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Hypotension in Preterm Neonates: The Relationship Between Early Postnatal Inotropic Support and Morbidity and Mortality

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Abstract

Objective: Hemodynamic instability is frequently observed during the early postnatal period in very low birth weight preterm infants. In this study, we aimed to evaluate the association between the requirement for early postnatal inotropic therapy and mid-term morbidities and mortality.

Methods: This retrospective cohort study included preterm neonates born at ≤32 weeks of gestation who were admitted to a level III neonatal intensive care unit between January 2020 and December 2023. Infants who died within the first 24 hours of life or had major congenital anomalies, genetic disorders, or perinatal asphyxia were excluded. Patients were classified according to the presence of hypotension and requirement for inotropic therapy within the first 72 hours of life. Hypotension was defined as a mean arterial pressure lower than the infant's gestational age in weeks, confirmed by at least two consecutive measurements. Clinical and maternal demographic data, respiratory support characteristics, and neonatal morbidities were recorded. Multivariable logistic regression analysis was performed to identify independent predictors of severe intraventricular hemorrhage.

Results: A total of 207 preterm neonates born at ≤32 weeks of gestation were included in the analysis, and 65 (32.3%) received inotropic therapy during the first 72 hours of life. Infants who received inotropic therapy had significantly lower birth weight (952 ± 328 g vs. 1120 ± 281 g, p = 0.01) and gestational age (26 ± 1.7 weeks vs. 27.8 ± 1.8 weeks, p < 0.01) compared with those who did not receive inotropes. Severe intraventricular hemorrhage (IVH) occurred significantly more frequently in the inotrope-treated group (29.2%, p < 0.01), and mortality was markedly higher in this group (43% vs. 11.3%, p < 0.01). Median vasoactive inotropic score (VIS) values were significantly higher both in non-survivors compared with survivors (20 vs. 10, p = 0.037) and in infants who developed severe IVH compared with those who did not (20 vs. 10, p = 0.025). Logistic regression analysis demonstrated that increasing gestational age was an independent protective factor against severe IVH (OR: 0.632, 95% CI: 0.433–0.924, p = 0.018). Mortality was independently associated with the presence of severe IVH (OR: 3.931, 95% CI: 1.462–10.565, p = 0.007).

Conclusion: Early postnatal hypotension and inotropic therapy requirement in preterm neonates were associated with increased rates of severe IVH and mortality, suggesting a poor prognosis in this population.

Keywords: Hypotension, inotropes, mortality, prematurity

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Prematüre Yenidoğanlarda Hipotansiyon: Postnatal Erken İnotrop Desteğinin Morbidite ve Mortalite ile İlişkisi

Öz

Giriş: Hemodinamik instabilite, çok düşük doğum ağırlıklı preterm bebeklerde erken postnatal dönemde sık olarak gözlenmektedir. Bu çalışmamızda, erken postnatal dönemde inotrop tedavisi gereksinimi ile orta dönem morbiditeler ve mortalite arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: Bu retrospektif kohort çalışmaya, Ocak 2020 ile Aralık 2023 tarihleri arasında üçüncü basamak yenidoğan yoğun bakım ünitesine yatırılan ve gebelik yaşı ≤32 hafta olan prematüre yenidoğanlar dahil edildi. Yaşamın ilk 24 saati içinde kaybedilen, majör konjenital anomalisi, genetik hastalığı veya perinatal asfiksi öyküsü bulunan bebekler çalışma dışı bırakıldı. Hastalar, yaşamın ilk 72 saati içinde hipotansiyon varlığı ve inotrop tedavisi gereksinimine göre sınıflandırıldı. Hipotansiyon, en az iki ardışık ölçümde ortalama arter basıncının bebeğin gebelik haftasından düşük olması olarak tanımlandı. Klinik ve maternal demografik veriler, solunum desteği özellikleri ve neonatal morbiditeler kaydedildi. Şiddetli intraventriküler kanamanın bağımsız belirleyicilerini araştırmak amacıyla çok değişkenli lojistik regresyon analizi uygulandı.

Bulgular: Analize gebelik yaşı ≤32 hafta olan toplam 207 prematüre yenidoğan dahil edildi ve bunların 65'ine (%32,3) yaşamın ilk 72 saatinde inotrop tedavisi uygulandı. İnotrop tedavisi alan bebeklerin doğum ağırlığı (952 ± 328 g'ye karşı 1120 ± 281 g, p = 0,01) ve gestasyon yaşı (26 ± 1,7 haftaya karşı 27,8 ± 1,8 hafta, p < 0,01), inotrop almayanlara göre anlamlı derecede daha düşüktü. Şiddetli intraventriküler kanama (İVK), inotrop tedavisi alan grupta anlamlı olarak daha sık görüldü (%29,2, p < 0,01) ve mortalite bu grupta belirgin şekilde daha yüksekti (%43'e karşı %11,3, p < 0,01). Medyan vazoaktif inotrop skor (VIS) değerleri hem kaybedilen hastalarda yaşayanlara göre (20'ye karşı 10, p = 0,037) hem de şiddetli IVK gelişen hastalarda gelişmeyenlere göre (20'ye karşı 10, p = 0,025) daha yüksekti. Lojistik regresyon analizinde artan gestasyon yaşının şiddetli IVK için bağımsız koruyucu bir faktör olduğu gösterildi (OR: 0,632, %95 GA: 0,433–0,924, p = 0,018).

Sonuç: Prematüre bebeklerde erken postnatal dönemde gelişen hipotansiyon ve inotrop tedavisi gereksinimi, ciddi IVK ve yüksek mortalite ile ilişkili bulunmuş olup, bu durumun kötü prognozun bir göstergesi olabileceği düşünülmektedir.

Anahtar kelimeler: Hipotansiyon, inotrop, mortalite, prematürite.

INTRODUCTION

Recent technological developments in neonatology have contributed to a decline in mortality among preterm infants; however, morbidity and mortality remain major challenges in clinical practice. Neurological complications, particularly intraventricular hemorrhage (IVH), remain key determinants of long-term neurodevelopmental outcomes, and early postnatal hypotension has been proposed as a potential contributor to these unfavorable outcomes[1,2]. Instability of cardiovascular status is commonly encountered in the first days following birth, especially in neonates born prematurely and with low birth weight. Although incidence rates vary across studies, hypotension remains prevalent in preterm infants within the initial 72 hours of life[1].

Defining hypotension and determining the appropriate indications for intervention in preterm infants remain challenging. Variations in systemic blood pressure can alter cerebral perfusion; however, interventions intended to normalize blood pressure may paradoxically increase the risk of cerebral injury when abrupt or excessive hemodynamic shifts occur. For this reason, both the recognition of hypotension and decisions regarding its treatment must be approached cautiously and tailored to the individual clinical context[3].

At present, no consensus exists regarding a single blood pressure threshold that reliably defines hypotension in preterm neonates. This lack of standardization has resulted in considerable variability in management strategies among neonatal intensive care units[3]. The early postnatal period, particularly the first three days of life, is recognized as a phase of heightened vulnerability, as most severe IVH

events occur during this interval. Consequently, timely identification of hypotension and a better understanding of its underlying pathophysiology are critical for improving neonatal outcomes[1,3].

Evidence from large multicenter randomized controlled trials the treatment of hypotension in extremely preterm infants in early life has demonstrated that although dopamine effectively elevates systemic blood pressure, this elevation has not been shown to improve survival, decrease major morbidities, or enhance long-term neurodevelopmental outcomes[1]. These findings challenge the practice of initiating therapy based solely on numerical blood pressure values and raise concerns regarding the clinical benefit of such an approach.

In preterm neonates, hypotension has also been linked to cerebral pathologies including IVH and periventricular leukomalacia[4]. Despite this observed association, a definitive causal relationship has not been clearly established[1]. One proposed explanation involves impaired cerebral autoregulation, whereby fluctuations in systemic circulation may predispose the immature brain to ischemia–reperfusion injury and subsequent structural damage[5].

In light of these considerations, the present study was designed to evaluate the association between early postnatal inotropic therapy and mid-term morbidity and mortality in preterm neonates.

METHODS

Study Design and Population

This retrospective cohort study evaluated preterm neonates born at or before 32 weeks of gestation who were hospitalized in a tertiary level neonatal intensive care unit between January 2020 and December 2023. Infants who died within the first 24 hours after delivery were excluded. Additional exclusion criteria included documented perinatal asphyxia, major structural congenital anomalies, and confirmed genetic syndromes. Relevant maternal, neonatal, and clinical data were extracted from the institutional electronic database.

Group Classification

Infants were stratified according to the occurrence of hypotension and exposure to inotropic therapy during the early postnatal period. The exposure group consisted of neonates who developed hypotension requiring pharmacological cardiovascular support within the first 72 hours of life. The comparison group included infants who maintained stable blood pressure values during the same period and did not receive vasoactive medications.

Normotension was defined as a mean arterial pressure (MAP) equal to or greater than the infant's gestational age expressed in weeks, in the absence of clinical or biochemical indicators of inadequate tissue perfusion during the first three postnatal days.

Blood Pressure Monitoring

Blood pressure was routinely assessed using oscillometric non-invasive bedside monitors. When clinically necessary, invasive arterial catheter monitoring was performed. Hypotension was diagnosed when MAP values were lower than the gestational age in weeks and confirmed by at least two consecutive measurements obtained through invasive monitoring or validated oscillometric techniques. MAP served as the principal hemodynamic parameter for hypotension diagnosis.

Hemodynamic Management and Inotropic Treatment

Hypotension management followed the clinical recommendations of the Turkish Neonatal Society. Initial evaluation included assessment of intravascular volume status, and fluid bolus therapy was administered when indicated.

Inotropic agents were initiated in infants with persistent hypotension despite adequate volume resuscitation or in those demonstrating clinical evidence of impaired perfusion, such as capillary refill time exceeding three seconds, metabolic acidosis, oliguria, or increased serum lactate concentrations.

Selection of vasoactive medications, including dopamine, dobutamine, or alternative agents, was determined based on individualized hemodynamic characteristics. Drug dosages were adjusted according to blood pressure trends, perfusion findings, and clinical response. Duration of inotropic therapy was defined as the cumulative time during which vasoactive medications were administered.

Data Collection

Demographic and perinatal variables were recorded for all patients. Maternal variables included antenatal corticosteroid administration, hypertensive disorders of pregnancy, gestational diabetes, medication exposure during pregnancy, premature rupture of membranes, and clinical or histopathological evidence of chorioamnionitis.

Clinical indications for inotropic treatment and the specific vasoactive agents used were documented. Infants were subsequently classified into two groups according to whether inotropic therapy was administered during the first 72 postnatal hours.

Vasoactive-Inotropic Score (VIS)

Inotropic treatment initiation in the study unit was guided by national clinical recommendations and implemented when hemodynamic and clinical criteria for hypotension were met. The overall intensity of cardiovascular pharmacological support was quantified using the Vasoactive-Inotropic Score (VIS), calculated using the following equation:

VIS = dopamine (μg/kg/min) + dobutamine (μg/kg/min) + 100 × epinephrine (μg/kg/min) + 100 × norepinephrine (μg/kg/min) + 10 × milrinone (μg/kg/min) + 10,000 × vasopressin (U/kg/min)

For each patient, the highest VIS value recorded within the first 72 hours of life was evaluated. VIS values were compared between infants with and without severe intraventricular hemorrhage (grade ≥3) and between survivors and non-survivors.

Outcome Measures

Primary and secondary neonatal outcomes were compared between the study groups. These included hemodynamically significant patent ductus arteriosus (hsPDA), severe intraventricular hemorrhage (grade ≥3), early- and late-onset neonatal sepsis, necrotizing enterocolitis (stage ≥2), moderate-to-severe bronchopulmonary dysplasia, retinopathy of prematurity requiring treatment, length of hospital stay, and mortality.

Additional evaluated variables included surfactant administration, duration of invasive and non-invasive respiratory support, development of pulmonary air leak syndromes, and total respiratory support duration.

Statistical Analysis

Data analyses were conducted using SPSS software (version 22). Categorical variables were presented as numbers and percentages, whereas continuous variables were summarized using mean ± standard deviation or median with interquartile ranges when appropriate.

Comparisons between groups were performed using the Chi-square test for categorical data. Continuous variables were analyzed using either the independent samples t-test or the Mann–Whitney U test based on distribution characteristics. Multivariable logistic regression models were constructed to determine independent predictors of severe intraventricular hemorrhage, including

gestational age, birth weight, and exposure to inotropic therapy. A two-sided p-value <0.05 was considered statistically significant.

The study protocol received approval from the Clinical Research Ethics Committee of the University of Health Sciences (approval date: 12 December 2024; approval number: 277). All procedures were performed in accordance with the ethical principles of the Declaration of Helsinki.

RESULTS

A total of 207 preterm infants born at or before 32 weeks of gestation were evaluated. Early postnatal inotropic therapy within the first 72 hours of life was administered to 65 infants (32.3%), while the remaining 141 infants (67.7%) did not require any inotropic support during this period.

Infants exposed to inotropic treatment were born at significantly lower gestational ages and had lower birth weights compared with those who were not treated with inotropes. The mean birth weight was 952 ± 328 g in the inotrope group versus 1120 ± 281 g in the non-inotrope group (p = 0.01). Similarly, mean gestational age was significantly lower among infants receiving inotropes (26 ± 1.7 weeks) compared with those who did not (27.8 ± 1.8 weeks; p < 0.01). No statistically significant differences were observed between the groups in terms of delivery mode, sex, maternal preeclampsia, gestational diabetes, or 5-minute Apgar scores (Table 1).

Table I: Demographic Characteristics of the Patients

Parameter	Early Inotrope Use (n=65)	No Early Inotrope Use (n=141)	p-value
Birth weight, g*	952±328	1120±281	0.01
Gestational age, weeks*	26±1.7	27.8±1.8	<0.01
Cesarean section, n (%)	42 (64.6)	95 (67.3)	0.22
Male sex, n (%)	26 (40)	58 (41.1)	0.601
Antenatal steroid use, n (%)	27 (41.5)	62 (44)	0.72
Preeclampsia, n (%)	5 (7.7)	10 (7)	0.78
Gestational diabetes, n (%)	3 (4.6)	2 (1.4)	0.64
Early membrane rupture, n (%)	11 (16.9)	30 (21.3)	0.57
Chorioamnionitis, n (%)	4 (6.2)	5 (3.5)	0.11
5-minute Apgar score, median (range)	5 (4-7)	6 (4-7)	0.21

**Mean ± standard deviation*

***Median (minimum–maximum)*

Respiratory support characteristics are detailed in Table 2. Infants who required inotropic support underwent significantly longer durations of invasive and non-invasive mechanical ventilation and had prolonged lengths of hospital stay compared with infants in the non-inotrope group. However, the proportion of infants receiving surfactant therapy and the total duration of respiratory support—defined as the cumulative time spent on invasive ventilation, non-invasive ventilation, and supplemental oxygen—were similar between groups.

Table II: Respiratory Support Parameters

	Early Inotrope Use (n=65)	No Early Inotrope Use (n=141)	p-value
Surfactant requirement, n (%)	54 (83)	121 (86)	0.56
Duration of invasive mechanical ventilation, days*	21± 10	13 ±4	0.041
Duration of non-invasive mechanical ventilation, days*	7±4	5±3	<0.01
Total duration of respiratory support, days*	35±6	33±5	0.14
Length of hospital stay, days*	47±7	36±5	0.014

** Mean ± Standard Deviation*

Short- and mid-term clinical outcomes are presented in Table 3. The incidence of periventricular leukomalacia, moderate-to-severe bronchopulmonary dysplasia, retinopathy of prematurity requiring treatment, osteopenia of prematurity, early-onset and late-onset sepsis, and necrotizing enterocolitis (stage ≥ 2) did not differ significantly between infants who received inotropes and those who did not. In contrast, severe intraventricular hemorrhage (grade ≥ 3) occurred significantly more frequently in the inotrope group (29.2%) compared with the non-inotrope group ($p < 0.01$). In addition, pneumothorax was observed more commonly among infants exposed to inotropic therapy ($p = 0.013$).

Table III: Short- and mid-term clinical characteristics of the patients

Clinical Feature	Early Inotrope Use (n=65)	No Early Inotrope Use (n=141)	p-value
Severe intraventricular Hemorrhage, n (%)	19 (29,2)	13 (9,2)	<0.01
Hemodynamically significant patent Ductus Arteriosus, n (%)	41 (63)	68 (48,2)	0.021
Retinopathy of Prematurity, n (%)	1 (0.15)	2 (0.14)	0.12
Moderete-severe bronchopulmonary Dysplasia, n (%)	21(32)	62 (44)	0.32
Air Leak, n (%)	10 (15,3)	6 (4,3)	0.013
Early Neonatal Sepsis, n (%)	16 (25)	32 (22.5)	0.44
Late Neonatal Sepsis, n (%)	26 (40)	42 (30)	0.12
Premature Osteopenia, n (%)	15 (23)	40 (28,3)	0.23
Periventricular Leukomalacia, n (%)	9 (13,8)	15 (11)	0.17
Necrotizing Enterocolitis, n (%)	5 (7,7)	10 (7)	0.78
Mortality, n (%)	28 (43)	16 (11.3)	<0.01

Mortality rates differed markedly between groups. Death occurred in 28 infants (43%) in the inotrope group, compared with 16 infants (11.3%) in the non-inotrope group, representing a statistically significant difference ($p < 0.01$). The vasoactive-inotropic score (VIS) was significantly higher in non-survivors than in survivors (median 20 vs. 10; $p = 0.037$). Likewise, infants who developed severe intraventricular hemorrhage had higher VIS values compared with those without severe IVH (median 20 vs. 10; $p = 0.025$) (Table 4).

Table IV: Evaluation of the relationship between vasoactive inotropic score and mortality and severe intraventricular hemorrhage in patients requiring inotropic support

	Exitus (n=28)	Survived (n=37)	p
Vasoactive inotropic score	20 (5-34)	10 (10-35)	0.037
	Severe IVH (n=19)	No severe IVH (n=46)	
Vasoactive inotropic score	20 (10-35)	10 (5-45)	0.025

Median (minimum-maximum)

In the logistic regression analysis performed to identify factors independently associated with severe intraventricular hemorrhage, increasing gestational age was identified as a significant protective factor, with a decreasing risk of severe IVH observed as gestational age increased (OR = 0.632, 95% CI: 0.433–0.924; p = 0.018). In contrast, after adjustment for confounding variables, inotropic therapy and VIS were not independently associated with severe IVH (Table 5).

Table V: Multivariable logistic regression analysis of factors associated with IVH/PVL

Variable	Beta (β)	S.E.	p-value	OR (Exp(B))	95% CI for OR (Lower–Upper)
Gestational age (weeks)	-0.458	0.193	0.018	0.632	0.433–0.924
Inotrope use	-0.635	0.921	0.491	0.530	0.087–3.223
Vasoactive Inotropic Score (per 1-point increase)	0.057	0.043	0.185	1.058	0.973–1.151

DISCUSSION

This study demonstrated that preterm infants who required early postnatal inotropic therapy experienced markedly higher incidences of severe intraventricular hemorrhage and mortality compared with those who remained hemodynamically stable without vasoactive treatment. These findings support the concept that early inotropic requirement is not merely a therapeutic intervention but may also reflect the severity of cardiovascular instability and overall clinical fragility in extremely premature infants.

The transition from fetal to neonatal circulation represents a physiologically demanding period, particularly in preterm neonates whose cardiovascular regulatory mechanisms are immature. During the first 72 hours of life, systemic and cerebral perfusion may be influenced by multiple interrelated factors such as respiratory support strategies, invasive monitoring procedures, and transitional circulatory conditions including ductal shunting. Because cerebral autoregulation remains underdeveloped in very preterm infants, even minor fluctuations in cerebral blood flow may predispose to ischemic-reperfusion injury and increase susceptibility to intraventricular hemorrhage[7,8].

In critically ill premature neonates, regulation of cerebral perfusion frequently becomes pressure-dependent rather than autoregulatory. Under these conditions, alterations in systemic blood pressure may directly affect cerebral circulation. The administration of vasoactive medications, although intended to improve systemic perfusion, may occasionally result in rapid hemodynamic changes that could adversely influence cerebral oxygen delivery, thereby potentially aggravating neurological injury during periods of heightened vulnerability[9].

In this study, preterm infants who required inotropic support were characterized by significantly lower gestational age and birth weight compared with those managed without vasoactive therapy. This finding is in agreement with accumulating evidence indicating that extreme prematurity is associated with underdeveloped cardiovascular structure and immature autonomic regulation, predisposing infants to circulatory instability. Prior cohort data have demonstrated that lower gestational age is associated with diminished myocardial performance and reduced systemic vascular resistance, thereby increasing vulnerability to hypotension and the subsequent need for pharmacologic circulatory support. Moreover, investigations focusing on the determinants of intraventricular hemorrhage have consistently

identified decreasing gestational age as a major risk factor for both hypotension and adverse neurological outcomes, highlighting the intrinsic biological fragility of this population[10]. In parallel, clinical studies have reported that lower birth weight and gestational age are strongly correlated with increased neonatal morbidity and a higher likelihood of requiring invasive therapeutic interventions, including inotropic agents, further supporting the close relationship between prematurity severity and hemodynamic compromise[11].

A key observation of the present study was the markedly higher rate of severe intraventricular hemorrhage among infants receiving inotropic therapy. This association has been reported in several recent investigations, which have identified hypotension requiring vasoactive support as a significant contributor to high-grade IVH. A systematic review and meta-analysis published in 2025 demonstrated that hypotension was associated with an almost fourfold increase in the risk of IVH in very low birth weight infants, a finding attributed to impaired cerebral autoregulation and unstable cerebral blood flow within the vulnerable germinal matrix[12]. Similarly, large cohort studies have confirmed that hypotension necessitating inotropic treatment constitutes an independent risk factor for severe IVH, underscoring the importance of careful circulatory management in extremely preterm neonates[13].

In our cohort, infants treated with inotropes also required significantly longer durations of both invasive and non-invasive mechanical ventilation and experienced prolonged hospitalization. This likely reflects the overall illness severity and multisystem immaturity commonly observed in hypotensive preterm infants. Previous studies have shown that hypotension requiring vasoactive support frequently coexists with more severe respiratory disease, leading to prolonged ventilator dependence. This interaction may be mediated by impaired pulmonary perfusion and an amplified systemic inflammatory response[12]. Additionally, mechanical ventilation itself can influence intrathoracic pressures and cerebral venous return, potentially exacerbating hemodynamic instability in premature infants. Consequently, prolonged respiratory support may serve as a marker of more profound systemic dysfunction, contributing to extended neonatal intensive care unit stays and increased healthcare utilization[13].

Recent evidence increasingly supports a physiology-based approach to neonatal hemodynamic management rather than reliance on fixed blood pressure thresholds alone. Several studies have demonstrated that reduced systemic blood flow may occur despite apparently normal blood pressure values and that such flow abnormalities are more closely associated with adverse outcomes, including severe IVH, bronchopulmonary dysplasia, and mortality[14,15]. Furthermore, data from randomized controlled trials and observational studies suggest that pharmacological elevation of blood pressure in isolation does not consistently translate into improved short- or long-term outcomes[1,3,16]. These findings advocate for individualized management strategies incorporating clinical perfusion assessment and targeted functional echocardiography.

In the present study, the incidences of necrotizing enterocolitis, retinopathy of prematurity, and bronchopulmonary dysplasia were comparable between infants who received inotropic therapy and those who did not. This observation is consistent with the findings of a Cochrane systematic review by Osborn et al., which reported no uniform differences in major neonatal morbidities between inotrope-exposed and non-exposed preterm infants[17].

Mortality was significantly higher among infants requiring inotropic support. This aligns

with existing literature suggesting that early hemodynamic instability represents a marker of severe systemic illness and impaired physiological adaptation. Recent studies have shown that refractory hypotension during the first postnatal week is strongly associated with both severe IVH and increased mortality, indicating that circulatory failure often reflects a global critical condition rather than an isolated cardiovascular disturbance[4].

Our findings also demonstrated that higher vasoactive inotropic burden was significantly associated with both mortality and severe IVH. In recent years, the VIS has emerged as a quantitative indicator of the intensity of cardiovascular support. Elevated VIS values in preterm neonates have been linked to increased risks of mortality, severe IVH, and bronchopulmonary dysplasia[18]–[22]. High VIS during the early postnatal period may reflect both the severity of cardiovascular dysfunction and the potential deleterious effects of aggressive vasoactive therapy. Although VIS could not be calculated in the present study due to its retrospective nature, incorporation of this parameter into future prospective studies may enhance risk stratification and support more precise therapeutic decision-making.

Multivariable analysis revealed that increasing gestational age was independently protective against severe IVH, whereas the presence of severe IVH substantially increased the risk of mortality. These findings are consistent with evidence demonstrating that immaturity of the germinal matrix and incomplete cerebrovascular autoregulation in extremely preterm infants predispose them to hemorrhagic brain injury. Findings from large population-based cohorts consistently show that severe IVH confers a significantly increased risk of mortality and adverse long-term neurodevelopmental outcomes. Furthermore, severe IVH has been linked to persistent cognitive and motor impairments, particularly when accompanied by refractory hypotension and additional systemic complications[4]. Together, these observations emphasize the importance of preventive strategies targeting both hemodynamic instability and secondary cerebral injury in this vulnerable population.

Our study has several limitations. The retrospective design precluded standardization of the timing, dosing, duration, and initiation thresholds of inotropic therapy, which may have influenced outcome interpretation. In addition, analyses according to the specific type or combination of inotropic agents could not be performed. The absence of serial VIS measurements limited comprehensive assessment of hemodynamic support intensity. Hypotension was defined without the use of advanced hemodynamic monitoring techniques. Finally, the single-center design and the absence of long-term neurodevelopmental outcome assessment represent additional limitations.

CONCLUSION

Among preterm infants, hypotension requiring inotropic therapy within the first 72 hours of life is associated with increased risks of severe intraventricular hemorrhage and mortality. Careful clinical assessment and individualized hemodynamic monitoring may help avoid unnecessary treatment in hemodynamically stable hypotensive infants while preserving outcomes comparable to those observed in normotensive neonates.

Ethical Approval: The study protocol received approval from the Clinical Research Ethics Committee of the University of Health Sciences (approval date: 12 December 2024; approval number: 277). All procedures were performed in accordance with the ethical principles of the Declaration of Helsinki.

Conflict of Interest: The authors declared no conflicts of interest.

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