposed to perinatal hypoxic event ($n = 50$)	Healthy neonates ($n = 26$)	p value
Gestational age (weeks)			
Mean ± SD	38.98 ± 2.62	39.57 ± 2.21	0.279
Median (IQR)	(38.857)	(39.071)	
Birth weight (g), (mean ± SD)	2560.94 ± 456.07	2830.19 ± 428.54	0.015
APGAR score			
1 min, median (IQR)	3	8	<0.001
5 min, median (IQR)	6	9	
Mode of delivery			
Spontaneous vaginal delivery	28	12	
Emergency cesarean section	22	14	

(PSV) of both right and left ACA and MCA. The exposure time for cranial Doppler sonography was ≤120 s.

Statistical analysis

Data were entered and analyzed by using Microsoft Excel version 2010 and Statistical Package for social science ver.16 (SPSS.16). Students t test, analysis of variance (ANOVA) with Chi-square t test were used to compare parametric and nonparametric continuous and categorical variables between groups. One-way ANOVA was used to find out the significant difference among multiple groups. A p value of <0.05 was considered statistically significant.

Results

Seventy-six newborns (M:F = 4:3) were included in this study with 26 control healthy neonates (Group A), 11 neonates who received DRR, and had low Apgar and without clinical evidence of encephalopathy (Group B) and 39 neonates with clinical findings suggestive of neonatal encephalopathy (Group C). Fifty neonates (M:F = 31:24) had Apgar score <7 at 5 min (Group B and C) of which 11 had no clinical evidence of encephalopthy whereas 9 had mild, 14 had moderate, and 16 had severe encephalopathy based on Sarnat classification.

Neonatal characteristics of the study population are summarized in Table 1. Mean birth weight and mean gestational age was significantly lower in neonates who received DRR for perinatal depression (Group B + C). The incidence of low birth weight was also higher in the depressed neonates. No significant difference was noted in the mode of delivery.

Table 2 summarizes the comparison of the mean value of the RI in each of the four arteries between the study group. Significantly higher RI was observed in the neonates who received DRR for perinatal depression (Group B and C) compared to the normal neonates (Group A). Also, Significantly higher RI was seen in the suspected encephalopathy group (Group C) compared to those who did not show clinical features of encepahlopathy (Group A + B). In the neonates with perinatal depression, RI was higher in suspected encephalopathy group (Group C) compared to Group B. The difference was statistically significant for left MCA and Left ACA whereas the difference was not significant for right-sided arteries.

Comparison of the RI values across the three groups of the encephalopathy severity showed that the mean RI is highest in the group with mild encephalopathy followed by moderate encephalopathy. Severe encephalopathy group showing the lowest mean RI. The difference was not statistically significant for all the four arteries.

A Scatter plot of RI values v/s groups of HIE is shown in Fig. 1. It showed that several (8/18) of the patients in severe encephalopathy group and 2/14 (14%) of the neonates in moderate encephalopathy group had RI values <0.6. None of the patients in group a, group b, or mild encephalopathy group revealed RI < 0.6.

A comparison of RI values of the patients with RI ≥ 0.6 showed that RI was significantly higher in the severe encephalopathy group (Table 3). ROC curve was drawn based on the RI values in cases that had RI > 0.6 to predict severe encephalopathy (Table 4, Fig. 2). ROC of all the four arteries showed a high area under the curve (0.89–0.98). Cutoff RI values of 0.82–0.83 were associated with severe encephalopathy with high sensitivity (87.5–100%) and high specificity (84.5–91.4%).

Peak Systolic velocities (PSV) was lower in patients in patients receiving DRR compared to the control group and also, PSV was lower in suspected encephalopathy group compared those without clinical features of encephalopathy (Table 5). PSV was lower in moderate encephalopathy compared to mild encephalopathy and further lower in severe encephalopathy group. However, the differences in PSV were not statistically significant between the various groups.

Table 2 Comparison of the resistive index (RI) of intracranial arteries between various study groups.

Groups	Right MCA	Left MCA	Right ACA	Left ACA
Comparison between healthy controls and neonates exposed to perinatal hypoxic event				
Group a (control) ($n = 26$)	0.7 ± 0.04	0.7 ± 0.04	0.69 ± 0.03	0.69 ± 0.04
Group b + c ($n = 50$)	0.74 ± 0.15	0.74 ± 0.15	0.74 ± 0.16	0.73 ± 0.15
p value	0.002	0.004	0.001	0.001
Comparison between neonates with and without clinical findings of neonatal encephalopathy at 24 h of birth				
Group a + b ($n = 37$)	0.71 ± 0.04	0.7 ± 0.04	0.70 ± 0.03	0.69 ± 0.03
Group c ($n = 39$)	0.74 ± 0.17	0.74 ± 0.17	0.74 ± 0.19	0.74 ± 0.17
p value	0.005	0.001	0.002	0.001
Comparison between neonates exposed to perinatal hypoxic event with and without clinical findings of neonatal encephalopathy at 24 h of birth				
Group b ($n = 11$)	0.74 ± 0.04	0.72 ± 0.03	0.72 ± 0.03	0.71 ± 0.03
Group c ($n = 39$)	0.74 ± 0.17	0.74 ± 0.17	0.74 ± 0.19	0.74 ± 0.17
p value	0.083	0.028	0.053	0.023
Comparison between mild, moderate, and severe neonatal encephalopathy subgroups				
Mild encephalopathy ($n = 9$)	0.81 ± 0.04	0.81 ± 0.03	0.81 ± 0.03	0.80 ± 0.05
Moderate encephalopathy ($n = 14$)	0.78 ± 0.10	0.77 ± 0.10	0.76 ± 0.10	0.78 ± 0.19
Severe encephalopathy ($n = 16$)	0.67 ± 0.24	0.68 ± 0.24	0.67 ± 0.27	0.66 ± 0.23
p value	0.10	0.13	0.15	0.07

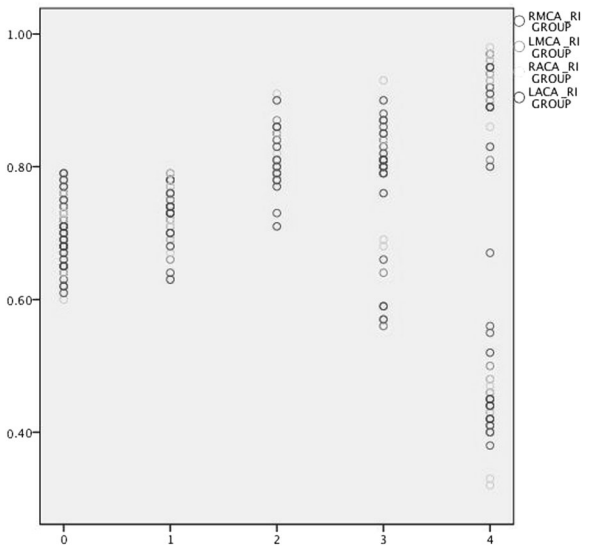

Fig. 1 Scatter plot of RI values of the four intracranial arteries (*y*-axis) in various study groups (*x*-axis). RI values of right middle cerebral artery (blue), left middle cerebral artery (green), right anterior cerebral artery (yellow), left anterior cerebral artery (purple) in controls (0), neonates with perinatal hypoxic exposure without suspected HIE (1), mild (2), moderate (3), and severe neonatal encephalopathy (4).

Discussion

Ultrasound imaging has gained worldwide acceptance as an essential component of the neonatal intensive care unit. Moreover, the neonatologists are becoming increasingly familiar with the interpretation and technique of cranial sonography. This provides an opportunity in the neonatal care units to utilize Sonography and Doppler imaging as an objective and point-of-care facility for neonates who are exposed to PA. Unfortunately, the implementation of this technique in patients with PA has been limited to rule out brain malformations or other mimics of hypoxia before the commencement of therapeutic hypothermia [9]. Over the last two decades, various researchers have tried to explore the utility of Doppler sonography in patients at risk of developing HIE. However, if imaging has to have a role in the management of suspected HIE, it has to be performed within the temporal therapeutic window for hypothermia therapy i.e., within 6 h of birth. Our study attempted to assess the changes in anterior and middle cerebral arteries during the first 6 h of life in the neonates who subsequently had clinical features suspicious of neonatal encephalopathy. We compared the data with that of normal healthy neonates as well as those with the perinatal hypoxic event who showed no subsequent abnormality on clinical assessment of neurological status.

Shortly after the perinatal hypoxic event, the child undergoes a period of profound apnea and bradycardia. Studies in lambs have demonstrated a period of cerebral recovery, which is implemented through vasoconstriction of peripheral arteries and vasodilatation of the cerebral arteries [10, 11]. This autoregulation response leads to the re-direction of blood into cerebral circulation and studies in animal subjects have emphasized that an impaired auto-regulation response might be an important factor in the genesis of the brain injury after hypoxia [10]. Possible causes of this impaired vasoreactivity might include the production of thromboxanes and leukotrienes or endothelial

Table 3 Comparison of the mean Resistive indices (RI) between mild, moderate, and severe neonatal encephalopathy subgruops (for cases with RI ≥ 0.6).

Grade	Right MCA	Left MCA	Right ACA	Left ACA
Mild encephalopathy ($n = 9$)	0.81 ± 0.04	0.81 ± 0.03	0.81 ± 0.03	0.80 ± 0.05
Moderate encephalopathy ($n = 12$)	0.82 ± 0.05	0.81 ± 0.05	0.80 ± 0.06	0.81 ± 0.03
Severe encephalopathy ($n = 8$)	0.90 ± 0.09	0.91 ± 0.04	0.93 ± 0.04	0.88 ± 0.05
p value	0.018	<0.001	<0.001	0.003

Table 4 Summery of Receiver operated characteristic (ROC) curve analysis of patients with RI > 0.6 to predict severe neonatal encephalopathy based on RI values.

Parameter	AUC	Cut off	Sensitivity	Specificity
Right MCA	0.89	0.83	87.5%	84.5%
Left MCA	0.97	0.82	87.5%	84.5%
Right MCA	0.98	0.83	100%	91.4%
Right MCA	0.94	0.82	87.5%	89.7%

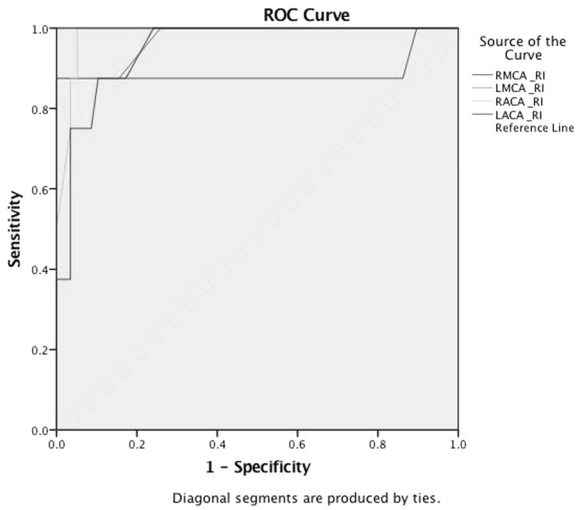

Fig. 2 Receiver operated characteristic (ROC) curves to predict severe neonatal encephalopathy. ROC curves were drawn based on the RI values of right middle cerebral artery (blue), left middle cerebral artery (green), right anterior cerebral artery (yellow), left anterior cerebral artery (purple) in cases with RI > 0.6 to predict severe neonatal encephalopathy.

vascular injury produced by free oxygen radicals [12–14]. Our data showed that ~50% of the severe encephalopathy patients had low RI (<0.6) in the cerebral arteries. This response was absent in patients exposed to the perinatal hypoxic event who did not develop neurological examination findings suspicious of encepahlopathy or had only mild encephalopathy. Low RI observed in cases of severe encephalopathy can be attributed to two possible mechanisms. Firstly, autoregulation response to severe hypoxic insult can result in vasodilatation of the intracranial arteries, however, this assertion may be counterintuitive because many of the previous studies have shown that the physiological autoregulation is impaired in cases of severe HIE. A second and more logical explanation of this observation can be the presence of systemic hypotension in many of the patients in suspected severe encephalopathy group and a decreased RI of the subjects may be due to impaired autoregulation and systemic hypotension in the most severely affected infants resulting into decrease RI of the vessels. This assumption is in concordance with that of a study by Rosenberg that demonstrated hypotension in the asphyxiated lambs and decreased oxygen delivery [10]. This paired with the fact that the measurement of RI varies directly with pulse pressure and inversely with vascular compliance can offer a plausible explanation of decreased RI. Unfortunately, we did not collect the data of systemic blood pressure and other cardiovascular parameters at the time of the Doppler scan in this study.

Over the last 2 decades, various studies have interrogated the utility of color Doppler for the evaluation of cerebral arteries in the neonates at risk of developing HIE. The observations of these studies have been summarized in Table 6 [15–27]. The results of all these studies seem widely inconsistent with half of these studies indicating lower RI of cerebral arteries in HIE and the other half demonstrating higher RI values associated with HIE or cerebral palsy. Our analysis provides some insight into this contrariety that can be due to various factors such as different study populations and different timing of the scan.

The study groups in the previous studies were widely inhomogeneous with some studies including exposure to perinatal hypoxic insult as their inclusion criteria while others including HIE or cerebral palsy in their study. We addressed this inconsonance by dividing our study population into three separate groups and further categorizing the encephalopathy group into mild, moderate, and severe encephalopathy. Our results showed that RI in cerebral vessels with perinatal hypoxic insult was significantly higher than normal neonates and further marginally higher in patients who eventually clinical features of neonatal encephalopathy. Presence of RI < 0.6 almost exclusively limited to and in half of the patients in the severe encephalopathy group. This indicated that the presence of lower RI might be used as a predictor for stage III Sarnat score at 24 h of birth. For patients with RI > 0.6, the RI values were highest in the severe encephalopathy group. RI value of 0.82–0.83 predicted severe encephalopathy with high sensitivity and specificity. Our analysis clarified the incongruence of the results of previous studies and indicated that

Table 5 Comparison of the peak systolic velocities (cm/s) of intracranial arteries between various study groups.

Groups	Right MCA	Left MCA	Right ACA	Left ACA
Comparison between healthy controls and neonates exposed to perinatal hypoxic event				
Group a ($n = 26$)	33.33 ± 6.1	32.3 ± 6.2	24.9 ± 3.6	24.6 ± 4.0
Group b + c ($n = 50$)	29.2 ± 6.7	28.1 ± 7.4	20.3 ± 4.8	19.7 ± 5.1
p value	0.37	0.15	0.21	0.23
Comparison between neonates with and without clinical findings of Neonatal encephalopathy at 24 h of birth				
Group a + b ($n = 37$)	32.6 ± 6.0	32.1 ± 6.3	24.6 ± 3.6	23.8 ± 4.0
Group c ($n = 39$)	28.7 ± 7.0	27.1 ± 7.4	19.2 ± 4.7	19.1 ± 5.4
p value	0.22	0.25	0.48	0.10
Comparison between neonates exposed to perinatal hypoxic event with and without clinical findings of neonatal encephalopathy at 24 h of birth				
Group b ($n = 11$)	30.9 ± 5.5	31.5 ± 6.8	23.9 ± 3.6	21.9 ± 3.5
Group c ($n = 39$)	28.7 ± 7.0	27.1 ± 7.4	19.2 ± 4.7	19.1 ± 5.4
p value	0.33	0.88	0.82	0.15
Comparison between mild, moderate, and severe neonatal encephalopathy subgroups				
Mild encephalopathy ($n = 9$)	31.9 ± 6.6	27.6 ± 5.4	20.8 ± 2.6	20.6 ± 2.9
Moderate encephalopathy ($n = 14$)	29.2 ± 5.9	28.7 ± 6.5	19.7 ± 6.3	19.5 ± 7.1
Severe encephalopathy ($n = 16$)	26.6 ± 7.8	25.5 ± 8.9	18.1 ± 3.7	17.7 ± 4.7
p value	0.20	0.48	0.34	0.41

infants with clinical features suspicious of severe HIE should be analyzed as an assemblage of two divergent groups.

Unlike the present study, none of these studies have performed the Doppler scan within the 1st 6 h of life and understandably, many of these studies are before the popularization of therapeutic hypothermia for HIE. To the best of our knowledge, this was the first study to perform the Doppler study of HIE patients within the recommended period for commencement of therapeutic hypothermia. A study by Pezzati et al. performed early Doppler in healthy neonates within 8 h of birth to establish the reference data of Doppler parameters and found a mean RI of 0.80 and 0.81 in term neonates ACA and MCA respectively, which was higher than our values in the control group [28]. This could be attributed to the difference between the geographical and demographic characteristics of the study population and highlights the need for more studies to generate reference data in different parts of the world.

Various Doppler parameters have been evaluated in the previous studies such as RI, PI, PSV, EDV, CBFV, and MV, however, most of the researchers recommend RI as an optimal parameter. We found that the RI was a better radiological marker for the analysis of cerebral vessels compared to PSV. RI takes both systolic and diastolic velocities into account and truly reflects the impedance of the individual arteries, as also demonstrated in the present study. Also, our data showed that the changes are mostly reflected similarly in all the four arteries, any of the four arteries can be evaluated for Doppler assessment, which will reduce the scan time, in keeping with ALARA (as low as reasonably achievable) principals.

We realize that our study had several limitations. The number of patients in the study was relatively low. Secondly, we considered the Sarnat and Sarnat criteria for grading of neonatal encephalopathy and did not perform a subsequent MRI or follow up for neurological evaluation. Moreover, a criterion for the selection of at-risk infants was based on a 5 min Apgar score <7 rather than a combination of evaluation for metabolic acidosis, Apgar score <5 at 10 min, or physical exam in the first 6 h. Thirdly, although the scans were performed in the early postpartum period, serial hourly scans would have more accurately demonstrated the trend for vasoreactivity in the early post hypoxic period. Also, we did not measure the systemic blood pressure and other cardiovascular parameters at the time of Doppler scan in the present study which could have offered a valuable insight into the mechanism of the vasodilatation observed in severe encephalopathy group. Lastly, none of the neonates included in this study received therapeutic hypothermia which impeded the ability of this study to assess the impact of Doppler scan on therapy of the HIE patients. The strength of the present study was its prospective nature, various categories of the study population, and most importantly, the expeditious Doppler scan.

Table 6 Results of the previous studies evaluating Doppler scan in HIE.

Study	Number of patients	Time of Doppler	Arteries and parameters evaluated	Significant results
Nishimaki et al. [15]	17	Between 24 and 48 h after birth	CBFV of BA, ACA	CBFV ratio of BA/ACA is higher in patients with asphyxia
Okumura et al. [16]	53	1st 72 h of life	MV and RI of ACA	Lower RI in patients with Periventricular leukomalacia
Kehrer et al. [17]	32 (preterm infants)	Days 1, 2, 3, 7, 14 of birth	CBF volume of VA and ICA	Increase of CBFV over 2 weeks with pronounced rise in 1st 2 days
Liu et al. [18]	40	Within 24 h of birth	RI of MCA	RI < 0.50 or RI > 0.9 suggested HIE RI > 1 associated with later brain death
Llves et al. [19]	47	Within 24 h of birth	Mean BFV and RI of ACA, MCA, BA, ICA	Increased BFV and decreased RI in severe HIE
Guan et al. [20]	158	Within 72 h	PSV and RI of MCA	Increased RI and decreases PSV in severe HIE
Wu [21]	55	Days 1, 2, 3	RI, PSV of MCA	Days 1 and 2: increased RI and decreased PSV in HIE Days 3: PSV and RI not statistically significant
Barseem et al. [22]	40	Within 12 h	RI, PSV, EDV of ACA, MCA	Higher RI and lower PSV in HIE
Kudrevičienė et al. [23]	78	Days 1, 2, 3, 4, 5	PSV, EDV, RI of ACA, MCA	Higher EDV, lower RI value associated with spastic quadrparesis
Pinto et al. [24]	31	Within 48 h	RI of ACA	Lower RI in patients with asphyxiated term neonates
Kumar et al. [25]	50	Within 72 h	RI of ACA	RI < 0.56 and >0.80 increased the risk of death/abnormal neurological outcome.
Kirimi et al. [26]	23	Within 12 h	RI of ACA	Lower PSV, EDV, and higher RI associated with cerebral palsy
Jongeling et al. [27]	125	Within 72 h	RI of ACA and ICA	RI < 0.56 associated with adverse neurological outcome
Present study	50	Within 6 h	PSV, RI of ACA, MCA	RI < 0.6 and >0.82 is associated with clinical features of severe neonatal encephalopathy

BA Basilar artery; *ACA* Anterior cerebral artery; *VA* Vertebral artery; *ICA* Internal cerebral artery; *MCA* Middle cerebral artery; *CBFV* cerebral blood flow velocity; *MV* mean velocity; *RI* Resitive index; *BFV* Blood flow velocity; *PSV* Peak systolic velocity; *EDV* End diastolic velocity.

To conclude, this study demonstrated that early Doppler can be utilized in patients exposed to perinatal hypoxic insult. Further, our data suggest that RI < 0.6 and >0.82 is associated with neonates subsequently classified as severe neonatal encephalopathy at 24 h as per Sarnat Classification.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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