






Peri-intraventricular hemorrhage in premature newborns: associated with immediate umbilical cord clamping, vaginal delivery and surfactant use

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Abstract

Objectives: to determine the incidence of peri-intraventricular hemorrhage (PIVH) and the risk factors in newborns weighing <1,500 g and/or gestational age <33 weeks.

Methods: a prospective cohort type study on premature newborns admitted to the type II neonatal intensive care unit at the Sistema Único de Saúde (SUS) (Public Health System) from January/2019 to December/2022. The dependent variable was PIVH, with determination of its incidence and associated risk factors. The project was approved by the Research Ethics Committee.

Results: a total of 503 neonates participated and the incidence of PIVH was 32.4%. The risk factors were: immediate clamping of the umbilical cord ($p=0.017$; $RR= 1.089$; $95\%CI=1.015-1.167$), vaginal delivery ($p=0.001$, $RR= 1.110$; $95\%CI= 1.041-1.183$) and surfactant use ($p<0.001$; $RR= 1.163$; $95\%CI= 1.092-1.239$).

Conclusion: the incidence of PIVH was high and was associated with immediate clamping of the umbilical cord, vaginal delivery and surfactant use, risk factors that can be modified by good perinatal care practices.

Key words Cerebral intraventricular hemorrhage, Infant premature, Umbilical cord clamping, Pulmonary surfactant-associated proteins



Introduction

The central nervous system (CNS) has a region called the germinal matrix, which is richly vascularized, with a large number of neuronal and glial cells. The small blood vessels in the germinal matrix form an immature vascular network. Fluctuations in cerebral blood flow caused by conditions such as anemia, hypoglycemia, asphyxia and abrupt rises in systemic blood pressure leaving the CNS prone to congestion and stasis, increasing cerebral venous pressure, causing peri-intraventricular hemorrhage (PIVH). This condition usually occurs in premature infants and is multifactorial: the presence of vulnerable vessels, hemodynamic alterations, inflammatory mediators, genetic predisposition, and among others.¹

The incidence of PIVH increases when gestational age (GA) is less, and is more frequent in patients younger than 32 weeks and with a birth weight of less than 1500g. Studies show that immediate clamping in these premature infants (< 30 seconds), the use of surfactant and vaginal delivery increase the risk of PIVH.²⁻⁵ Gestational hypertension and the use of prenatal magnesium sulphate also decrease this risk.^{6,7}

The first classification of PIVH was written by Papile⁸ in 1978, where it was divided into grades I, II, III and IV. The one most used today is the one published by Volpe⁹ in 1989, in which there was a change regarding to grade IV. Grades I and II are considered milder conditions, while grade III and ventricular hemorrhage with associated hemorrhagic infarction (formerly grade IV) are more serious, with a higher risk of death and negative neurodevelopmental outcomes.⁹

Regarding clinical presentation, most patients are asymptomatic. Therefore, for diagnosis, it is necessary to perform a transfontanellar ultrasound (TFUS) early, in the first week of life. In a survey of severe PIVH cases (grade III and IV),¹⁰ in Brazil and worldwide, between 2007 and 2013, the frequency of cases was similar. In Brazil, around 10% of premature newborns (PTNBs) have grade III and IV PIVH,¹¹ as in Spain and Canada. In Israel, 12% of hemorrhage cases were classified as more severe.¹² In more recent studies in Brazil, between 2013 and 2018, cases of severe PIVH were around 32.2%.¹³

Due to the importance of this morbidity and the negative neurological outcomes associated with its occurrence,¹⁴ the aim of this study was to determine the incidence of PIVH in PTNBs in a type II neonatal intensive care unit (NICU) at the *Sistema Único de Saúde* (SUS) (Public Health System) in the Northeast of Brazil, as well as to identify risk factors associated with its occurrence. Carrying out this research will help track cases better and reinforce preventive care and proper management of these children, in an attempt to avoid complications and

promote the best quality of life, without compromising neurodevelopment.

Methods

This was a prospective cohort study of newborns (NB) admitted to the NICU at a high-risk maternity hospital in the city of Natal - RN, in the Northeast of Brazil, from January 2019 to December 31, 2022. It has 20 beds, is classified as type II and attends exclusively for SUS patients. Patients were followed from the moment of birth until the final outcome (discharge, transfer to another hospital unit or death).

The inclusion criteria were PTNBs with a GA of less than 33 weeks and/or a birth weight of less than 1,500g. The cut-off point adopted for gestational age and birth weight was based on the higher morbidity and mortality seen in these groups at the institution where the research was carried out.

The exclusion criteria were: carriers of congenital infections (STORCH: syphilis, toxoplasmosis, rubella, cytomegalovirus and herpes, as well as arboviruses, HIV and Sars-Cov 2 infection), major congenital malformations and/or chromosomopathies, genetic syndromes, inborn errors of metabolism, non-performance of TFUS during hospitalization and coming from other services more than 24 hours after birth. Major congenital malformations are those that have medical and/or social implications and generally require surgical treatment or have an increased risk of death due to the severity and complexity of the malformation.¹⁵

The dependent variable was PIVH according to Volpe's classification⁹ in 1989, as shown in Table 1.

The diagnosis was made by means of TFUS performed using Philips Affiniti 50 ultrasound equipment, with a Linear L12-4 transducer (4 - 12 MHz). The tests were carried out at the patient's bedside in the NICU by two doctors, ultrasonographers from the institution with specific training to carry out such tests and extensive experience in the field. The first TFUS was carried out in the first week of life and the following tests were carried out at intervals according to the results of the first test, or when there was clinical suspicion of intracranial bleeding.

The independent maternal variables analyzed were: maternal age; prenatal care and number of visits; type of pregnancy (single or multiple); presence of hypertensive syndromes and diabetes during pregnancy; use of antenatal corticosteroids, with number of doses administered; use of magnesium sulphate for neuroprotection.

The neonatal variables analyzed were: route of delivery (cesarean or vaginal); time of ruptured pouch; time of umbilical cord clamping, considered immediate when performed < 30 seconds, according to the *Sociedade*

Table 1

Classification of peri-intraventricular hemorrhage.	
Grade	Description
I	Hemorrhage only in the germinal matrix or intraventricular hemorrhage in up to 10% of the ventricular area.
II	Hemorrhage in the germinal matrix and ventricular hemorrhage between 10-50% of the ventricular area
III	Hemorrhage in the germinal matrix and involving more than 50% of the ventricular area, with ventricular distension.
Hemorrhagic heart attack	Ipsilateral peri-intraventricular hemorrhagic heart attack in the white matter, and large intra-ventricular hemorrhage (referred to in this study as grade IV for ease of understanding).

Source: Volpe.⁹

Brasileira de Pediatria;¹⁶ (Brazilian Society of Pediatrics) sex of the NB; GA and birth weight; classification of weight in relation to GA using the Intergrowth-21st Project curves.¹⁷ Participants were classified as small for GA when their weight was less than the 10th percentile for GA; neonatal resuscitation and Apgar score in the 1st and 5th minute of life; axillary temperature in the first hour of life; use of intra-tracheal surfactant for respiratory distress shortly after birth and inspired oxygen fraction greater than 30%; analysis of the occurrence of infections, according to criteria defined by the *Agência Nacional de Vigilância Sanitária* (ANVISA) (National Health Surveillance Agency), which are considered early when they manifest in the first 48 hours of life and late when they occur after this period;¹⁸ pulmonary hemorrhage (PH): presence of blood in the orotracheal tube associated with the need to increase ventilatory parameters and/or hemodynamic support;¹⁹ patent ductus arteriosus: patent ductus arteriosus with flow on echocardiogram after 72 hours of life, a diagnosis made by the pediatric cardiologists at the institution using GE's Vivid I echocardiogram machine (all NBs with symptoms such as the presence of a heart murmur, pulmonary hemorrhage, tachycardia, wide pulses, signs of congestive heart failure, hypotension and the need to use vasoactive drugs were assessed for this morbidity); use of vasoactive drugs in the first week of life.

Descriptive analysis was carried out using the mean, standard deviation (Mean \pm SD), absolute and relative frequencies. Point estimates with 95% confidence intervals were used to calculate the incidence of PIVH. The Student's t-test for independent samples was applied to continuous variables with a normal distribution. The homogeneity of variances was checked using Levene's test. In the presence of heterogeneity of variances, Welch's t-test was applied. The chi-square test was used to analyze the association between categorical variables.

For results that showed significance in the t-test, Cohen's d effect size was calculated by dividing the mean difference by the standard deviation of the difference. The values were assessed according to Cohen's scale: up to

0.19 = negligible; between 0.20 and 0.39=small; between 0.40 and 0.79=moderate and ≥ 0.80 =large. The effect size for significant associations was assessed by calculating the Relative Risks (RR) and respective 95% Confidence Intervals (95%CI) using robust Poisson regression. The robust Poisson regression model was also used in the multivariate analysis. The initial model was adjusted for the independent variables that showed a significance level ≤ 0.20 in the bivariate analysis.

In a second adjustment stage, variables with a *p*-value of <0.10 were selected. For the final model, equidispersion assumptions were checked and the quality of the fit was assessed using the Wald chi-square test, Deviance analysis and the ROC curve. The variables selected were those with significant associations ($p<0.05$). A 5% significance level was adopted for all analyses. The software used for the analyses was SPSS (Statistical Package for the Social Sciences, Chicago, USA), version 28.0.

The study was approved by the Research Ethics Committee at the hospital, CAAE: 11177019.7.0000.5292, and by the Teaching and Research Management.

Results

In the period studied, 647 NB were admitted with a GA of less than 33 weeks and/or a birth weight of less than 1500g. The following were excluded: 21 because they were admitted to the service more than 24 hours after birth; 12 due to a diagnosis of genetic syndromes (trisomies 13, 18 and 21, Cri Du Chat syndrome and Jarcho Levin syndrome); 27 with a diagnosis of severe congenital malformations; six with STORCH-type congenital infections; one with lysosomal storage disease and three guardians refused to take part. A total of 74 babies did not undergo TFUS and could not be included in the study. Therefore, the final sample consisted of 503 participants.

The incidence of IVH found was 32.4%, corresponding to 163 patients (95%CI= 28.3%-36.5%). Bleeding was classified as mild (I or II) and severe (III or IVHF with associated venous infarction) in 74.2% (121) and 25.8%

(42), respectively. The average GA and birth weight were 29.5 weeks \pm 2.5 and 1251 grams \pm 385, respectively. The average follow-up time for patients until the final outcome was 56.05 \pm 32.27 days (Table 2).

Comparing the group of NBs with and without hemorrhage, it was found that mothers who had been diagnosed with hypertensive syndromes in pregnancy and received two doses of antenatal corticosteroids and magnesium sulfate for neuroprotection had a lower incidence of PIVH. The number of prenatal consultations was lower for the group of patients diagnosed with PIVH (4.4 \pm 2.1) compared to the group of neonates not diagnosed with PIVH (4.9 \pm 2.4), a statistically significant difference (Table 3).

PIVH was also associated with vaginal delivery, immediate clamping of the umbilical cord, neonatal resuscitation, Apgar less than 7 in the first and fifth minute of life, use of mechanical ventilation, use of surfactant and vasoactive drugs in the first week of life, pulmonary hemorrhage and Persistent Patent Ductus Arteriosus (PDA). On the other hand, the use of nasal

CPAP (Continuous Positive Airway Pressure) in the delivery room proved to be a protective factor against the occurrence of this morbidity. The GA at birth was lower for the group of patients diagnosed with PIVH (28.8 \pm 2.8) compared to the group of neonates without this diagnosis (29.9 \pm 2.4), $p < 0.01$. Birth weight was also lower for the group of patients diagnosed with PIVH (1.194 \pm 408) compared to the neonates group without the diagnosis (1.279 \pm 371), a statistically significant difference, $p = 0.020$ (Table 4).

The multivariate regression model was not statistically significant by the Omnibus test ($p = 0.089$), however, by analyzing the Deviance and ROC Curve, the model showed an acceptable fit (Deviance/Grades of freedom = 0.145; Area under the curve = 67.2%). The results indicated an increased risk of PIVH in neonates with an umbilical cord clamping time of < 30 seconds (RR = 1.09; 95%CI = 1.02-1.17), who used surfactant (RR = 1.16; 95%CI = 1.09-1.24) and who were born by vaginal (RR = 1.11; 95%CI = 1.04-1.18), all with $p < 0.05$ (Table 5).

Table 2

Characterization of pregnant women and neonates admitted to the neonatal intensive care unit of a high-risk maternity hospital. Natal, RN, 2019-2022.

Categorical variables	n	%
Maternal age (years)	501	100.0
< 20	76	15.2
20 - 35	342	68.3
>35	83	16.6
Neonate's sex	503	100.0
Male	255	50.7
Female	248	49.3
Gestational age at birth	503	100.0
Up to 28 weeks and 6 days	189	37.6
≥ 29 weeks	314	62.4
Birth weight (grams)	503	100.0
Up to 999	153	30.4
$\geq 1,000$	350	69.6
Quantitative variables	$\bar{x} \pm SD$	
Maternal age (years)	27.8 \pm 7.2	
Prenatal consultations (number)	4.7 \pm 2.3	
Gestational age at birth (weeks)	29.5 \pm 2.5	
Birth weight (grams)	1.251 \pm 385	
Follow-up time to final outcome (days)	56.05 \pm 32.27	

Continuous data is expressed as mean and standard deviation; categorical data is expressed as absolute (n) and relative (%) frequency.

Table 3

Obstetric characterization of pregnant women of preterm neonates admitted to the neonatal intensive care unit at a high-risk maternity hospital according to diagnosis of peri-intraventricular hemorrhage (PIVH). Natal, RN, 2019-2022.

Variables	N	Group		p ^a
		With PIVH	Without PIVH	
Maternal age (years)	501	27 ± 7	28 ± 7	0.410
Maternal age (years); n (%)	501			0.216
< 20	76	31 (40.8)	45 (59.2)	
20 - 35	342	104 (30.4)	238 (69.6)	
> 35	83	27 (32.5)	56 (67.5)	
Prenatal consultations; (number)	409	4.4 ± 2.1	4.9 ± 2.4	0.,033
Gestational hypertension; n (%)	502			0.020
Yes	219	59 (26.9)	160 (73.1)	
No	283	104 (36.7)	179 (63.3)	
Gestational diabetes; n (%)	502			0.988
Yes	71	23 (32.4)	48 (67.6)	
No	431	140 (32.5)	291 (67.5)	
Antenatal corticoid; n (%)	493			0.050
Complete cycle	282	82 (29.1)	200 (70.9)	
No or incomplete cycle	211	79 (37.4)	132 (62.6)	
Magnesium sulphate; n (%)	491			0.043
Yes	187	50 (26.7)	137 (73.3)	
No	304	108 (35.5)	196 (64.5)	

^aSignificance of difference between groups by Student's t-test (continuous variables) or Pearson's chi-squared test (categorical variables); Continuous data are expressed as mean and standard deviation; categorical data are expressed as absolute (n) and relative (%) frequency.

Table 4

Characterization of neonates admitted to the neonatal intensive care unit at a high-risk maternity hospital according to diagnosis of peri-intraventricular hemorrhage (PIVH). Natal, RN, 2019-2022.

Variables	N	Group		p ^a
		With PIVH	Without PIVH	
Sex; n (%)	503			0.074
Male	255	92 (36.1)	163 (63.9)	
Female	248	71 (28.6)	177 (71.4)	
Gestational age at birth (weeks)	503	28.8 ± 2.8	29.9 ± 2.4	<0.01
Gestational age at birth; n (%)	503			0.004
Up to 28 weeks and 6 days	189	76 (40.2)	113 (59.8)	
≥29 weeks	314	87 (27.7)	227 (72.3)	
Birth weight (grams)	503	1.194 ± 408	1.279 ± 371	0.020
Birth weight (grams); n (%)	503			0.005
Up to 999	153	63 (41.2)	90 (58.8)	
≥1.000	350	100 (28.6)	250 (71.4)	
Small for gestational age; n (%)	503			0.284
Yes	110	31 (28.2)	79 (71.8)	
No	393	132 (33.6)	261 (66.4)	
Type of delivery; n (%)	503			0.008
Cesarean section	325	92 (28.3)	233 (71.7)	
Vaginal	178	71 (39.9)	107 (60.1)	

Time of ruptured sac (hours)	498	22.9 ± 75.6	26.7 ± 82.8	0.621
Type of pregnancy; n (%)	503			0.528
Multiple	88	26 (29.5)	62 (70.5)	
Singleton	415	137 (33.0)	278 (67.0)	
Umbilical cord clamping time 2; n (%)	459			0.002
Immediate (< 30 seconds)	324	123 (38.0)	201 (62.0)	
≥30 seconds	135	31 (23.0)	104 (77.0)	
Resuscitation in delivery room; n (%)	485			<0.01
Yes	280	108 (38.6)	172 (61.4)	
No	205	47 (22.9)	158 (77.1)	
Temperatura de admissão; n (%)	470			0.951
< 36.5	383	123 (32.1)	260 (67.9)	
36.5 – 37.5	76	24 (31.6)	52 (68.4)	
>37.5	11	4 (36.4)	7 (63.6)	
Admission temperature; (degrees)	467	35.4 ± 1.3	35.6 ± 1.1	0.097
Apgar score at 1 st minute; n (%)	498			0.003
< 7 points	235	92 (39.1)	143 (60.9)	
≥7 points	263	70 (26.6)	193 (73.4)	
Apgar score at 5 th minute; n (%)	498			0.001
< 7 points	80	40 (50.0)	40 (50.0)	
≥7 points	418	122 (29.2)	296 (70.8)	
Use of mechanical ventilation; n (%)	503			<0.01
Yes	293	119 (40.6)	174 (59.4)	
No	210	44 (21.0)	166 (79.0)	
Respiratory distress syndrome (surfactant use); n (%)	503			<0.01
Yes	221	100 (45.2)	121 (54.8)	
No	282	63 (22.3)	219 (77.7)	
Pulmonary hemorrhage; n (%)	503			<0.01
Yes	85	41 (48.2)	44 (51.8)	
No	418	122 (29.2)	296 (70.8)	
Persistent ductus arteriosus; n (%)	497			<0.01
Yes	120	54 (45.0)	66 (55.0)	
No	377	105 (27.9)	272 (72.1)	
Use of vasoactive drugs; n (%)	501			<0.01
Yes	155	72 (46.5)	83 (53.5)	
No	346	91 (26.3)	255 (73.7)	
Use of CPAP in the delivery room; n (%)	502			<0.01
Yes	319	77 (24.1)	242 (75.9)	
No	183	86 (47.0)	97 (53.0)	

*Significance of difference between groups by Student's t-test (continuous variables) or Pearson's chi-squared test (categorical variables); Continuous data are expressed as mean and standard deviation; categorical data are expressed as absolute (n) and relative (%) frequency; nasal CPAP (Continuous Positive Airway Pressure).

Table 5

Robust Poisson Regression Model adjusted for the occurrence of peri-intraventricular hemorrhage in premature newborns in the neonatal intensive care unit at a high-risk maternity hospital. Natal, RN, 2019-2022.

Parameter	B	Standard Error	χ^2	p	RR	95%CI
(Intercept)	.117	.0330	12.705	<.001	1.125	1.054-1.200
Clamping time < 30 sec.	.085	.0356	5.693	.017	1.089	1.015-1.167
Clamping time \geq 30 sec. (reference)						
Use of surfactant	.151	.0322	22.015	<.001	1.163	1.092-1.239
No use of surfactant (reference)						
Vaginal delivery	.104	.0327	10.139	.001	1.110	1.041-1.183
Cesarean delivery (reference)						

Relative risks (RR) calculated by the Robust Poisson Regression model and adjusted for the variables: type of delivery, time of umbilical cord clamping and use of surfactant; Chi-square (3) = 6.524, $p=0.089$; ROC curve = 67.2%.

Discussion

In this present study, the incidence of PIVH in premature infants was high compared to the national average. However, the frequency of more severe hemorrhages was lower and morbidity was more common in patients with lower gestational age and birth weight.

A national study using data from the *Rede Brasileira de Pesquisa Neonatal* (Brazilian Neonatal Research Network), carried out between 2013 and 2018¹³ showed that 30.4% of patients had PIVH, ranging from mild to severe. The severe form was diagnosed in 32.2%, a high incidence with an increasing trend over the years in a population with an average gestational age of 29 weeks and an average weight of 1,085 grams. The occurrence of bleeding was also higher in patients with lower gestational ages and birth weights (28 weeks and 815 grams).

The risk factors that remained associated with PIVH in the multivariate analysis were: immediate umbilical cord clamping (< 30 seconds), the use of surfactant and vaginal delivery compared to cesarean section.

In the literature, we have seen that timely umbilical cord clamping (>30 seconds in premature NBs under 34 weeks of gestational age, according to the recommendations of the *Programa de Reanimação Neonatal da Sociedade Brasileira de Pediatria*)¹⁶ (Neonatal Resuscitation Program of the Brazilian Society of Pediatrics) brings benefits for the patient, as it increases the transfer of blood from the cord to the NB, increasing hematocrit levels and preventing early anemia. In addition, immediate clamping decreases intravascular volume, favoring cerebral hypoperfusion.² For this reason, it is recommended that in premature infants under 34 weeks, clamping be performed between 30 seconds and one minute of life. However, for this to happen, it is necessary for the NB to have good vitality at birth, characterized by the presence of regular breathing and good muscle tone, which sometimes does not occur in premature infants under 34 weeks, especially

those who did not receive prenatal corticosteroids.^{20,21} In the institution studied, the pediatricians in the delivery room are trained periodically with neonatal resuscitation courses, indicating that the care provided to newborns is adequate. However, many premature newborns are not born with good vitality and in these situations there is a need for immediate umbilical cord clamping according to national guidelines.¹⁶

Many extreme preterm infants have respiratory distress syndrome (RDS), and the main treatment recommended is the use of surfactant to recruit pulmonary alveoli, associated with ventilatory support (invasive or not). However, despite its benefits, one of the side effects is hemorrhage, such as PIVH and pulmonary hemorrhage.³ Many of the PTNB <33 weeks in the unit studied received at least one dose of surfactant. It is important to note that in the institution where the research was carried out, surfactant is administered primarily through orotracheal intubation (InSurE-Intubate Surfactant Extubate technique), and minimally invasive techniques such as MIST (Minimally Invasive Surfactant Therapy) are not routinely used. With the InSurE technique, the patient is intubated to administer the medication, after which they must be extubated, but the risk of keeping the patient intubated is greater, causing harm due to the invasive ventilation time.²²

Recent studies have shown that using a less invasive technique to administer surfactant, such as MIST, reduces the need for invasive ventilation, reduces the length of hospital stay and is less likely to develop pulmonary bronchodysplasia and severe PIVH. The MIST technique consists of using a thin endotracheal catheter, introduced into the trachea under direct visualization through the laryngoscope. This catheter is then removed after administration of the medication. Throughout the procedure, the patient has a nasal prong with positive pressure in non-invasive ventilation and maintains spontaneous breathing.²²

It has also been shown that the route of delivery contributes to the occurrence of PIVH. There are controversial results in the scientific literature; some authors have also found the same result with an increased risk of PIVH in PTNBs born vaginally, but with no association with more severe bleeding. Vaginal delivery favors the rupture of the NB's vessels, and in an elective cesarean delivery this risk would be lower. However, the best route of delivery should always take into account the risk of maternal complications, as well as the risks to the fetus.^{4,5,23}

Minimum or essential handling protocols, especially in the first 72 hours of life, have been indicated as a neuroprotective strategy and to reduce the risk of PIVH.^{24,25} These protocols, are known as bundles, generally include: maintaining the supine position and head in a neutral position, avoiding painful and stressful procedures, aspirating the tracheal tube only if there is excessive secretion/obstruction, arterial catheterization in addition to venous catheterization in those with a birth weight of <1,000g (for the administration of medication and to avoid repeated punctures for test collection), not collecting cerebrospinal fluid, essential manipulation and care bundling. Bundles are a set of good practices, such as those listed above, and are used in NB care. It is a low-cost solution that contributes to improving the quality of care.²⁶ The studies showed that the use of these care measures was effective in reducing cases of PIVH, but that there is still a need for continuing education for the team caring for the NB, emphasizing the importance of this care and that these are simple actions that can be adopted and maintained.

For the management of children diagnosed with PIVH, it is recommended to: maintain adequate mean arterial perfusion; oxygenation and ventilation according to the condition; adequate water support, metabolic and nutritional support; treat seizures in timely manner to avoid hypoxia or hypotension; continuous surveillance with TFUS for early detection of post-hemorrhagic ventricular dilation to assess the need for ventricular shunt.²⁷

Severe PIVH is considered harmful to the child's neurological development, and can delay the achievement of developmental milestones, and compromise speech, hearing and vision, and among others. For this reason, follow-up with the multidisciplinary team after hospital discharge is very important.²⁸

By evaluating the results of this longitudinal study, we can contribute to changes in the care of premature patients, in order to provide better quality care, reducing prenatal risk factors, increasing the use of corticosteroids for example, and controlling postnatal risk factors such as the use of ventilatory support with protective strategies,

the administration of surfactant in a less invasive way and with stress and pain control and the timely umbilical cord clamping.²⁹

With regard to limitations, the study was single-center, but with a large sample size and prospectively constructed. Some approaches could not be well analyzed, such as the use of vasoactive drugs, for example, which in the literature and in our statistical analysis is associated with an increased risk of PIVH,³⁰ but the indications for their use were not well documented, compromising the evaluation of data for future interventions, with the aim of improving care.

In conclusion, we would like to point out that the incidence of PIVH was high. The risk factors identified for its occurrence are similar to those described in the literature and can be minimized through bundles of care for the premature infant including timely umbilical cord clamping, prevention of hypothermia, application of good practices in vaginal delivery or indication of cesarean delivery in cases of extreme prematurity, considering the associated maternal risks and protocol for indication and administration of tracheal surfactant, preferably through minimally invasive techniques and with adequate management of stress and pain during the procedure.

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Authors' contribution

Sousa DAS and Barreto ACNG: conception and design of the study, data collection, filling in the spreadsheets, analysis and interpretation of the results, writing and critical revision of the content of the manuscript. Ferreira PLM: statistical analysis of the data, analysis and interpretation of the results, writing and critical revision of the content of the manuscript. Camargo JDAS: design of the research methodology, statistical analysis of the data, analysis and interpretation of the results, writing and critical revision of the content of the manuscript. Silveira SLA: research design, writing and critical revision of the content of the manuscript. All the authors have approved the final version of the article and declare no conflicts of interest.

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