



ANTERIOR CEREBRAL ARTERY RESISTIVE INDEX AND GRAYSCALE CRANIAL ULTRASOUND FINDINGS IN PRETERM NEONATES: A PROSPECTIVE DESCRIPTIVE STUDY AT A NATIONAL MILITARY REFERRAL HOSPITAL IN JAKARTA, INDONESIA

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ABSTRACT

Introduction: Immature cerebral autoregulation renders the preterm brain vulnerable to haemodynamic injury. The Doppler resistive index (RI) of the anterior cerebral artery (ACA) is a bedside surrogate of cerebrovascular resistance, yet no Indonesian data exist. This study described ACA RI and grayscale cranial ultrasound (CUS) findings in preterm neonates.

Methods: This prospective descriptive study enrolled preterm neonates (<37 weeks) admitted to the neonatal intensive care unit of RSPAD Gatot Soebroto, Jakarta, from May to July 2026. Grayscale CUS and pulsed-wave Doppler of the bilateral ACA (A2 segment, ≥ 3 cardiac cycles per side) were performed within the first seven days of life. RI was summarised by gestational age

(GA) and categorised as low, normal or high against GA-specific bands.

Results: Of 45 neonates, 30 were analysed (32–<37 weeks, 60.0%; 28–31 weeks, 36.7%; <28 weeks, 3.3%). Respiratory distress syndrome (40.0%) and sepsis (36.7%) were the leading comorbidities; asphyxia was absent. Median ACA RI was 0.64 (IQR 0.09) at 32–<37 weeks, 0.68 (IQR 0.07) at 28–31 weeks and 0.86 in the single infant <28 weeks. Low RI predominated (53.3%; 95% CI 36.1–69.8); high RI occurred in 13.3%. Cerebral oedema was the commonest grayscale finding (56.7%), followed by normal scans (40.0%) and grade I haemorrhage (3.3%); periventricular leukomalacia and ventriculomegaly were absent.

Discussion: ACA RI showed a descriptive inverse gradient with GA, and Doppler abnormalities occurred in grayscale-normal brains, although inter-stratum differences were not statistically significant.

Conclusion: Integrated grayscale–Doppler CUS yields locally derived cerebral haemodynamic data for Indonesian preterm neonates; larger multicentre studies are warranted.

Keywords: *preterm infant; cranial ultrasonography; Doppler ultrasonography; anterior cerebral artery; resistive index*

INTRODUCTION

Background

Preterm birth, defined as delivery before 37 completed weeks of gestation, affected an estimated 13.4 million live births (9.9%) worldwide in 2020, and complications of prematurity remain the leading cause of death in children younger than five years. Indonesia contributes one of the largest absolute burdens globally, with approximately 675,700 preterm births annually, ranking fifth worldwide; prematurity accounts for roughly one-third of neonatal deaths in a setting where the neonatal mortality rate approximates 15 per 1,000 live births.¹⁻⁴

Gatot Soebroto Central Army Hospital (RSPAD Gatot Soebroto), the national military referral hospital in Jakarta, manages preterm neonates across the full spectrum of severity; 64 preterm infants were admitted to its neonatal intensive care unit (NICU) between January and March 2026 alone, 43 of whom had complications, underscoring the need for locally applicable neuroimaging data.⁵

The preterm brain is disproportionately vulnerable to injury. The subventricular germinal matrix is a highly vascular yet structurally fragile zone composed of thin-walled capillaries with sparse pericyte and astrocytic end-foot support, and cerebral autoregulation operates within a narrow plateau. Consequently, cerebral blood flow becomes pressure-passive and tracks fluctuations in systemic arterial pressure, predisposing to both ischaemia (hypoperfusion) and haemorrhage (hyperperfusion or reperfusion), particularly in the context of respiratory distress syndrome (RDS), germinal matrix–intraventricular haemorrhage (GMH-IVH), perinatal asphyxia and sepsis (Figure 1).⁶⁻⁹

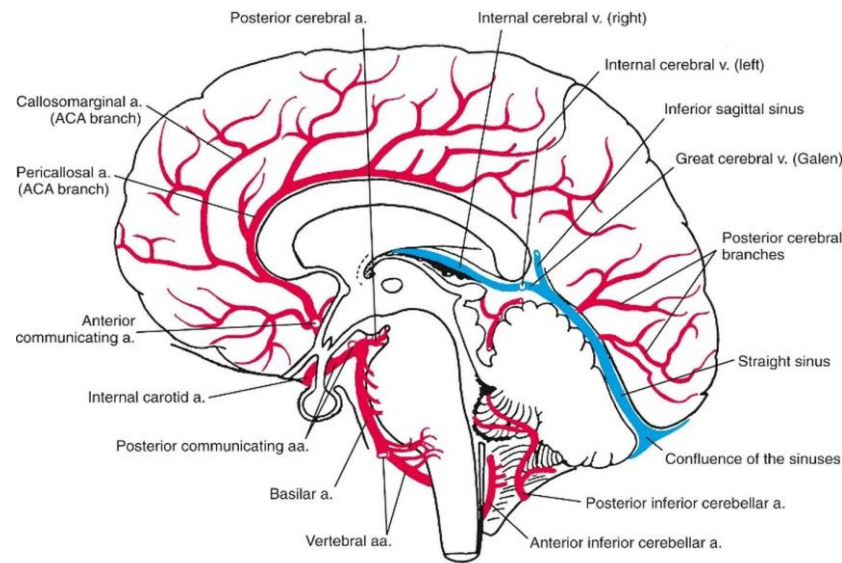


Figure 1. Arterial supply of the neonatal brain. Schematic of the internal carotid and vertebrobasilar systems giving rise to the anterior (ACA), middle (MCA) and posterior (PCA) cerebral arteries, together with the pericallosal and callosomarginal branches of the ACA and the deep venous system (internal cerebral veins, vein of Galen, straight sinus), all of which can be interrogated through the anterior fontanelle. Reproduced from the cited literature for educational illustration.^{7,10-12}

Cranial ultrasonography (CUS) is the recommended first-line neuroimaging modality in preterm neonates in preference to magnetic resonance imaging (MRI) and computed tomography because it is non-invasive, free of ionising radiation, portable, repeatable at the bedside and inexpensive. Scanning through the open anterior fontanelle provides a direct acoustic window to supratentorial structures, supplemented by the posterior and mastoid fontanelles for the occipital horns and posterior fossa. Grayscale (B-mode) imaging depicts haemorrhage, ventricular size, periventricular echogenicity, cysts and gyral maturation, whereas spectral Doppler quantifies cerebral haemodynamics.^{7,10,13,14}

The resistive index (RI; Pourcelot index), calculated as (peak systolic velocity – end-diastolic velocity)/peak systolic velocity, reflects downstream cerebrovascular resistance and is most reproducibly measured in the anterior cerebral artery (ACA), which is readily insonated on midsagittal or parasagittal planes at a near-zero angle. Abnormally high RI suggests increased distal

resistance (raised intracranial pressure, vasoconstriction, severe hypotension or ductal steal), whereas low RI suggests vasodilatation or luxury perfusion, classically following asphyxia. Gill et al. (2024) reported day-3 ACA RI of 0.76–0.78 across gestational strata but no significant difference between preterm neonates with and without early comorbidities; Akın et al. (2023) found no association between ACA RI and early near-infrared spectroscopy (NIRS) cerebral oxygenation but higher day-1 RI in infants who died early; and Pal et al. (2025) observed higher RI within 36 hours of life in infants <29 weeks who developed IVH.^{15–19}

Problem statement

Despite a growing international evidence base, published ACA RI data derive predominantly from European, North American, Turkish and South Asian cohorts with differing demographic, genetic and obstetric–neonatal practice profiles, and reported values vary considerably with postnatal age, insonated segment, fontanelle pressure and haemodynamic status. No study has described ACA RI together with grayscale CUS findings in Indonesian preterm neonates. The research question was therefore: what is the profile of Doppler ACA RI in preterm neonates at RSPAD Gatot Soebroto, Jakarta?^{17,20–22}

Research objectives

The general objective was to describe ACA RI in preterm neonates at RSPAD Gatot Soebroto. The specific objectives were to: (i) describe demographic characteristics (gestational age [GA], sex, birth weight, mode of delivery, head circumference and 5-minute Apgar score); (ii) describe clinical comorbidities (RDS, neonatal sepsis and asphyxia); (iii) measure and summarise ACA RI by GA stratum as local reference data; (iv) describe the distribution of RI categories (low, normal, high) by GA; and (v) describe grayscale CUS findings, including cerebral oedema, GMH-IVH, ventriculomegaly, periventricular leukomalacia (PVL) and other anatomical abnormalities.^{4,23}

Research benefits

Academically, the study provides the first Indonesian descriptive dataset on ACA RI in preterm neonates, supporting curricula and training in neonatal cranial Doppler for radiology residents. Clinically, it provides a basis for a standard operating procedure (SOP) for neonatal CUS with routine Doppler at RSPAD Gatot Soebroto and for a structured neuroradiological screening

programme for preterm neonates. For the investigator, it consolidates competence in the technique and interpretation of neonatal cranial Doppler.^{10,24}

Hypotheses

As a descriptive study, no confirmatory hypothesis was tested. Two a priori working hypotheses, grounded in the developmental physiology of cerebral autoregulation, guided interpretation: (H1) ACA RI is inversely related to GA, being highest in the most immature infants; and (H2) a proportion of preterm neonates exhibit ACA RI outside GA-specific reference bands even when grayscale CUS is normal, indicating that Doppler adds haemodynamic information not captured by morphology alone.^{6,17,25}

Research gap

Three gaps justify this study. First, a population gap: searches of PubMed, Google Scholar and Indonesian national journal repositories identified no published ACA RI data for Indonesian or other Southeast Asian preterm neonates. Second, a spectrum gap: most cohorts restrict enrolment to very or extremely preterm infants (<29–35 weeks), leaving moderate-to-late preterm neonates (32–<37 weeks), who constitute the majority of preterm births, under-represented. Third, an integration gap: Doppler indices are frequently reported without systematic grayscale correlation, whereas pictorial and consensus reviews describe morphology without quantitative Doppler data.^{13,17,19–21}

METHODS

Study design, setting and period

This was a prospective, descriptive observational study conducted in the Department of Radiology and the NICU of RSPAD Gatot Soebroto, Central Jakarta, Indonesia, from May to July 2026. A descriptive design was selected because the primary aim was to characterise the distribution, central tendency and GA-stratified profile of ACA RI rather than to test causal hypotheses. Grayscale CUS findings and clinical comorbidities were collected as complementary descriptive variables to contextualise RI values.²⁶

Population, sampling and eligibility

The target population comprised all preterm neonates (GA <37 weeks) treated at the NICU of RSPAD Gatot Soebroto; the accessible population comprised those admitted during May–July

2026. Consecutive (purposive, total) sampling was applied: every neonate meeting the eligibility criteria during the study period was enrolled, so that the sample size equalled the number of eligible neonates. Inclusion criteria were: (i) GA <37 weeks, born at or referred to RSPAD Gatot Soebroto during the study period; (ii) relatively stable haemodynamic status at examination (not in cardiac arrest or undergoing active resuscitation); and (iii) written informed consent from a parent or guardian. Neonates with congenital malformations or syndromes (e.g., congenital hydrocephalus, anencephaly, holoprosencephaly) were excluded.^{4,10}

Variables and operational definitions

The primary variable was ACA RI. Complementary variables comprised demographic characteristics, clinical comorbidities and grayscale CUS findings. GA was classified according to WHO categories as extremely preterm (<28 weeks), very preterm (28–31 weeks) and moderate-to-late preterm (32–<37 weeks); birth weight as low (LBW, 1,500–2,499 g), very low (VLBW, 1,000–1,499 g) and extremely low (ELBW, <1,000 g). GMH-IVH was graded according to Papile, and ventriculomegaly was defined as a ventricular index >4 mm above the 97th centile (Levene). ACA RI was categorised as low, normal or high relative to GA-specific reference bands pre-specified in the study protocol (32–<37 weeks: 0.62–0.75; 28–31 weeks: 0.70–0.80; <28 weeks: 0.76–0.85). Operational definitions are provided in Table 1.^{4,23,27–29}

Table 1. Operational definitions of study variables

Variable	Operational definition	Measurement	Categories / result	Scale
ACA resistive index (primary)	Index from PW spectral Doppler through the anterior fontanelle reflecting distal cerebrovascular resistance; $RI = (PSV - EDV)/PSV$	PW Doppler, A2 segment, bilateral, ≥ 3 cycles/side, angle <60°; RI = mean of valid bilateral values	Low / normal / high vs GA band: 32–<37 wk 0.62–0.75; 28–31 wk 0.70–0.80; <28 wk 0.76–0.85	Ordinal (numeric for summary)

Gestational age	Completed weeks at birth from LMP or first-trimester US	Delivery record	<28; 28–31; 32–<37 weeks	Numeric / ordinal
Birth weight	Weight within the first hour before intravenous fluids	Calibrated digital scale	ELBW <1,000 g; VLBW 1,000–1,499 g; LBW 1,500–2,499 g	Numeric / ordinal
Sex	Biological sex by external genitalia/record	Record / examination	Male; female	Nominal
Head circumference	Occipitofrontal circumference at birth	Tape measure (cm)	cm by GA stratum	Ratio
Apgar score (5 min)	Sum of heart rate, respiration, tone, reflex irritability and colour (0–2 each)	Delivery record	7–10 reassuring; 4–6 moderately abnormal; 0–3 low	Ordinal
Perinatal asphyxia	Hypoxic–ischaemic insult before/during delivery (cord pH <7.0 or base deficit $\leq$ -12 mmol/L, 5-min Apgar <7, or active resuscitation)	Medical record	Present / absent	Nominal
RDS	Acute respiratory failure due to surfactant deficiency	Medical record	Present / absent	Nominal
Neonatal sepsis	Positive blood culture or strong clinical suspicion	Medical record, laboratory	Present / absent	Nominal

	with leukocytosis/leukopenia and raised CRP			
GMH-IVH	Echogenic haemorrhage in germinal matrix and/or ventricles on B-mode	Coronal and sagittal grayscale	None; Papile I– IV	Ordinal
Ventriculomegaly	Ventricular index >4 mm above the 97th centile (Levene) on coronal plane	Callipers, grayscale	Present / absent	Nominal
PVL	Persistent periventricular hyperechogenicity (non- cystic) or periventricular cysts (cystic, usually after 2–3 weeks)	Grayscale	Present / absent	Nominal
Cerebral oedema	Diffusely increased parenchymal echogenicity with narrowed sulci, compressed ventricles and reduced gray–white differentiation	Grayscale	Present / absent	Nominal

ACA, anterior cerebral artery; CRP, C-reactive protein; EDV, end-diastolic velocity; ELBW/VLBW/LBW, extremely low/very low/low birth weight; GA, gestational age; GMH-IVH, germinal matrix–intraventricular haemorrhage; LMP, last menstrual period; PSV, peak systolic velocity; PVL, periventricular leukomalacia; PW, pulsed-wave; RDS, respiratory distress syndrome; RI, resistive index; US, ultrasonography.^{15,23,27,28,30,31}

Equipment and image acquisition

Examinations were performed with the ultrasound systems of the Department of Radiology using a microconvex/phased-array transducer (5–10 MHz) sized to the anterior fontanelle and a high-frequency linear transducer (7.5–12 MHz) for superficial structures. B-mode imaging was used to confirm anatomy before Doppler; colour Doppler flow imaging (CDFI) localised the ACA; and pulsed-wave (PW) spectral Doppler generated range-gated velocity spectra from which peak systolic velocity (PSV), end-diastolic velocity (EDV) and RI were calculated automatically. Systems underwent routine institutional calibration, and electronic callipers were used for ventricular measurements. Standard acoustic windows and coronal/sagittal scanning planes are illustrated in Figure 2.^{7,10,12,14}

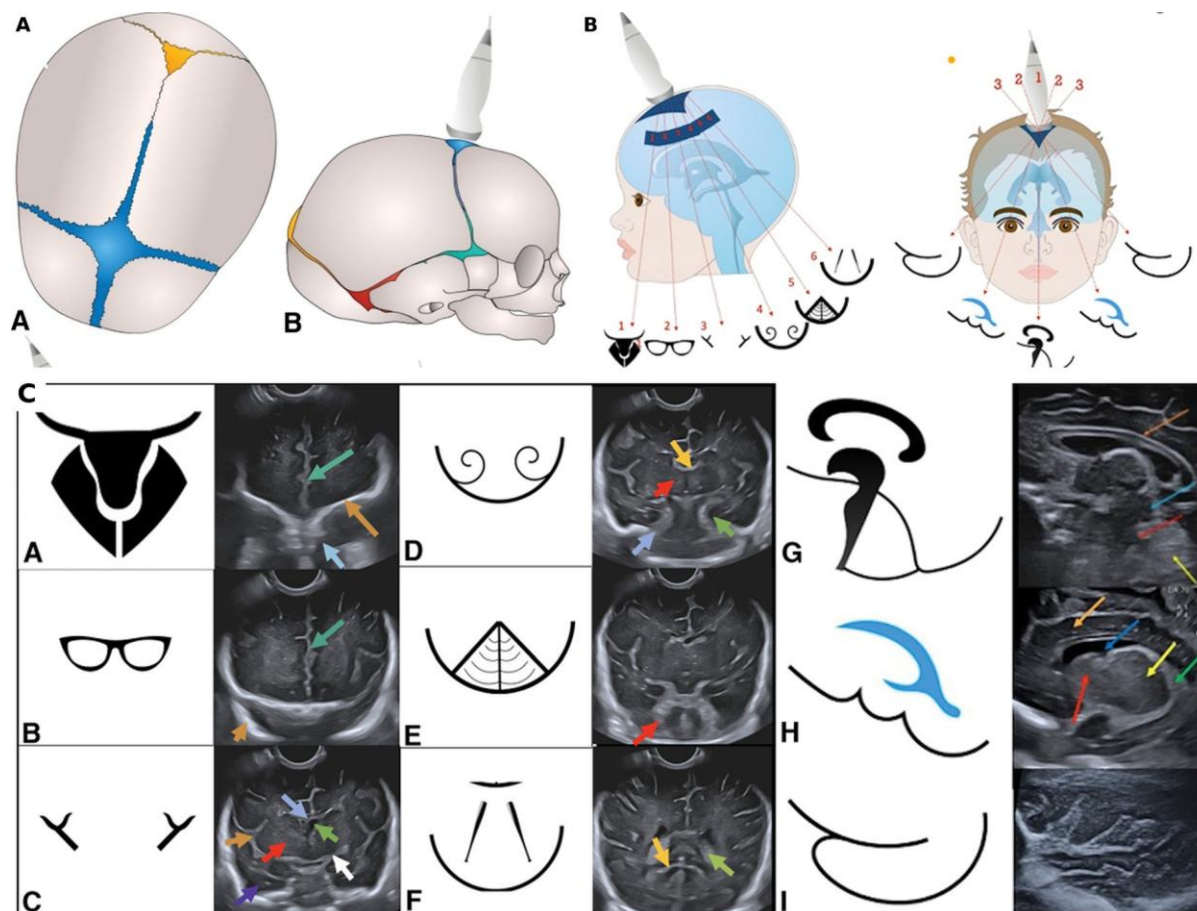


Figure 2. Standardised neonatal cranial ultrasound technique. (A) Acoustic windows: anterior, posterior and mastoid fontanelles and the temporal window. (B) Sequential coronal and sagittal scanning planes through the anterior fontanelle. (C) Reference images of the standard planes; internal labels A–F denote the basic coronal planes (‘bull’s horn’, ‘spectacles’, bilateral ‘Y’, bilateral ‘C’, inverted ‘V’ and ‘basket’ configurations) and G–I the midsagittal, 15° parasagittal and lateral sagittal planes. Panels reproduced from the cited literature for educational illustration.^{10,14,28}

For reference, characteristic grayscale and Doppler patterns of the principal preterm brain pathologies against which scans were interpreted (GMH-IVH, periventricular white matter injury/PVL, diffuse cerebral oedema, hypoxic–ischaemic injury and sepsis-associated echogenic lesions) are summarised in Figure 3.^{8,9,30,31}

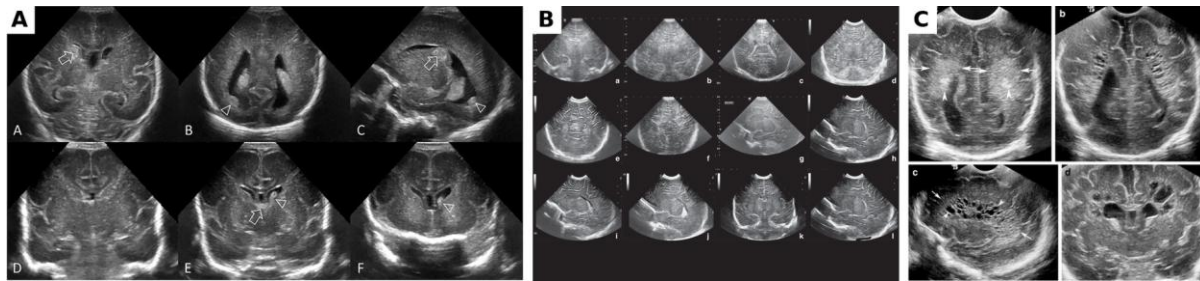


Figure 3. Reference grayscale patterns of preterm brain injury. (A) Grade II germinal matrix–intraventricular haemorrhage at the caudothalamic groove. (B) Diffuse cerebral oedema with increased parenchymal echogenicity and loss of gray–white differentiation. (C) Cystic periventricular leukomalacia. Panels reproduced from the cited literature for educational illustration.^{8,13,30,31}

Standardised Doppler protocol for RI measurement

(1) Subject preparation: infants were examined supine in a quiet state; examinations were deferred during active crying because crying artefactually modifies RI. (2) Transducer placement: sterile water-based gel was applied and a floating-probe technique with minimal pressure was used to avoid iatrogenic elevation of intracranial pressure, which increases RI. (3) ACA identification: on midsagittal/parasagittal planes the ACA was visualised by CDFI as a flow signal directed towards the transducer along the corpus callosum. (4) Sample gate: the PW sample volume was positioned on the A2 segment with an insonation angle kept as small as possible (<60°). (5) Recording and calculation: at least three consecutive representative cardiac cycles with a consistent waveform were selected; RI was computed automatically by the formula below, measured bilaterally, and the final RI for each infant was the mean of all valid bilateral measurements (Figure 4). Examinations were performed within the first seven days of life.^{15,16,22,32}

$$RI = (PSV - EDV) / PSV \quad (\text{Equation 1})$$

$$PI = (PSV - EDV) / V_{mean} \quad (\text{Equation 2})$$

PSV, peak systolic velocity (maximum velocity in systole); EDV, end-diastolic velocity (velocity at end-diastole); V_{mean} , time-averaged mean velocity over one cardiac cycle; PI, pulsatility index (reported for completeness; not analysed).¹⁵

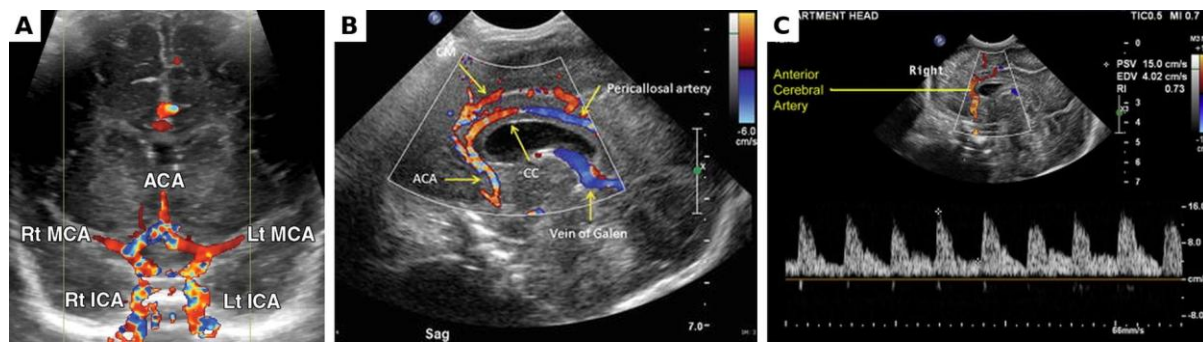


Figure 4. Transfontanellar Doppler of the cerebral arteries. (A) Colour Doppler depiction of the circle of Willis (ACA, right and left MCA and ICA). (B) Sagittal colour Doppler of the ACA/pericallosal artery along the corpus callosum together with the vein of Galen. (C) Pulsed-wave spectral Doppler of the ACA with automatic calculation of PSV, EDV and RI. Panels reproduced from the cited literature for educational illustration.^{14,15}

Data collection and observer standardisation

Data were recorded on a purpose-designed case report form (identity, demographic and clinical characteristics, bilateral RI per measurement, grayscale findings and comorbidities) and transferred to Microsoft Excel 2021. All examinations were performed or directly supervised by radiology residents standardised in neonatal cranial Doppler under consultant radiologist supervision; a calibration session preceded enrolment, and discordant interpretations were resolved by consensus with the supervising radiologist.^{24,33}

Statistical analysis

Analyses were performed with IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Normality of RI was assessed with the Shapiro–Wilk test ($n < 50$) supplemented by histograms, box plots and Q–Q plots. Normally distributed variables are presented as mean $\pm$ standard deviation (SD) and non-normal variables as median (interquartile range, IQR); categorical variables as n (%). RI was summarised overall and by GA stratum (mean $\pm$ SD with 95% confidence interval [CI], median [IQR], minimum–maximum, skewness and kurtosis), and the frequency of low, normal and high RI was tabulated by GA. To aid interpretation, 95% CIs for key proportions were calculated using the Wilson score method, and post hoc exploratory comparisons

between the two adequately populated strata (28–31 vs 32–<37 weeks) were performed on the aggregated data (Welch t-test with Hedges' g effect size and Fisher–Freeman–Halton exact test); these were not powered and are hypothesis-generating only. Formulae: $RI = (PSV - EDV)/PSV$; $\bar{x} = \sum x_i/n$; $SD = \sqrt{[\sum (x_i - \bar{x})^2/(n - 1)]}$; $\% = (n \text{ category}/N \text{ total}) \times 100$.²⁶

Ethical considerations

The protocol was reviewed and approved by the Health Research Ethics Committee of RSPAD Gatot Soebroto (Ethical Approval No. 316/VI/KEPK/2026) in accordance with the seven WHO 2011 standards and the 2016 CIOMS guidelines. Written informed consent was obtained from a parent or legal guardian of every participant.¹⁰

RESULTS

Recruitment

Forty-five preterm neonates were admitted to the NICU during May–July 2026. Fifteen were not enrolled: nine were haemodynamically unstable at the time of examination, five had congenital anomalies, and one infant born at 23 weeks died shortly after birth. Thirty neonates were therefore enrolled and analysed, with no missing data (Figure 5).

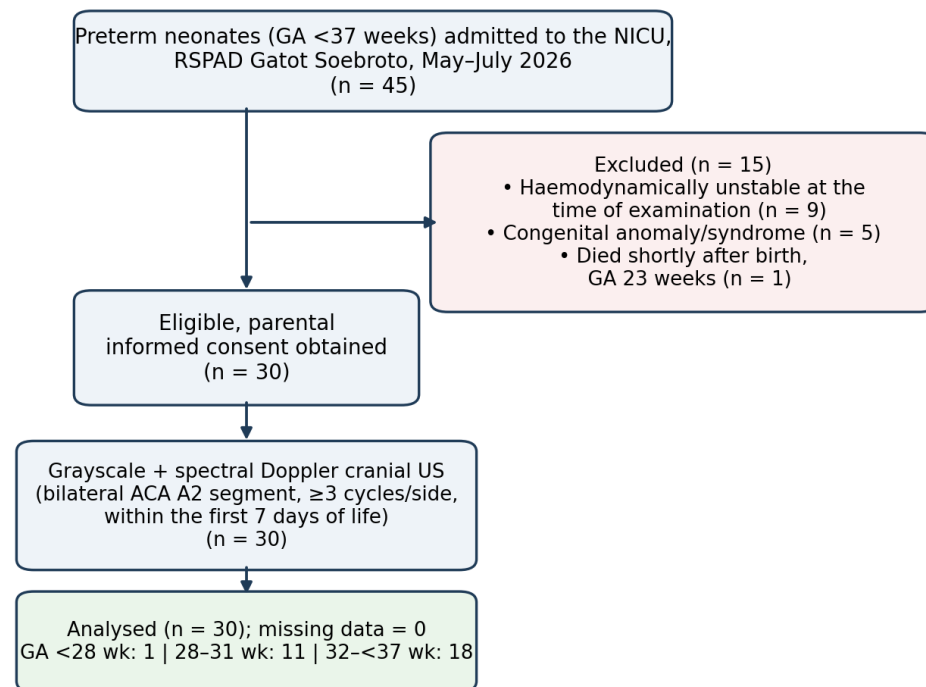


Figure 5. Flow diagram of subject recruitment. ACA, anterior cerebral artery; GA, gestational age; NICU, neonatal intensive care unit; US, ultrasonography.

Demographic characteristics

Sex distribution was balanced (15 males and 15 females). Most infants were moderate-to-late preterm (32–<37 weeks; 18/30, 60.0%), followed by very preterm (28–31 weeks; 11/30, 36.7%) and extremely preterm (<28 weeks; 1/30, 3.3%). Nineteen infants (63.3%; 95% CI 45.5–78.1) were LBW and 11 (36.7%) VLBW; none was ELBW. Caesarean delivery predominated (20/30, 66.7%; 95% CI 48.8–80.8). Median birth head circumference was 28 cm (IQR 2) in both the 32–<37-week and 28–31-week strata and 24 cm in the extremely preterm infant; overall mean head circumference was 28.40 ± 1.83 cm (range 24–31). The median 5-minute Apgar score was 8 (IQR 1; range 7–10), with no infant scoring <7 (Table 2).^{4,23}

Table 2. Demographic characteristics of the study subjects (N = 30)

Characteristic	Category	n (%) or median (IQR)
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Sex	Male	15 (50.0)
	Female	15 (50.0)
Gestational age	32–<37 weeks	18 (60.0)
	28–31 weeks	11 (36.7)
	<28 weeks	1 (3.3)
Birth weight	LBW (1,500–2,499 g)	19 (63.3)
	VLBW (1,000–1,499 g)	11 (36.7)
	ELBW (<1,000 g)	0 (0.0)
Mode of delivery	Spontaneous vaginal	10 (33.3)
	Caesarean section	20 (66.7)
Head circumference at birth (cm)	32–<37 weeks	28 (2)
	28–31 weeks	28 (2)
	<28 weeks (n = 1)	24
	Overall, mean $\pm$ SD (range)	28.40 $\pm$ 1.83 (24–31)
Apgar score at 5 min	Median (IQR)	8 (1)
	Score 7 / 8 / 9 / 10	2 (6.7) / 17 (56.7) / 9 (30.0) / 2 (6.7)

Numeric data are median (IQR) unless stated; categorical data are n (%). Head circumference was non-normally distributed (Shapiro–Wilk $p = 0.001$). ELBW, extremely low birth weight; IQR, interquartile range; LBW, low birth weight; SD, standard deviation; VLBW, very low birth weight.^{4,23}

Clinical comorbidities

RDS was the most frequent comorbidity (12/30, 40.0%; 95% CI 24.6–57.7), followed by neonatal sepsis (11/30, 36.7%; 95% CI 21.9–54.5); seven infants (23.3%) had no comorbidity, and no case fulfilled the operational criteria for perinatal asphyxia. Within the 32–<37-week stratum, eight infants (44.4%) had RDS, six (33.3%) sepsis and four (22.2%) no comorbidity; within the 28–

31-week stratum, four (36.4%) had RDS, four (36.4%) sepsis and three (27.3%) no comorbidity; the extremely preterm infant had sepsis (Table 3).^{29,34}

Table 3. Clinical comorbidities by gestational age stratum

GA stratum	No comorbidity	RDS	Neonatal sepsis	Asphyxia	Total
32–<37 weeks	4 (22.2)	8 (44.4)	6 (33.3)	0 (0.0)	18 (100)
28–31 weeks	3 (27.3)	4 (36.4)	4 (36.4)	0 (0.0)	11 (100)
<28 weeks	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	1 (100)
Total, n (%) [95% CI]	7 (23.3) [11.8–40.9]	12 (40.0) [24.6–57.7]	11 (36.7) [21.9–54.5]	0 (0.0)	30 (100)

Data are n (% within GA stratum); 95% CI by the Wilson score method. The total for neonatal sepsis is corrected to 36.7% (11/30). GA, gestational age; RDS, respiratory distress syndrome.²⁹

ACA resistive index by gestational age

RI values were not normally distributed on Shapiro–Wilk testing; medians were therefore used as the principal summary measure. In the 32–<37-week stratum (n = 18), mean RI was 0.665 ± 0.055 (95% CI 0.638–0.692), median 0.64 (IQR 0.09) and range 0.61–0.76. In the 28–31-week stratum (n = 11), mean RI was 0.693 ± 0.074 (95% CI 0.643–0.743), median 0.68 (IQR 0.07) and range 0.60–0.82. The single extremely preterm infant had an RI of 0.86. RI thus showed a descriptive inverse gradient with GA (0.86 → 0.68 → 0.64). In exploratory analysis, the mean difference between the 28–31-week and 32–<37-week strata was 0.028 (95% CI –0.027 to 0.082; Welch t = 1.07, p = 0.30; Hedges' g = 0.43, 95% CI –0.33 to 1.19), indicating a small-to-moderate but statistically non-significant effect (Table 4).^{17,26}

Table 4. Anterior cerebral artery resistive index by gestational age stratum

GA stratum	n (%)	Mean $\pm$ SD	95% CI of mean	Median (IQR)	Min–max	Skewness (SE)	Kurtosis (SE)
32–<37 weeks	18 (60.0)	0.665 ± 0.055	0.638–0.692	0.64 (0.09)	0.61–0.76	0.551 (0.536)	–1.282 (1.038)

28–31 weeks	11 (36.7)	0.693 ± 0.074	0.643– 0.743	0.68 (0.07)	0.60– 0.82	0.570 (0.661)	–0.466 (1.279)
<28 weeks	1 (3.3)	0.86	—	0.86	0.86	—	—

RI is the mean of bilateral ACA (A2 segment) measurements, ≥ 3 cardiac cycles per side. RI was non-normally distributed (Shapiro–Wilk); medians are the principal summary measure. Exploratory comparison 28–31 vs 32–<37 weeks: mean difference 0.028 (95% CI –0.027 to 0.082), Welch $t = 1.07$, $df = 16.7$, $p = 0.30$; Hedges' $g = 0.43$ (95% CI –0.33 to 1.19). CI, confidence interval; IQR, interquartile range; SD, standard deviation; SE, standard error.²⁶

Distribution of RI categories

Overall, low RI was the most frequent category (16/30, 53.3%; 95% CI 36.1–69.8), followed by normal RI (10/30, 33.3%; 95% CI 19.2–51.2) and high RI (4/30, 13.3%; 95% CI 5.3–29.7). Low RI occurred in 10/18 (55.6%) infants at 32–<37 weeks and 6/11 (54.5%) at 28–31 weeks; high RI occurred in 1/18 (5.6%), 2/11 (18.2%) and 1/1 (100%) infants in the 32–<37-week, 28–31-week and <28-week strata, respectively. The proportion with high RI was therefore greatest in the least mature strata (3/12 [25.0%] at <32 weeks vs 1/18 [5.6%] at ≥ 32 weeks; Fisher exact $p = 0.27$). The distribution of RI categories did not differ between the 28–31-week and 32–<37-week strata (Fisher–Freeman–Halton exact $p = 0.64$) (Table 5).

Table 5. Distribution of RI categories by gestational age stratum

GA stratum (reference band)	Low RI	Normal RI	High RI	Total
32–<37 weeks (0.62–0.75)	10 (55.6)	7 (38.9)	1 (5.6)	18 (100)
28–31 weeks (0.70–0.80)	6 (54.5)	3 (27.3)	2 (18.2)	11 (100)
<28 weeks (0.76–0.85)	0 (0.0)	0 (0.0)	1 (100)	1 (100)
Total, n (%) [95% CI]	16 (53.3) [36.1–69.8]	10 (33.3) [19.2–51.2]	4 (13.3) [5.3–29.7]	30 (100)

Data are n (% within GA stratum); 95% CI by the Wilson score method. Reference bands were pre-specified in the study protocol and are not validated normative values. Exploratory tests:

28–31 vs 32–<37 weeks, Fisher–Freeman–Halton exact $p = 0.64$; high RI at <32 weeks (3/12) vs ≥ 32 weeks (1/18), Fisher exact $p = 0.27$. GA, gestational age; RI, resistive index.

Grayscale cranial ultrasound findings

Cerebral oedema was the commonest grayscale finding (17/30, 56.7%; 95% CI 39.2–72.6), followed by normal scans (12/30, 40.0%) and grade I GMH-IVH (1/30, 3.3%). Neither PVL nor ventriculomegaly, nor any other structural anomaly, was detected. Oedema was observed in 10/18 (55.6%), 6/11 (54.5%) and 1/1 (100%) infants in the 32–<37-week, 28–31-week and <28-week strata, respectively; the only GMH-IVH occurred at 32–<37 weeks (Table 6). Representative images are shown in Figures 6–9: oedema with RI of 0.86, 0.76 and 0.66 at 27, 30 and 35 weeks (Figure 6); grade I GMH-IVH with RI 0.80 (Figure 7); normal scans with RI 0.64 at 34 weeks and 0.70 at 30 weeks (Figure 8); and, notably, a morphologically normal brain with a markedly reduced RI of 0.51 (Figure 9).^{27,31}

Table 6. Grayscale cranial ultrasound findings by gestational age stratum

GA stratum	Normal	Cerebral oedema	GMH-IVH	PVL	Ventriculomegaly	Total
32–<37 weeks	7 (38.9)	10 (55.6)	1 (5.6)	0 (0.0)	0 (0.0)	18 (100)
28–31 weeks	5 (45.5)	6 (54.5)	0 (0.0)	0 (0.0)	0 (0.0)	11 (100)
<28 weeks	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
Total, n (%)	12 (40.0)	17 (56.7)	1 (3.3)	0 (0.0)	0 (0.0)	30 (100)
[95% CI]	[24.6–57.7]	[39.2–72.6]	[0.6–16.7]			

Data are n (% within GA stratum); 95% CI by the Wilson score method. The single GMH-IVH was Papile grade I. Examinations were performed within the first 7 days of life. GMH-IVH, germinal matrix–intraventricular haemorrhage; PVL, periventricular leukomalacia.²⁷

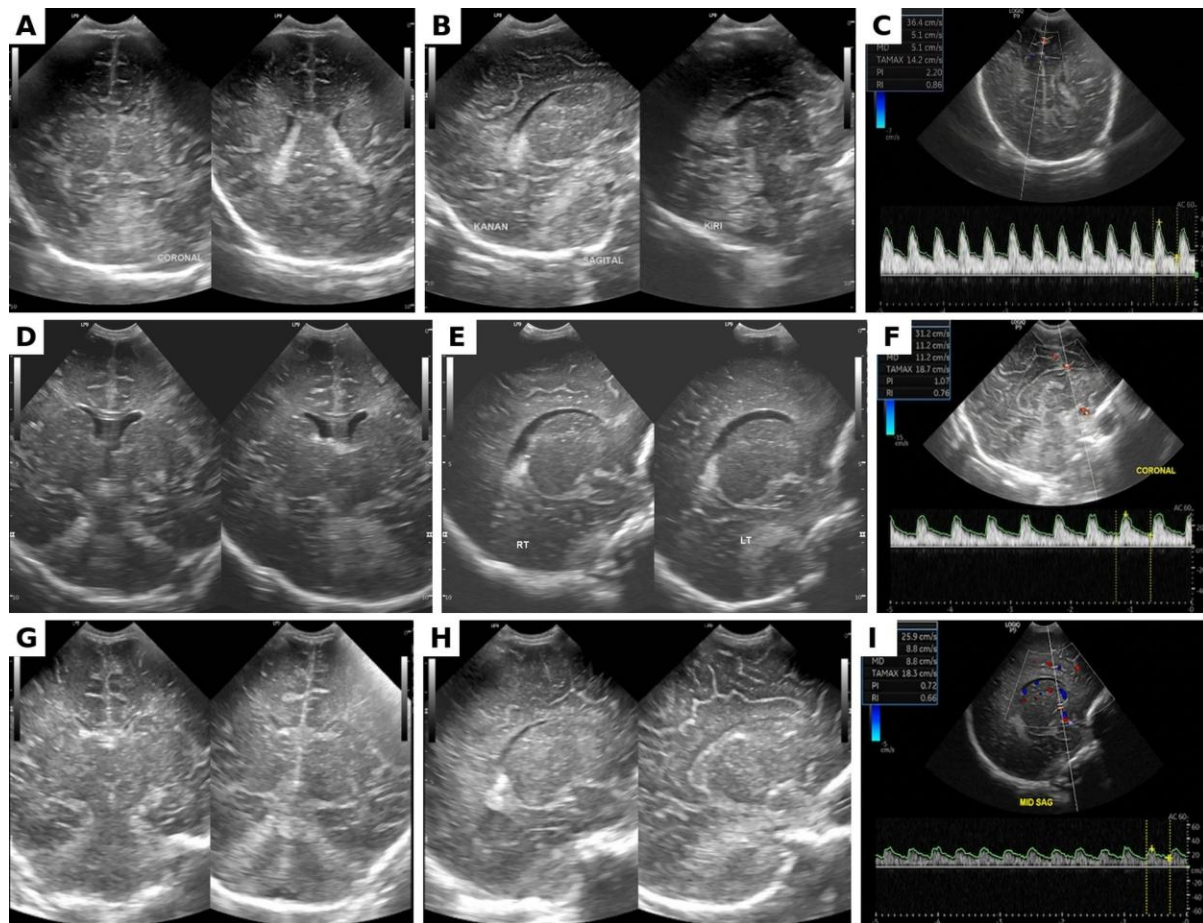


Figure 6. Cerebral oedema with corresponding ACA spectral Doppler. Row 1 (A–C): GA 27 weeks, coronal and sagittal grayscale showing diffusely increased parenchymal echogenicity; ACA RI 0.86. Row 2 (D–F): GA 30 weeks; ACA RI 0.76. Row 3 (G–I): GA 35 weeks; ACA RI 0.66.

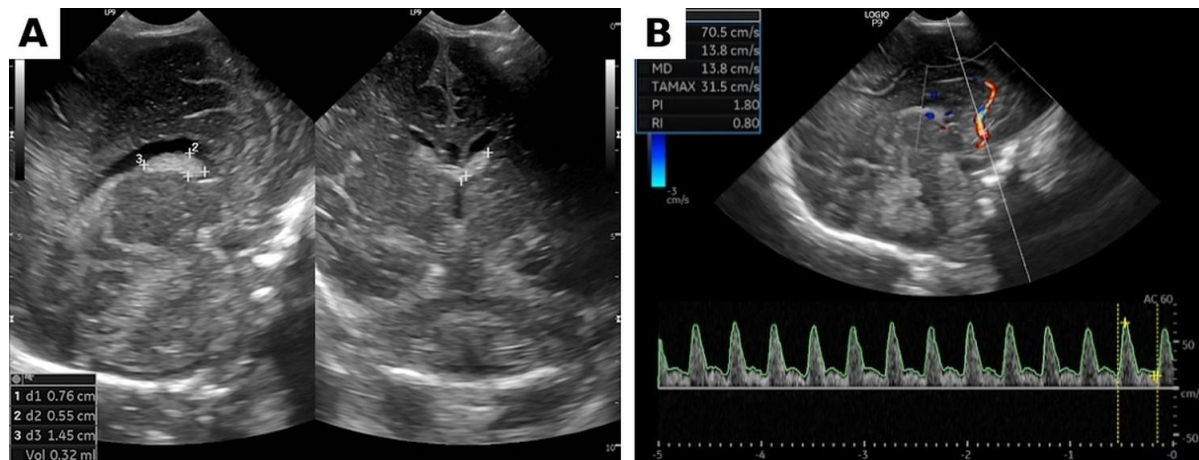


Figure 7. Grade I germinal matrix haemorrhage. (A) Coronal and parasagittal grayscale showing an echogenic focus confined to the germinal matrix region without ventricular extension. (B) ACA spectral Doppler; RI 0.80.²⁷

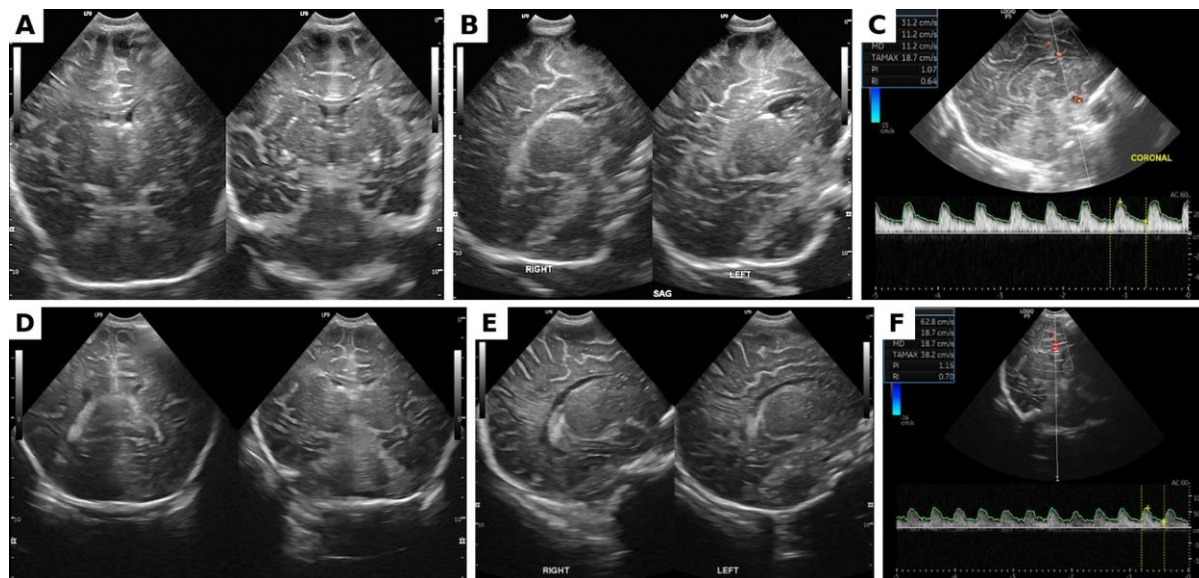


Figure 8. Normal grayscale cranial ultrasound with ACA Doppler. Row 1 (A–C): GA 34 weeks; RI 0.64. Row 2 (D–F): GA 30 weeks; RI 0.70.

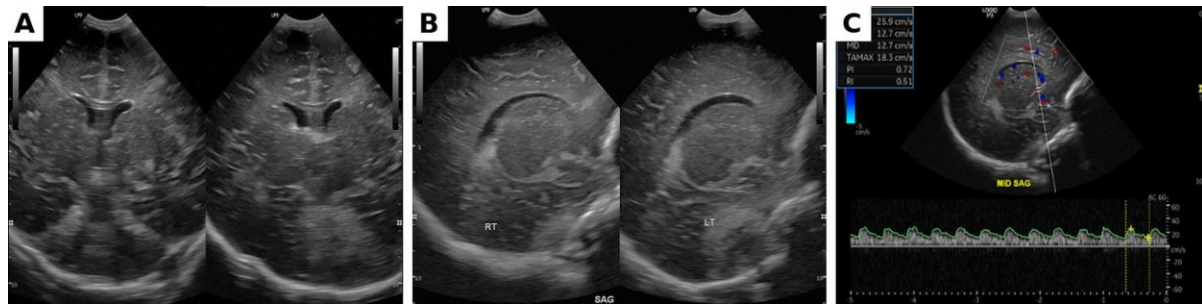


Figure 9. Normal grayscale morphology with markedly reduced ACA resistive index. (A, B) Coronal and sagittal grayscale images without structural abnormality. (C) ACA spectral Doppler with elevated diastolic flow; RI 0.51.

DISCUSSION

This is, to our knowledge, the first prospective description of ACA RI integrated with grayscale CUS in Indonesian preterm neonates. Four principal findings emerged: (i) a descriptive inverse gradient of RI with GA; (ii) a predominance of RI values below the protocol-specified GA bands, with high RI concentrated in the least mature infants; (iii) diffuse cerebral oedema as the dominant grayscale abnormality, with a low prevalence of GMH-IVH and no PVL or ventriculomegaly within the first week; and (iv) Doppler abnormalities in morphologically normal brains, supporting the incremental value of haemodynamic assessment.^{15,20}

Demographic and clinical profile

The cohort was dominated by moderate-to-late preterm, LBW infants delivered by caesarean section, with balanced sex distribution and absence of ELBW infants. This pattern mirrors global epidemiology, in which the large majority of preterm births are moderate-to-late preterm, and is consistent with referral-centre practice in which maternal or fetal indications frequently prompt operative delivery. The smaller head circumference in the extremely preterm infant is expected from intrauterine growth trajectories. The median 5-minute Apgar score of 8 indicates generally favourable immediate adaptation, although Apgar components (tone, reflex irritability, colour) are maturation-dependent and should not be used in isolation to diagnose asphyxia or predict neurological outcome in preterm infants. Because this study was descriptive, the distribution of

delivery mode cannot be interpreted causally; notably, Akin et al. reported higher day-1 ACA RI after caesarean than vaginal delivery, a potential confounder for future analytic studies.^{1,4,18,23}

RDS and sepsis as dominant comorbidities

RDS (40.0%) and neonatal sepsis (36.7%) were the leading comorbidities, whereas asphyxia was absent. RDS reflects surfactant deficiency and pulmonary immaturity and affects approximately 93% of infants <28 weeks, 50% at 28–32 weeks and 20–30% at 32–34 weeks; the larger absolute number of RDS cases in the 32–<37-week stratum reflects its larger denominator rather than higher risk. Hypoxaemia and hypercapnia in RDS provoke reactive cerebral vasodilatation that increases EDV and lowers RI, which normalises after surfactant or ventilatory stabilisation. Sepsis was present in every GA stratum; immune immaturity and invasive NICU procedures heighten susceptibility, and sepsis perturbs cerebral haemodynamics bidirectionally—vasodilatation lowers RI, whereas septic myocardial dysfunction and raised distal resistance increase it, as shown by Singh et al., who found significantly higher ACA RI and lower EDV in late-onset sepsis. These opposing mechanisms plausibly contribute to the heterogeneity of RI observed here. The absence of asphyxia is consistent with the Apgar distribution (all ≥ 7) and with the exclusion of haemodynamically unstable neonates requiring active resuscitation.^{17,29,30,34}

ACA RI and gestational age

RI declined descriptively from 0.86 (<28 weeks) to 0.68 (28–31 weeks) and 0.64 (32–<37 weeks), a direction consistent with H1 and with developmental physiology: with advancing maturity, pericyte coverage and vascular smooth-muscle maturation, capillary density and metabolic vasodilatory capacity increase, raising diastolic flow and reducing impedance. Gill et al. likewise found that day-3 ACA RI increased as GA decreased (0.78, 0.76 and 0.76 at ≤ 28 , 28–32 and 32–35 weeks), although, as in our exploratory analysis ($p = 0.30$), the gradient was not statistically significant; the relationship reached significance only for birth weight. The literature is not uniform: Pezzati et al. reported RI rising with GA during the first eight hours of life, Ecury-Goossen et al. showed that, in infants <29 weeks, RI varied according to the intubated artery and ductal status, and Elmfors et al. observed lower RI after 35 weeks. These discrepancies emphasise

that RI is a composite index governed by GA, postnatal age, ductal status, carbon dioxide tension, feeding state and insonation technique, and that GA-stratified interpretation is necessary.^{6,17,21,25,32,35}

Absolute RI values in our moderate-to-late and very preterm strata (medians 0.64 and 0.68) were lower than day-3 values reported by Gill et al. (0.76–0.78) and Akin et al. (0.75–0.77), but close to those of Pal et al. in infants <29 weeks without IVH (0.65 ± 0.05), Ortiz Borda et al. in very preterm infants at 72 hours (0.667) and Zamora et al. in clinically unremarkable preterm infants (mean 0.70; range 0.54–0.86) (Table 7). Postnatal age is a key determinant: Gill et al. documented a significant rise from 0.77 on day 3 to 0.82 on day 7, and the protocol-prescribed avoidance of fontanelle compression in our study is also relevant, because compression elevates RI by approximately 6–7%. Timing heterogeneity within our 7-day window, a floating-probe technique and population differences may therefore all have contributed to the lower values.^{17–19,22,32,36}

Table 7. Comparison of ACA resistive index with published preterm cohorts

Study (country)	Population	Timing	ACA RI	Principal finding
Present study (Indonesia)	n = 30; GA <37 wk	≤7 days	Median 0.64 (32–<37 wk); 0.68 (28–31 wk); 0.86 (<28 wk, n = 1)	Descriptive inverse gradient with GA; low RI predominant; Doppler abnormal despite normal grayscale
Gill et al. 2024 (India)	n = 73; GA ≤35 wk	Days 3 and 7	Day 3: 0.78 / 0.76 / 0.76 (≤28 / 28–32 / 32–35 wk); day 7: 0.82–0.83	No association with comorbidities; RI rose from day 3 to day 7
Akin et al. 2023 (Turkey)	n = 96; GA <32 wk	Days 1, 3, 7	0.76 / 0.75 / 0.77	No association with NIRS Csat; day-1 RI 0.83 in early deaths

Pal et al. 2025 (USA)	n = 30; GA <29 wk	<36 h	0.65 ± 0.05 (no IVH) vs 0.70 ± 0.04 (IVH)	Higher early RI associated with IVH
Ecury-Goossen et al. 2016 (Netherlands)	n = 235; GA <29 wk	Days 1–3, then weekly	Median 0.75 (no PDA) vs 0.82 (hsPDA)	RI differs by artery; higher with hsPDA
Zamora et al. 2014 (USA)	n = 129; preterm and term	Baseline and fontanelle compression	Preterm mean 0.70 (0.54–0.86); term 0.66	Compression raised RI by ≈6–7%
Ortiz Borda et al. 2020 (Peru)	n = 56; very preterm	24, 48, 72 h	0.695 / 0.69 / 0.667	Stable-to-declining RI over first 72 h
Hsia et al. 2026 (Taiwan)	n = 386; mean GA 35 wk	≤24 h	Bands <0.6 / 0.6–0.8 / >0.8; low 4.1%, high 21.0%	Low RI independently associated with hypotension and fluid resuscitation

Csat, cerebral oxygen saturation; hsPDA, haemodynamically significant patent ductus arteriosus; IVH, intraventricular haemorrhage; NIRS, near-infrared spectroscopy.^{17–19,21,22,36,37}

Distribution of RI categories

More than half of the infants (53.3%) had RI below the protocol-specified bands, whereas high RI (13.3%) clustered in the least mature infants (25.0% at <32 weeks vs 5.6% at ≥32 weeks). High RI reflects reduced diastolic flow and increased distal resistance and has been associated with haemodynamically significant patent ductus arteriosus (hsPDA), early IVH and early mortality: Ecury-Goossen et al. reported median ACA RI 0.82 with hsPDA vs 0.75 without (a pattern replicated in an Indian cohort by Rafiq et al.), Akın et al. found day-1 RI of 0.83 in infants who died early, and Pal et al. linked higher early RI to IVH. Correspondingly, the grade I GMH-IVH case in our cohort had an RI of 0.80, above the band for its GA stratum. Low RI, conversely, suggests cerebral vasodilatation—a physiological or compensatory response to hypoxaemia, hypercapnia,

anaemia or sepsis—and, in a large Taiwanese NICU cohort, low early ACA RI (<0.6) was independently associated with systemic hypotension and the need for fluid resuscitation. Importantly, the predominance of low RI must be interpreted in light of the reference bands used: these protocol-specified bands are not a validated normative standard, and contemporary cohorts report higher day-3 values; a local, age-specific reference curve is needed before the frequency of “low RI” can be regarded as pathological.^{18–21,37–39}

Grayscale findings

Diffuse cerebral oedema was the dominant grayscale finding (56.7%) across all strata. In preterm infants, altered parenchymal echogenicity may reflect immature autoregulation, haemodynamic fluctuation and perinatal inflammatory or hypoxic stress. However, the sonographic diagnosis of diffuse oedema and non-cystic white matter echogenicity is subjective: the normal preterm brain is relatively echogenic with immature sulcation, periventricular “flaring” may be physiological, inter-observer agreement for non-cystic echogenicity is poor (κ 0.20–0.32), and persistent echogenicities do not reliably predict reduced brain growth. The high oedema prevalence therefore warrants cautious interpretation and, ideally, blinded dual reading with quantitative echogenicity measures in future work.^{9,13,31,33,40}

GMH-IVH was identified in only one infant (grade I) and no PVL or ventriculomegaly was observed. GMH-IVH incidence rises steeply with decreasing GA, reaching 20–25% in VLBW infants, so the low prevalence here is expected in a cohort dominated by moderate-to-late preterm infants, with a single extremely preterm infant and exclusion of haemodynamically unstable neonates who carry the highest risk. Moreover, cystic PVL typically becomes evident only after two to three weeks, post-haemorrhagic ventricular dilatation evolves over days to weeks, and CUS is less sensitive than MRI for mild and diffuse white matter injury. Absence of these findings within the first week therefore does not exclude evolving injury, and serial CUS to term-equivalent age, complemented by MRI where indicated, is recommended.^{8,24,27,31,41}

Incremental value of Doppler

In several infants with morphologically normal grayscale scans, spectral Doppler revealed markedly reduced RI (e.g., 0.51; Figure 9), supporting H2. Doppler provides functional information

on cerebral perfusion that may precede or occur without structural change, and RI correlates inversely with regional cerebral oxygenation measured by NIRS in the first 24 hours after birth. Nevertheless, a systematic review found insufficient evidence to support routine RI measurement for predicting brain injury or long-term neurodevelopment in preterm infants, while confirming that elevated RI signals hsPDA; in term hypoxic–ischaemic encephalopathy, the prognostic value of abnormal Doppler indices has been systematically evaluated with heterogeneous results. Doppler should therefore be regarded as an adjunct that refines haemodynamic phenotyping and prompts clinical correlation (ductal assessment, blood gases, blood pressure, haemoglobin), rather than as a stand-alone diagnostic test.^{15,20,39,42,43}

Strengths and limitations

Strengths include the prospective design, a standardised bilateral A2-segment protocol with at least three cycles per side and a floating-probe technique, consultant supervision with consensus reading, complete data, integration of Doppler with grayscale morphology, and inclusion of the full preterm spectrum including moderate-to-late preterm infants. Limitations are substantial. The sample was small and single-centre, with a markedly unbalanced GA distribution (one extremely preterm infant), precluding inference in that stratum and limiting power (the exploratory analyses were not powered). Purposive consecutive sampling in a tertiary military hospital and exclusion of unstable infants limit generalisability and probably underestimate injury prevalence. Postnatal age at examination varied within the first week and was not analysed; PDA status, blood gases, blood pressure, haemoglobin, ventilatory support and feeding state—recognised determinants of RI—were not recorded. The GA-specific RI bands were protocol-defined rather than validated normative references. Grayscale interpretation, particularly of diffuse oedema, is subjective and inter-observer agreement was not formally quantified. Finally, no MRI or neurodevelopmental follow-up was available.^{20,21,33,35}

Clinical implications

Adding spectral Doppler to routine neonatal CUS at RSPAD Gatot Soebroto is feasible, inexpensive and adds haemodynamic information to morphology. RI should be interpreted against GA and postnatal age, with standardised acquisition (same artery and segment, quiet state, no

fontanelle compression) and correlation with the clinical haemodynamic context. These data provide a starting point for an institutional SOP and for a structured, serial preterm neuro-imaging pathway consistent with international consensus recommendations.^{10,15,24}

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

(1) The 30 preterm neonates had balanced sex distribution and were predominantly moderate-to-late preterm, LBW and delivered by caesarean section, with a median 5-minute Apgar score of 8; no ELBW infant was enrolled, and head circumference was smaller at lower GA. (2) RDS was the most frequent comorbidity, followed by neonatal sepsis; asphyxia was absent. (3) ACA RI was 0.665 ± 0.055 (median 0.64, IQR 0.09) at 32–<37 weeks and 0.693 ± 0.074 (median 0.68, IQR 0.07) at 28–31 weeks, with a single RI of 0.86 at <28 weeks, demonstrating a descriptive inverse gradient with GA. (4) RI above the GA-specific band was most frequent in the least mature infants, in keeping with cerebrovascular immaturity, whereas low RI predominated overall. (5) Diffuse cerebral oedema was the commonest grayscale finding, GMH-IVH was rare, and PVL and ventriculomegaly were not detected within the first week of life.^{15,17}

Recommendations

(1) Cranial ultrasonography should be considered as a routine screening examination for preterm neonates at RSPAD Gatot Soebroto to enable early detection of cerebral abnormalities. (2) Cranial ultrasonography should routinely include spectral Doppler of the ACA, with RI interpreted according to GA and postnatal age. (3) Future studies should recruit over longer periods and across multiple centres with balanced GA strata, particularly extremely preterm infants, and should include serial examinations at predefined postnatal ages. (4) Analytic designs should examine associations between RI and GA, birth weight, sex, delivery mode, PDA status, blood gases and grayscale findings using multivariable models, and should establish local normative RI curves linked to MRI and neurodevelopmental outcomes.^{10,20,24}

DECLARATIONS

Ethics approval and consent to participate: Approved by the Health Research Ethics Committee of RSPAD Gatot Soebroto (No. 316/VI/KEPK/2026). Written informed consent was obtained from the parents or guardians of all participants.

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Author contributions: FS: conceptualisation, methodology, data acquisition, formal analysis, writing – original draft. Supervisors: supervision, validation, writing – review and editing. All authors approved the final manuscript.

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