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## ORIGINAL ARTICLE

# Intraventricular hemorrhage in preterm newborns: a multicenter study in four Brazilian hospitals ☆

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### KEYWORDS

Cerebral intraventricular hemorrhage;  
Infant, premature;  
Cranial ultrasonography;  
Body temperature regulation

### Abstract

**Objective:** To identify the incidence, demographic characteristics, and risk factors for intraventricular hemorrhage (IVH) in preterm infants admitted to Brazilian neonatal intensive care units (NICUs).

**Methods:** This prospective, observational cohort study was conducted over a one-year period in four NICUs in Brazil. All newborns with gestational age (GA) < 32 weeks or birth weight (BW) < 1500 g, born between September 2023 and September 2024, were included. Demographic data and short-term outcomes were collected. Multinomial logistic regression was performed to evaluate associations between clinical variables and IVH severity.

**Results:** A total of 268 newborns were enrolled. The mean BW and GA were 1138 g (SD ±388 g) and 29 weeks and 1 day (SD ±3 weeks and 1 day), respectively. Normal cUS were seen in 54.1%, mild IVH in 20.5%, severe IVH in 10.4%, and 8.2% died prior to a cUS being performed. Infants with the outcome of severe IVH or death prior to cUS exhibited lower BW, GA, Apgar scores, rates of cesarean section, fewer complete courses of antenatal steroids, and were more likely to have undergone advanced resuscitation in the delivery room and significant interventions in the early neonatal period. Hypothermia was prevalent across all groups. Infants with severe IVH had significantly higher rates of death prior to hospital discharge and longer length of stay.

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*Conclusions:* Identifying risk factors for IVH is essential for developing strategies to optimize outcomes. Implementation of a standardized IVH prevention bundle in Brazilian NICUs focusing on factors shown to adversely affect outcomes is warranted.

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## 1 Introduction

2 Intraventricular hemorrhage (IVH) is a common and severe  
3 complication of prematurity due to the fragility of the ger-  
4 minal matrix and the immature cerebrovascular system[1]  
5 and remains a significant cause of morbidity and mortality,  
6 particularly in infants born before 32 weeks of gestation or  
7 weighing <1500 g [2]. Despite substantial advances in neo-  
8 natal care, IVH continues to affect up to 50% of very low  
9 birth weight infants in many settings, with severe grades of  
10 IVH strongly associated with poor neurodevelopmental out-  
11 comes, such as cerebral palsy, cognitive impairment, and  
12 sensory deficits [3,4]. IVH is a multifactorial condition influ-  
13 enced by antenatal, perinatal, and postnatal factors, includ-  
14 ing antenatal exposure to steroids, mode of delivery, tra-  
15 cheal intubation, and inotropic use [5,6].

16 Most epidemiological data on IVH originate from high-  
17 income countries with well-established neonatal networks  
18 with consistent quality of care and distinct population char-  
19 acteristics. However, in low- and middle-income countries  
20 (LMICs), the incidence and outcomes of IVH may differ due  
21 to resource constraints, limited access to specialized neonat-  
22 al care, and disparities in the implementation of evidence-  
23 based practices [7].

24 Brazil, as an LMIC with heterogeneity in perinatal care,  
25 offers a unique setting to understand the burden of IVH in  
26 preterm neonates. The Brazilian Neonatal Research Network  
27 has documented that 30.4% of preterm infants in Brazil  
28 experience IVH, with significant variations in severity and  
29 outcomes across neonatal intensive care units (NICUs).  
30 Moreover, trends from 2013 to 2018 indicate an increasing  
31 incidence of IVH, reflecting the increased rate of survival of  
32 lower GA infants, the complexity of neonatal care, and pos-  
33 sible gaps in resource allocation and clinical protocols [8].

34 To address this knowledge gap, the authors conducted a  
35 multicenter cohort study in four Brazilian NICUs, including  
36 both private and public centers, to identify the rates and  
37 severity of IVH among infants born at < 32 weeks' gestation  
38 or < 1500 g, and secondarily, to identify the demographic,  
39 maternal, prenatal, delivery, and neonatal risk factors for  
40 IVH in these Brazilian NICUs.

## 41 Methods

42 This observational, prospective cohort study was conducted  
43 in four NICUs in Brazil from September 2023 to September  
44 2024. The study was approved by the Research Ethics Com-  
45 mittees of all participating hospitals and followed the  
46 STROBE (Strengthening the Reporting of Observational Stud-  
47 ies in Epidemiology) guideline.

48 One center was based in the state of Goiás (Central-West  
49 region) and three in São Paulo (Southeast region). Brazil's

healthcare system is characterized by a dual structure with 50  
both public and private sectors. Of the four participating 51  
NICUs, three were public hospitals integrated into the Bra- 52  
zilian Unified Health System (Sistema Único de Saúde – 53  
SUS), and one was a private facility. All centers are referral 54  
institutions for high-risk pregnancies and provide level III 55  
neonatal care. The inclusion of centers from different geo- 56  
graphic regions and with distinct organizational structures 57  
and resource availability was intentional, aiming to capture 58  
the heterogeneity of neonatal care in Brazil and enhance 59  
the external validity of the findings. Prior to the study initia- 60  
tion, training sessions were held with the center's investiga- 61  
tors to standardize the data collection process. A shared 62  
protocol and centralized database were used to ensure data 63  
consistency across centers. 64

65 The study population consisted of preterm infants born at  
66 < 32 weeks' gestation or with birth weight < 1500 g, admit-  
67 ted to the participating NICUs during the one-year study  
68 period. Infants with congenital malformations or genetic  
69 syndromes were excluded.

70 Antenatal, in-hospital, and outcome data were collected  
71 from the patients' medical records, including information on  
72 invasive interventions in the NICU, such as the use of seda-  
73 tives or analgesics, inotropes, fluid bolus, and mechanical  
74 ventilation. Antenatal steroid exposure was categorized as  
75 complete when two doses were administered, irrespective  
76 of the time interval between doses. Exposure was consid-  
77 ered incomplete when fewer than two doses were adminis-  
78 tered, regardless of timing. The most severe IVH grade  
79 identified on cranial ultrasound (cUS) during NICU stay was  
80 included in the analysis. The diagnosis and classification of  
81 IVH were based on Papile's classification system [9]. Grades I  
82 and II IVH were considered to be mild IVH, and grades III and  
83 IV were considered to be severe IVH [9]. Post-hemorrhagic  
84 ventricular dilatation was also classified as a severe finding.

85 Descriptive analyses were conducted using frequencies  
86 for categorical variables and means, medians, standard  
87 deviations, and interquartile ranges for continuous vari-  
88 ables, according to data distribution. The results of cUS were  
89 divided into normal (no evidence of IVH), mild, and severe.  
90 To avoid exclusion of high-risk infants, those who died before  
91 cUS assessment were included in a composite outcome of  
92 severe IVH or death prior to cUS. Infants with leukomalacia  
93 and no IVH were excluded from this comparison.

94 Multinomial logistic regression was performed to evaluate  
95 associations between clinical variables and IVH severity.  
96 Crude associations were estimated using univariate models.  
97 Subsequently, domain-specific multivariable models were  
98 constructed a priori based on clinical plausibility. A baseline  
99 demographic model included gestational age (GA), sex,  
100 mode of delivery, and hospital sector. Separate models eval-  
101 uated prenatal exposures, perinatal variables, and early  
102 postnatal interventions within the first 72 h of life, all

adjusted for baseline variables. GA and birth weight were not included simultaneously due to their biological collinearity. Multicollinearity was assessed using the variance inflation factor (VIF), and variables with  $VIF > 5$  were excluded. Results are presented as relative risk ratios (RRR) with 95% confidence intervals (CI), and statistical significance was defined as  $p < 0.05$ .

## Results

### Baseline characteristics

A total of 268 preterm infants were included in the study, and 142 (53%) were male. The mean birth weight was 1138 g (SD  $\pm 388$  g), and the mean GA was 29 weeks (SD  $\pm 3$ ). Cesarean sections accounted for 163 (61%) deliveries, and 182 (92%) neonates were inborn. A detailed flowchart on patient selection is presented in Supplemental Figure 1, and baseline characteristics are described in Table 1.

### Antenatal care and delivery room events

Only 126 newborns (47%) were exposed to a complete course of antenatal steroids, 69 (25.7%) to a partial course, and 134 (50%) were exposed to antenatal magnesium sulfate. During the delivery room resuscitation, 53 (20%) received only positive pressure ventilation, 104 (43%) received endotracheal intubation, and 10 (4.1%) received chest compressions. Hypothermia, defined as a temperature  $< 36.5^\circ \text{C}$ , occurred in 131 (49%) of the neonates in the delivery room. Detailed information on antenatal care and delivery room events is shown in Table 2.

### First 72 h of life

Within the first 72 h, 84% ( $n = 224$ ) of the infants were exposed to caffeine, 20.5% ( $n = 55$ ) sedatives or analgesics, 87% ( $n = 233$ ) parenteral nutrition, 21% ( $n = 56$ ) fluid bolus, and 25% ( $n = 68$ ) inotropes. Mechanical ventilation was used in 45.5% ( $n = 122$ ). Parental touch was applied to 84% ( $n = 223$ ) of newborns, and 77% ( $n = 207$ ) were cared for using minimal handling protocols. Hypothermia was observed in 66% ( $n = 177$ ) of newborns at NICU admission and in 88% ( $n = 235$ ) within the first 72 h.

### Cranial ultrasound findings and in-hospital outcomes

During NICU stay, 246 (91.7%) infants underwent cUS, and 22 (8.2%) patients died prior to performing a cUS. The median days to death for these patients was 2 days (IQR 0–4). Among the patients that underwent cUS, the first exam was performed at a median of 5 days of life (DOL) (IQR 3–6), and the worst exam was documented at a median of 14 DOL (IQR 5–29). Characteristics and incidence of cUS findings are shown in Figure 1.

In survivors, a normal cUS was observed in 145 (59%) infants, mild IVH in 55 (22.4%), severe IVH in 28 (11.4%), and leukomalacia with no IVH in 18 (7.3%). Infants with severe IVH or death tended to have lower birth weight and GA and lower Apgar scores. Cesarean delivery and exposure to a complete course of antenatal steroids were less frequent in infants with severe IVH or death, whereas intubation in the delivery room was more common. Antenatal and delivery room data are displayed in Table 2.

In the first 72 h after birth, infants with the combined outcome of death or severe IVH were less frequently exposed to caffeine and more frequently exposed to sedative or analgesics, mechanical ventilation, inotropes, and fluid boluses. Detailed information on the neonatal care in the first 72 h after birth is summarized in Table 2.

Hypothermia was common in the delivery room (39%), at NICU admission (66%), and in the first 72 h after admission (88%). Although hypothermia appeared more frequently among infants with severe IVH, differences between groups were modest (Table 2).

Infants with severe IVH had higher rates of death prior to hospital discharge, with a median age at death of 32 days (IQR 18–40). Length of stay among survivors was also longer in infants with severe IVH, with a median of 95 days (IQR 51–114).

In univariate analyses (Table 3), lower GA and birth weight, advanced resuscitation in the delivery room, mechanical ventilation, endotracheal intubation, sedation or opioid use, inotrope use, and fluid bolus administration were associated with increased relative risk of severe IVH or death. Cesarean delivery was associated with a lower relative risk of any IVH or death.

In multinomial regression models (Table 4), lower GA remained independently associated with severe IVH or death

**Table 1** Baseline characteristics.

Variables	All Subjects N = 268	N total (cUS + death) = 250		
		Normal cUS N = 145 (58%)	Mild IVH N = 55 (22%)	Severe IVH OR death N = 50 (20%)
Public	190 (70.9)	97 (66.9)	38 (69.1)	42 (84.0)
Private	78 (29.1)	48 (33.1)	17 (30.9)	8 (16.0)
Male, n (%)	142 (53.0)	74 (51.0)	30 (54.5)	28 (56.0)
Cesarean section, n (%)	163 (61.0)	100 (69.0)	29 (52.7)	24 (48.0)
Birth weight, grams, mean (SD)	1138 ( $\pm 388$ )	1220 ( $\pm 342$ )	1150 ( $\pm 391$ )	884 ( $\pm 383$ )
Gestational age, weeks, mean (SD)	29 1/7 ( $\pm 3$ 1/7)	29 6/7 ( $\pm 2$ 6/7)	29 1/7 ( $\pm 2$ 6/7)	26 4/7 ( $\pm 3$ 0/7)
Apgar 1', median (IQR)	6 (4–8)	7 (5–8)	6 (5–8)	3 (2–6)
Apgar 5', median (IQR)	8 (7–9)	9 (8–9)	8 (8–9)	7 (5–8)
Apgar 10', median (IQR)	8 (7–9)	9 (8–9)	8 (7–9)	7 (6–8)

**Table 2** Antenatal and delivery room events in the study population.

Variables	All Subjects No = 268	N total (cUS + death) = 250		
		cUS Normal No = 145 (58%)	Mild IVH No = 55 (22%)	Severe IVH OR death No = 50 (20%)
<b>Antenatal care</b>				
Antenatal steroids:				
Complete course, n (%)	126 (47.0)	77 (53.1)	24 (43.6)	16 (32.0)
Partial steroids, n (%)	69 (25.7)	35 (24.1)	14 (25.5)	16 (32)
No steroids, n (%)	73 (27.2)	33 (22.8)	17 (30.9)	18 (36)
Antenatal magnesium sulfate, n (%)	134 (50)	72 (49.7)	29 (52.7)	25 (50.0)
<b>Delivery room events</b>				
Hypothermia (T < 36 °C) in the delivery room, n (%)	131 (49)	72/115 (62.6)	23/40 (57.5)	25/33 (75.8)
Positive pressure ventilation only, n (%)	53 (19.8)	38 (26.2)	10 (18.2)	5 (10)
Positive pressure ventilation + Intubation, n (%)	104 (43.0)	47 (32.4)	17 (30.9)	34 (68.0)
Positive pressure ventilation + intubation + Chest compressions, n (%)	10 (4.1)	2 (1.4)	2 (3.6)	4 (8.0)
<b>Neonatal care in the first 72 h after birth</b>				
Caffeine, n (%)	224 (84.0)	124 (85.5)	50 (90.9)	35 (70.0)
Sedation or analgesic, n (%)	55 (20.5)	22 (15.2)	14 (25.4)	19 (38)
Mechanical ventilation, n (%)	122 (45.5)	60 (41.4)	28 (50.9)	45 (90.0)
Parenteral nutrition, n (%)	233 (87.0)	129 (89.0)	52 (94.5)	38 (76.0)
Fluid bolus, n (%)	56 (21.0)	21 (14.5)	14 (25.5)	19 (38.0)
Inotropes, n (%)	68 (25.0)	18 (12.4)	15 (27.3)	32 (64.0)
Parental touch, n (%)	223 (84.0)	125 (86.2)	47 (85.5)	36 (72.0)
Minimal handling, n (%)	207 (77.0)	113 (77.9)	39 (70.9)	41 (82.0)
Hypothermia at NICU admission, n (%)	177 (66.0)	87/143 (60.8)	38/55 (69)	40/50 (80)
n = 144				
Hypothermia within 72 h after admission, n (%)	235 (88.0)	126/143 (88.1)	49/55 (89.1)	46/48 (95.8)

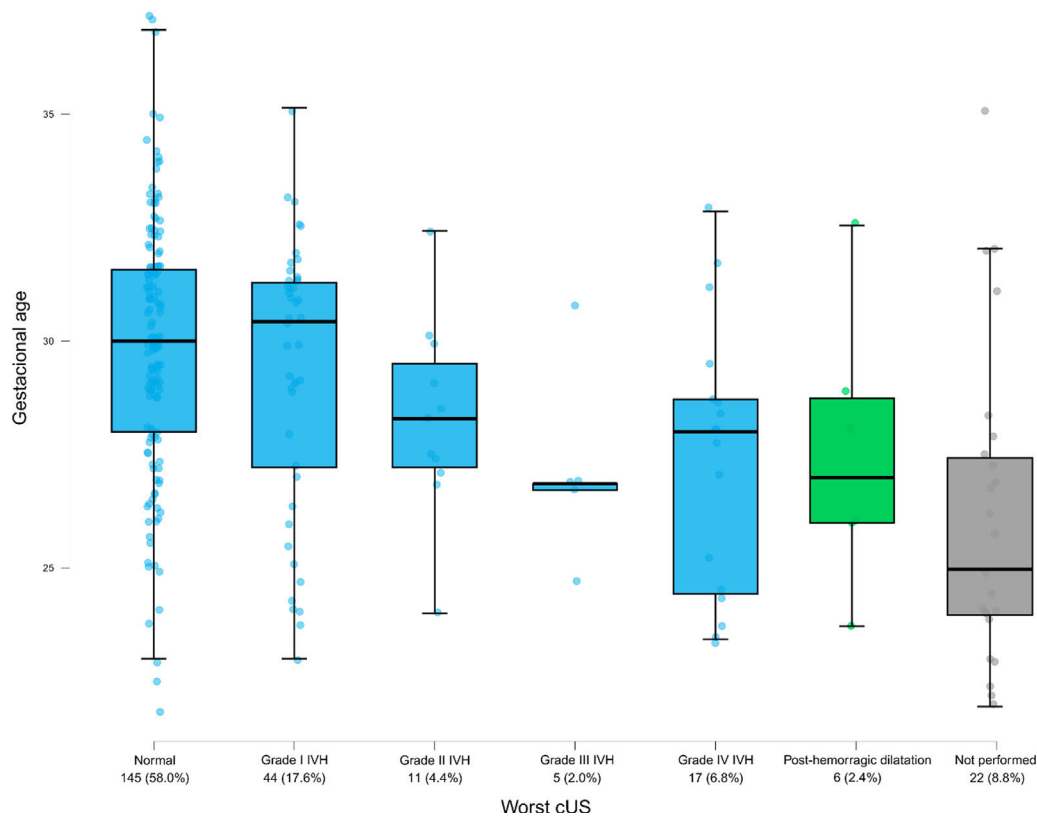
182 in the baseline and antenatal care models (models 1 and 2).  
 183 Advanced resuscitation in the delivery room was strongly  
 184 associated with severe IVH or death in Model 3 (RRR 13.4,  
 185 95% CI 2.62–68.50,  $p = 0.002$ ). In the model evaluating neo-  
 186 natal care (model 4) within the first 72 h of life, the use of  
 187 inotropes was independently associated with severe IVH or  
 188 death (RRR 4.14, 95% CI 1.28–13.39,  $p = 0.018$ ).

## 189 Discussion

190 This prospective multicenter study conducted in four Brazil-  
 191 ian NICUs revealed a 36.4% incidence of IVH among preterm  
 192 infants born at < 32 weeks' gestation or weighing < 1500 g,  
 193 with the combined outcome of severe IVH or death prior to

cUS occurring in 20%. Infants with this combined outcome  
 were characterized by lower birth weight and GA, lower  
 Apgar scores, and lower rates of cesarean delivery, and were  
 less likely to be exposed to a complete course of antenatal  
 corticosteroids and more likely to have undergone advanced  
 resuscitation in the delivery room and more invasive inter-  
 ventions in the NICU, such as use of sedatives or analgesics,  
 inotropes, fluid bolus, and mechanical ventilation. Hypo-  
 thermia was prevalent across all groups, but particularly  
 elevated among those with severe IVH or death. In multino-  
 mial regression analyses, lower GA, advanced resuscitation  
 in the delivery room, and early use of inotropes were inde-  
 pendently associated with severe IVH or death.

The IVH rates seen in this study align with global and local  
 reports. A previous meta-analysis of 64 studies including



**Figure 1** cUS findings during hospitalization by gestational age.

The box shows where most values are concentrated, while the whiskers show the typical range of the data. Points beyond the whiskers represent more extreme values.

209 data from 9633 preterm infants  $\leq 32$  weeks GA born after  
 210 2007, reported a global IVH occurrence of 31% (95% CI 25-  
 211 36%) and 11% (95% CI 8–14%) of severe IVH [2]. A multicenter  
 212 cohort study including very low birth weight newborns <  
 213 1500 g, published by the Brazilian Network on Neonatal  
 214 Research, reported a similar overall rate of IVH in 30.4%,  
 215 with 9.8% classified as severe [8]. These findings highlight  
 216 that a substantial proportion of preterm infants remain at  
 217 high risk for severe brain injury.

218 In this analysis, infants with severe IVH or death pre-  
 219 sented more frequently with lower birth weight, GA, and  
 220 Apgar scores. In the adjusted multinomial analyses, GA  
 221 emerged as the most consistent independent predictor of  
 222 severe IVH or death. These findings are consistent with pre-  
 223 viously identified risk profiles for adverse neonatal outcomes  
 224 [10,11]. The fragility of the vessels in the germinal matrix at  
 225 early GA and the instability of cerebral blood flow place pre-  
 226 term newborns at a higher risk for brain injury [10].

227 In the studied cohort, cesarean delivery appeared less  
 228 frequent among infants with severe IVH or death; however,  
 229 this association was not maintained after adjustment for  
 230 other perinatal factors. Previous studies have reported con-  
 231 flicting findings regarding the protective role of cesarean  
 232 delivery in extremely preterm infants [12–14]. While some  
 233 suggest that cesarean delivery may reduce hemodynamic  
 234 instability during birth, as vaginal delivery may expose frag-  
 235 ile cerebral vessels to significant fluctuations in cerebral  
 236 blood flow and oxygen saturation, others have shown that  
 237 the association disappears after adjustment for GA and

perinatal condition [13–16]. These findings suggest that the  
 relationship between delivery mode and IVH risk is likely  
 confounded by the clinical circumstances leading to preterm  
 birth rather than reflecting a direct causal effect of delivery  
 method.

238 While some risk factors for IVH are inherent to the unpre-  
 239 dictability of preterm birth, many are modifiable through  
 240 clinical practice. Of particular concern in the studied cohort  
 241 were the low rate of antenatal corticosteroid administration  
 242 (47%), high rates of inotrope use (25%), delivery room intu-  
 243 bation (43%), and postnatal hypothermia (up to 88% within  
 244 72 h), all of which are strongly associated with increased  
 245 risk for IVH and adverse neonatal outcomes [12–17].

246 Previous studies have demonstrated that the use of anten-  
 247 atal corticosteroids significantly reduces the incidence of  
 248 IVH and improves survival in preterm infants by enhancing  
 249 pulmonary and cerebrovascular stability [15–18]. As shown in  
 250 a large population-based cohort from the California Perinatal  
 251 Quality Care Collaborative (CPQCC), including 44,028 pre-  
 252 term infants, antenatal corticosteroid exposure was the only  
 253 factor independently associated with a reduced risk of severe  
 254 IVH across all GA groups [15]. Although infants exposed to a  
 255 complete course of antenatal corticosteroids in the present  
 256 cohort showed lower crude rates of severe IVH or death, this  
 257 association was not maintained in adjusted analyses. This  
 258 may reflect the relatively small number of severe IVH cases or  
 259 residual confounding related to the timing of steroid adminis-  
 260 tration and perinatal condition. Nonetheless, the relatively  
 261 low rate of complete antenatal corticosteroid exposure

**Table 3** Univariate logistic regression analysis.

Variables	IVH severity	RRR (95% CI)	p-value
Private Sector	Mild	0.90 (0.46 – 1.76)	0.767
	Severe / Death	0.44 (0.16 – 1.23)	0.117
Cesarean delivery	Mild	0.50 (0.27 – 0.95)	0.034
	Severe / Death	0.34 (0.15 – 0.77)	0.010
Gestational age	Mild	0.91 (0.82 – 1.01)	0.084
	Severe or death	0.68 (0.60 – 0.77)	<0.001
Birth weight	Mild	1.00 (0.99 – 1.00)	0.231
	Severe or death	1.00 (0.996 – 0.998)	<0.001
Female sex	Mild	0.87 (0.47 – 1.62)	0.657
	Severe / Death	0.67 (0.30 – 1.54)	0.350
Complete course of antenatal corticosteroid	Mild	0.61 (0.29 – 1.27)	0.185
	Severe / Death	0.59 (0.22 – 1.60)	0.299
Magnesium sulfate	Mild	1.13 (0.61 – 2.11)	0.698
	Severe / Death	0.88 (0.39 – 1.98)	0.755
Advanced resuscitation in DR	Mild	0.86 (0.46 – 1.61)	0.641
	Severe / Death	18.00 (2.38 – 136.15)	0.005
Mechanical Ventilation	Mild	1.47 (0.79 – 2.74)	0.227
	Severe / Death	18.42 (4.21 – 80.56)	<0.001
Orotracheal intubation	Mild	1.55 (0.83 – 2.89)	0.172
	Severe / Death	32.32 (4.28 – 244.24)	0.001
Caffeine	Mild	1.69 (0.61 – 4.74)	0.316
	Severe / Death	1.41 (0.39 – 5.10)	0.599
Sedation or Opioids	Mild	1.91 (0.89 – 4.07)	0.094
	Severe / Death	3.11 (1.27 – 7.61)	0.013
Use of inotropes	Mild	2.65 (1.22 – 5.73)	0.013
	Severe / Death	9.41 (3.84 – 23.06)	<0.001
Volume expansion	Mild	2.02 (0.94 – 4.32)	0.072
	Severe / Death	3.82 (1.57 – 9.29)	0.003
Positive touch	Mild	0.94 (0.39 – 2.28)	0.891
	Severe / Death	0.96 (0.30 – 3.06)	0.945
Minimal handling	Mild	0.69 (0.34 – 1.39)	0.301
	Severe / Death	1.70 (0.55 – 5.25)	0.357
Hypothermia in the DR	Mild	0.81 (0.39 – 1.68)	0.568
	Severe / Death	1.49 (0.54 – 4.14)	0.441
Hypothermia within 72 h after admission	Mild	1.10 (0.41–2.96)	0.847
	Severe / Death	1.75 (0.38–8.06)	0.470

Abbreviations: RRR, Relative risk ratio; CI, Confidence interval; DR, Delivery room.

267 observed in this cohort (47%) highlights an important opportunity 286  
 268 for improvement in perinatal care.

269 The need for advanced resuscitation in the delivery room 287  
 270 was strongly associated with severe IVH or death in the 288  
 271 adjusted analysis. This association likely reflects the severity 289  
 272 of cardiorespiratory compromise immediately after birth, 290  
 273 which may lead to abrupt fluctuations in cerebral blood flow 291  
 274 during the transitional period. Previous observational studies 292  
 275 have similarly demonstrated that extensive resuscitation 293  
 276 and multiple intubation attempts in the delivery room are 294  
 277 associated with increased risk of severe IVH in very preterm 295  
 278 infants [15,19]. These findings underscore the importance of 296  
 279 gentle stabilization strategies and minimizing hemodynamic 297  
 280 instability during the immediate postnatal transition. 298

281 Similarly, early hemodynamic instability also appears to 299  
 282 play a central role in IVH pathogenesis [17]. In the adjusted 300  
 283 models, the use of inotropes within the first 72 h of life 301  
 284 remained independently associated with severe IVH or 302  
 285 death. Fluctuations in cerebral blood flow and systemic 303  
 304

286 blood pressure during the early neonatal period have been 287  
 288 strongly implicated in the development of germinal matrix 289  
 289 hemorrhage [19–21]. A previous prospective study of 497 290  
 290 extremely preterm infants ( $\leq 29$  weeks) found that early 291  
 291 inotrope use was associated with significantly increased 292  
 292 odds of severe brain injury, including IVH of any grade [21]. 293

294 Hypothermia was highly prevalent in the studied cohort, 295  
 295 occurring in nearly half of the infants in the delivery room 296  
 296 and in the majority during the first 72 h after admission. 297  
 297 Maintaining normothermia in the immediate postnatal 298  
 298 period is critical, as hypothermia is linked to impaired cardiorespiratory 299  
 299 transition and increased morbidity in preterm neonates [22,23]. A systematic review including over 300  
 300 300,000 very preterm infants reported that admission hypothermia was associated with increased mortality and higher 301  
 301 risk of IVH, bronchopulmonary dysplasia, retinopathy of prematurity, and sepsis [23]. Although hypothermia was not 302  
 302 independently associated with IVH severity in these models, 303  
 303 its high prevalence underscores the importance of improving 304

**Table 4** Adjusted multinomial logistic regression models.

Variables	Outcome Category	RRR (95% CI)	p-value
<b>Model 1: Baseline characteristics.</b>			
Private Sector	Mild	1.07 (0.52–2.22)	0.847
	Severe / Death	0.40 (0.13–1.26)	0.116
Cesarean delivery	Mild	0.56 (0.27–1.13)	0.106
	Severe / Death	0.77 (0.29–2.01)	0.590
Gestational age	Mild	0.93 (0.83–1.05)	0.226
	Severe / Death	0.73 (0.61–0.86)	< 0.001
Female sex	Mild	0.89 (0.47–1.67)	0.707
	Severe / Death	0.54 (0.22–1.34)	0.185
<b>Model 2: Antenatal care.</b>			
Private Sector	Mild	0.62 (0.26–1.47)	0.277
	Severe / Death	0.24 (0.05–1.01)	0.051
Cesarean delivery	Mild	0.71 (0.30–1.68)	0.434
	Severe / Death	1.00 (0.29–3.47)	0.997
Gestational age	Mild	0.98 (0.86–1.13)	0.816
	Severe / Death	0.76 (0.62–0.94)	0.012
Female sex	Mild	0.71 (0.34–1.49)	0.371
	Severe / Death	0.64 (0.23–1.84)	0.412
Complete course of antenatal steroids	Mild	0.63 (0.26–1.53)	0.306
	Severe / Death	0.56 (0.15–2.12)	0.392
Magnesium sulfate	Mild	1.30 (0.54–3.14)	0.564
	Severe / Death	1.68 (0.46–6.19)	0.435
<b>Model 3: Delivery room events.</b>			
Private Sector	Mild	0.98 (0.41–2.31)	0.959
	Severe / Death	0.44 (0.11–1.71)	0.236
Cesarean delivery	Mild	0.67 (0.28–1.57)	0.353
	Severe / Death	0.48 (0.15–1.54)	0.218
Gestational age	Mild	0.87 (0.75–1.03)	0.101
	Severe / Death	0.90 (0.73–1.10)	0.285
Female sex	Mild	1.08 (0.51–2.26)	0.845
	Severe / Death	0.70 (0.24–2.10)	0.530
Advanced resuscitation in the DR	Mild	0.96 (0.39–2.39)	0.936
	Severe / Death	13.4 (2.62–68.50)	0.002
Hypothermia in the DR	Mild	0.71 (0.31–1.66)	0.433
	Severe / Death	0.54 (0.16–1.89)	0.338
<b>Model 4: Neonatal care in the first 72 h after birth.</b>			
Private Sector	Mild	1.47 (0.61–3.55)	0.392
	Severe / Death	0.53 (0.11–2.55)	0.430
Cesarean delivery	Mild	0.51 (0.24–1.06)	0.073
	Severe / Death	0.79 (0.27–2.26)	0.654
Gestational age	Mild	0.97 (0.83–1.14)	0.720
	Severe / Death	0.88 (0.71–1.09)	0.248
Female sex	Mild	0.84 (0.42–1.68)	0.620
	Severe / Death	0.59 (0.21–1.63)	0.305
Mechanical ventilation	Mild	0.57 (0.15–2.19)	0.413
	Severe / Death	1.53 (0.20–11.89)	0.686
Orotracheal intubation	Mild	1.41 (0.38–5.23)	0.608
	Severe / Death	9.20 (0.64–131.43)	0.102
Caffeine	Mild	1.54 (0.46–5.11)	0.482
	Severe / Death	0.47 (0.86–2.57)	0.383
Sedation or opioids	Mild	1.64 (0.66–4.08)	0.286
	Severe / Death	1.06 (0.33–3.36)	0.925
Use of inotropes	Mild	2.18 (0.76–6.25)	0.148
	Severe / Death	4.14 (1.28–13.39)	0.018
Fluid bolus	Mild	1.18 (0.45–3.06)	0.737
	Severe / Death	1.08 (0.37–3.17)	0.886
Early nutrition <72h	Mild	1.64 (0.41–6.53)	0.479
	Severe / Death	1.16 (0.09–13.70)	0.905

**Table 4** (Continued)

Variables	Outcome Category	RRR (95% CI)	p-value
Positive touch	Mild	1.44 (0.47–4.39)	0.519
	Severe / Death	1.07 (0.20–5.80)	0.940
Minimal handling	Mild	0.49 (0.21–1.15)	0.103
	Severe / Death	1.06 (0.27–4.12)	0.933
Hypothermia within 72h hours after admission	Mild	0.97 (0.34–2.77)	0.951
	Severe / Death	1.06 (0.18–6.26)	0.950

RRR, Relative risk ratio; CI, Confidence interval; DR, delivery room.

Footnote: Multicollinearity was assessed using variance inflation factors (VIF). All variables included in the models presented VIF values < 5.

Reference category = absence of exposure unless otherwise specified.

305 thermal management practices in the delivery room and  
306 early NICU care.

307 Taken together, the present findings highlight urgent  
308 opportunities for improvement in perinatal and neonatal  
309 practices in Brazilian NICUs. Multiple studies have consis-  
310 tently demonstrated that evidence-based interventions sig-  
311 nificantly reduce the incidence of IVH in preterm infants  
312 [24,25]. A recognized strategy to mitigate these multifactor-  
313 ial risks is to implement care bundles [17,26–28]. Rather  
314 than focusing on single interventions, bundles combine mul-  
315 tiple evidence-based practices and training across the peri-  
316 natal continuum to maximize neuroprotection. A previously  
317 published quality improvement study in Canada has shown a  
318 substantial reduction in the use of inotropes, fluid boluses,  
319 and opioids. These changes were associated with a 69%  
320 decrease in IVH rates [17]. Increasing the uptake of these  
321 evidence-based practices has the potential to yield substan-  
322 tial improvements in survival without severe morbidity  
323 among the most vulnerable preterm newborns [4,10,14].

324 A major strength of this study lies in its prospective  
325 design and inclusion of both public and private hospitals in  
326 an LMIC. This approach allows for a more comprehensive  
327 and realistic representation of neonatal care across differ-  
328 ent healthcare settings in Brazil, capturing systemic chal-  
329 lenges and institutional variability. The multicenter nature  
330 and standardized methodology enhance the external validity  
331 of the findings and support their application in guiding local  
332 and national strategies for IVH prevention in similar con-  
333 texts. However, the study sample may not fully represent all  
334 regions of the country, as differences in NICU resources and  
335 clinical practices could affect generalizability.

336 Nonetheless, certain limitations must be acknowl-  
337 edged. First, as an observational study, causal inferences  
338 cannot be firmly established. Second, a significant pro-  
339 portion of infants (8.2%) did not undergo cUS, possibly  
340 due to early mortality or limited access to imaging in the  
341 first DOL, potentially leading to underestimation of IVH  
342 incidence. Third, although several variables traditionally  
343 considered risk factors for severe IVH did not reach sta-  
344 tistical significance in multinomial analyses, the sample  
345 size and number of outcome events may have limited the  
346 statistical power to detect modest associations; there-  
347 fore, these findings should be interpreted with caution.  
348 These limitations underscore the need for systemic  
349 improvements in education, clinical practice, and access  
350 to early neuroimaging in Brazilian NICUs to improve mor-  
351 tality and mortality due to IVH.

In conclusion, this multicenter cohort study highlights the  
352 persistent burden of IVH among preterm infants in Brazilian  
353 NICUs and identifies key factors associated with severe IVH  
354 or death, including lower GA, advanced delivery room resus-  
355 citation, and early hemodynamic instability. These findings  
356 support the development and implementation of standard-  
357 ized IVH prevention bundles, focused on optimizing antena-  
358 tal corticosteroid administration, thermoregulation, gentle  
359 resuscitation, and judicious hemodynamic management for  
360 preterm infants in Brazil. Future studies should prospec-  
361 tively assess the impact of such interventions on IVH inci-  
362 dence and neonatal outcomes in Brazilian NICUs.  
363

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### Data availability

The data that support the findings of this study are avail-  
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## Conflicts of interest

The authors declare no conflicts of interest.  
370  
371

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