International Journal of Current Research and Review
DOI: https://doi.org/10.31782/IJCRR.2023.151703

Research Article

IJCRR
Section: Healthcare

Evaluation of Blood Pressure in Preterm Newborn and Long-Term Impacts of Hypotension on Neonatal Health

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ABSTRACT

Introduction: Blood pressure values of too low or too high can be related with serious morbidity and mortality. Neonatal hypotension has been found to be related with serious short term as well as significant long term health complications. Thus identifying this low blood pressure in preterm neonates with its long term impacts is crucial.

Objectives: To evaluate blood pressure values in preterm newborn and long-term impacts of hypotension on neonatal health.

Methods: This prospective observational study was conducted in Neonatal Intensive Care Unit (NICU) of Bangabandhu Sheikh Mujib Medical University a tertiary care hospital of Dhaka city after approval from Institutional Review Board for a period of two years. Neonates having gestation<37 completed weeks admitted in NICU of BSMMU were enrolled in the study after getting informed consent from the parents. Proper antenatal and postnatal history was recorded in data collection form. Blood pressure was measured by non-invasive oscillometric method in all neonates within 24 hours after birth by ideal procedure. Blood pressure was monitored at an interval of 12 hours or more frequently when required till discharge or death. Assessment of neurodevelopmental status was performed by an assigned psychologist from Institute of Pediatric Neuro-disorder and Autism at 12 months and 18 months of corrected gestational age using the Bayley Scales of Infant and Toddler Development, Third Edition (BSITD-III).

Results: A total of 114 preterm neonates were studied during the study period, among them 61 (53.5%) had normal blood pressure and 53(46.5%) had hypotension. Among the enrolled patients,15(13.2%) patients died, 3(2.6%) left against medical advice, 11(9.6%) patients were lost to follow up and neurodevelopmental assessment was done of remaining 85 (74.6%) at 12 months and 18months of age (59 in normotensive group and 26 in hypotensive group). Motor impairment, cognitive impairment, language delay, visual impairment, hearing impairment and overall global developmental delay were significantly high among the hypotensive group. Short time outcomes like culture proven sepsis, use of inotropes, need for oxygen support and assisted ventilation, feeding intolerance, Necrotizing enterocolitis, intraventricular hemorrhage, retinopathy of prematurity and duration of hospital stay were significantly higher in hypotensive group. Mortality was also higher in hypotensive group than normotensive group (26.4% vs 3.3%, p <0.001).

Conclusion: Neurodevelopmental impairment at 12 months and18 months was higher among preterm neonates with hypotension. Hypotension in preterm neonates was also associated with significant mortality and morbidity in early post-natal period.

Key Words: Preterm, Hypotension, Neurodevelopmental Outcome, Morbidity, Mortality, Hemodynamic.

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ISSN: 2231-2196 (Print) **ISSN:** 0975-5241 (Online)

Received: 05.08.2023 **Revised:** 19.08.2023 **Accepted:** 29.08.2023 **Published:** 11.09.2023

INTRODUCTION

Blood pressure (BP) measurements is the most commonly used surrogate of end-organ perfusion and have been increasingly used across neonatal intensive care units to determine and monitor hemodynamic status in neonates. [1] It is considered a vital sign, as values too low or too high can be related with serious morbidity and mortality.[2,3] Several maternal and neonatal factors influence neonatal blood pressure. Maternal conditions, including hypertension and preeclampsia have some impact on neonatal BP and maternal drugs, in particular antenatal steroids also have a strong influence. Among the neonatal factors, gestational age, postconceptual age and birth weight have the strongest influence on blood pressure. [4] Hypotension is common in newborn infants. Common conditions leading to systolic hypo-tension include those that lead to low left ventricular preload, poor myocardial contractility or high left ventricular after load. [1] In pathological conditions such asphyxia and sepsis, poor myocardial contractility and pulmonary hypertension, which can further be aggravated by acidosis, cause hypotension and tissue hypo-perfusion. Systemic vasodilation or vasoplegia is often found in sepsis, profound hypoxia and in post operative period. Sick neonates often have impaired auto regulation or a redistribution of organ blood flow that alters the relationship between blood pressure, cardiac output and organ perfusion. [5] The major argument to treat low blood pressure in new born infants is the aim to preserve or restore adequate organ perfusion, with special emphasis on cerebral blood flow. This is based on the observed association between systemic hypotension and neuro-morbidity, such as intracranial hemorrhage, white matter injury, hearing loss and impaired neurologicdevelopment.[6] Thus, hypotension has been identified as important factors in the pathophysiology of cerebral injury.[6] Neonatal hypotension has been found to be related with serious long-term neuro-developmental sequel. On the basis of previous literature, it has been seen that hypotension pose significant short term as well as long term health complications to neonates. Thus identifying this low blood pressure in neonates with its long term impacts is crucial. As per my knowledge, there is paucity of information about relationship between low blood pressure and related morbidities and mortalities of preterm neonates in Bangladesh. So this study aimed to identify low blood pressure related health outcomes in neonates and long-term impact on neurodevelopmental outcome.

METHODOLOGY

Study design: This Prospective Observational study was conducted in the Department of Neonatology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka, Bangladesh over a period of two years from January 2021 to December 2022. All preterm neonates having gestational age < 37 completed weeks admitted in the NICU of BSMMU during the study period were enrolled in first 6 months and follow up was done over rest 18 months of study period. Out born neonates and neonates with major congenital anomalies were excluded from the study.

Study procedure: After enrollment detail antenatal, natal and post-natal history was recorded in data collection form. Blood pressure was measured by non-invasive oscillometric method in all neonates within 24 hours after birth. Blood pressure calf was applied to the right upper extremity. Bladder length covered 75% to 80% of arm circumference and bladder width was measured by measuring mid upper arm circumference. Blood pressure was measured 1.5hours after feeding or a medical intervention preferably during sleep or in a quiet state, lying prone or supine. Neonate was allowed to rest undisturbed after cuff placement for 15minutes and 3 successive BP readings was taken at 2- minute intervals. Final blood pressure was considered as the mean of three readings. Blood pressure was monitored at an interval of 12hours or more frequently when required till discharge or death. The eligible infant who fulfilled the inclusion criteria were divided into two strata: normotensive group and hypotensive group. Those who developed hypotension, the name of drugs with dose administered were recorded. Assessment of neurodevelopmental status was performed by an assigned psychologist from Institute of Pediatric Neuro-disorder and Autism at12 months and 18 months of corrected age using the Bayley Scales of Infant and Toddler Development, Third Edition (BSITD-III).

Primary outcome was neurodevelopmental delay, such as language delay, cognitive impairment, hearing impairment, visual impairment and global developmental delay at 12months and 18 months of corrected. Secondary outcomes were death, development of short-term complications like intra ventricular hemorrhage, retinopathy of prematurity, necrotizing enterocolitis, chronic lung disease, acute kidney injury etc. The study was conducted under good clinical practice of Bangladesh guideline. Reference, Directorate General of Drug Administration, Ministry of Health and Family Welfare, Govt. of the people's Republic of Bangladesh.

Statistical Analysis: After collecting the data, it was entered in a personal computer. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 25.

Continuous variables were presented as mean ± SD for normally distributed data. Categorical variables were presented as frequencies and percentages. The unpaired Student *t* test was-used for quantitative variables with a normal distribution and the chi-square test was performed for qualitative variables. A result was considered statistically significant if values of-$p<0.05$

RESULTS

A total of 114 preterm neonates were studied during the study period, among them 61(53.5%) had normal blood pressure and 53 (46.5%) had hypotension.

Table 1: Baseline Characteristics of enrolled neonates (N=114)

Characteristics	Normotensive group, n=61	Hypotensive group, n=53	P value
Gestational age, mean ± SD (weeks)	31.934 ± 2.24	33.208 ± 2.152	**0.511**
Gestational age category			**0.518**
Moderate to late preterm, n (%)	32(52.5)	31(58.5)	
Very preterm, n (%)	29(47.5)	22(41.5)	
Birth weight, mean ± SD (gram)	1562.034 ± 323.269	1487.528 ± 324.971	**0.123**
Birth weight category			**0.119**
Low birth weight, n (%)	31(50.8)	18(34)	
Very low birth weight, n (%)	28(45.9)	30(56.6)	
Extreme low birth weight, n (%)	2(3.3)	5(9.4)	
Male, n(%)	35(57.4)	25(47.2)	**0.276**
Small for gestational age, n (%)	18(29.5)	21(39.6)	**0.256**
Appropriate for gestational age, n (%)	43(70.5)	32(60.4)	
Multiple births, n (%)	16(31.4)	25(49)	**0.069**
Cesarean delivery, n (%)	54(88.5)	49(92.5)	**0.479**
Maternal hypertension, n (%)	23(37.7)	25(47.2)	**0.307**
Antenatal corticosteroid, n (%)	47(77)	42(79.2)	**0.777**
Resuscitation needed at birth, n (%)	4(6.6)	3(5.7)	**0.578**

The baseline characteristics of the preterm neonates are shown in Table-1. Among the baseline characteristics like gestational age, birth weight, sex, multiple births, mode of delivery, resuscitation at birth and maternal hypertension showed no significant difference in between two groups.

Table 2: Short term outcome of the study population (N=114)

Outcome	Normotensive group, n=61,	Hypotensive group, n=53	p value
Use of oxygen, n (%)	48(78.7%)	49(92.5%)	**0.040**
Use of inotropes, n (%)	1(1.6%)	48(90.6%)	**<0.001**
Use of Assisted ventilation, n (%)	17(27.9%)	33(62.3%)	**<0.001**
Feeding intolerance, n (%)	8(13.1%)	28(52.8%)	**<0.001**
Culture proven sepsis, n (%)	5 (8.2%)	43(81.1%)	**<0.001**
Necrotizing enterocolitis, n (%)	0(0%)	14(26.4%)	**<0.001**
Intraventricular hemorrhage, n (%)	1(1.6%)	7(13.2%)	**<0.001**
Retinopathy of prematurity, n (%)	4(6.6%)	10(18.9%)	**<0.001**
Duration of hospital stay, mean ± SD (days)	7.737 ± 3.439	17.773 ± 9.039	**<0.001**
Death, n (%)	2(3.3%)	14(26.4%)	**<0.001**

Short time outcomes like need for oxygen support, use of inotropes, need for assisted ventilation, feeding intolerance, culture proven sepsis, necrotizing enterocolitis, intraventricular hemorrhage, retinopathy of prematurity and duration of hospital stay were significantly higher in hypotensive group (table-2). Mortality was also higher in hypotensive group than normotensive group (26.4% vs 3.3%, p<0.001). Among total114 patients,15 (13.2%) patients died, 3 (2.6%) left against medical advice, 11 (9.6%) patients were lost to follow up and neurodevelopmental assessment was done of remaining 85 (74.6%) at 12 months and 18 months of age (59 in normotensive group and 26 in hypotensive group) (Table-2).

Table 3: Neurodevelopmental outcomes of the study population at 12 months of age (N=114)

Outcome	Normotensive group, n=59,	Hypotensive group, n=26	p value
Motor impairment, n (%)	3 (5.1%)	9(34.6%)	0.001
Cognitive impairment, n (%)	0(0%)	9(34.6 %)	<0.001
Language delay, n (%)	6(10.2%)	15(57.7%)	<0.001
Visual impairment, n (%)	6(10.2%)	10(38.5%)	0.004
Hearing impairment, n (%)	5(8.5%)	10(38.5%)	0.002
Global developmental delay, n (%)	3(5.1%)	10(38.5%)	<0.001

Table 4: Neurodevelopmental outcomes of the study population at 18months of age (N=114)

Outcome	Normotensive group, n=59,	Hypotensive group, n=26	p value
Motor impairment, n (%)	3 (5.1%)	9(34.6%)	0.001
Cognitive impairment, n (%)	0(0%)	9(34.6 %)	<0.001
Language delay, n (%)	6(10.2%)	15(57.7%)	<0.001
Visual impairment, n (%)	6(10.2%)	10(38.5%)	0.004
Hearing impairment, n (%)	0(0%)	6(23.1%)	<0.001
Global developmental delay, n (%)	3(5.1%)	10(38.5%)	<0.001

Neurodevelopmental outcomes of 85 patients were assessed at 12 months and 18 months of age. Motor impairment, cognitive impairment, language delay, visual impairment, hearing impairment and overall global developmental delay were significantly high among the hypotensive group (Table 3 and 4).

DISCUSSION

Medical conditions, medications prescribed and the mortality rate is significantly higher among preterm and low birth weight neonates admitted in the NICU in resource limited countries. [7] This prospective observational study was conducted to find out the short term and long-term effect of hypotension among preterm neonates. The data suggested that hypotension was significantly associated with short term adverse morbidity and long-term neurodevelopmental impairment among preterm neonates. We also found that the smallest, least mature infants were most likely to have hypotension. Our finding that early postnatal hypotension is associated with developmental delay at follow-up agrees with conclusions from some prior studies [8] and contrasts with the conclusions of several others. [9] Zubrow and coworkers reported almost a decade ago a strong association between birth weight, gestational age, and blood pressure. In recent years there has been increasing focus on the untoward effects of low blood pressure in this population, especially on cerebral blood flow. Munro and coworkers, for example, recently found that cerebral autoregulation was functional in normotensive but not hypotensive ELBW infants. Other factors which increase the risk of hypotension include lack of antenatal steroids, perinatal blood loss, large patent ductus arteriosus and higher-pressure ventilation. Hypotension occurs commonly among ventilated preterm neonates because of iatrogenic fluid restriction, impaired venous return caused by positive intrathoracic pressure (often with inadvertent PEEP), limited myocardial contractility, decreased adrenocortical responses, and comorbidities such as sepsis and pulmonary hemorrhage. Infants with hypotension were more likely to have significant IVH, delayed motor development, impaired cognition and hearing loss. This may be due to the impairment of vascular autoregulation which leaves cerebral blood flow at the mercy of perfusion pressure. Furthermore, the deficits in cerebral blood flow may be profound even in the presence of mild systemic hypotension.[10] Symptomatic hypotension has been clinically tied to IVH in the past, but very few study reported an association with hearing loss. Potential mechanisms for this finding include either ischemic injury to the cochlear nuclei or hemorrhage involving the auditory nerve. Additional studies are needed to fully elucidate the relationship among the multiple factors involved in this injury. Hunt and coworkers reported in one study that low early postnatal blood flow to the upper body and brain may be one factor in the causal pathway of impaired preterm neurodevelopmental outcome. The strengths of our study include the use of prospectively collected data, defined by gestational age and the use of follow-up data collected by examiners who were trained in the standardized administration of the BSID-III. A potential limitation of our study is the lack of a consistent method for obtaining Mean Arterial Pressure. Mean Arterial Pressure measurements were obtained by oscillometry which overestimates blood pressure where standard is to measure by intra-arterial method. Hypotension affects close to half (46.5%) of all preterm infants in our study, yet there is lack of consistency or agreement on its definition. Nomograms have been useful in other areas of neonatology. It is important to establish normative values for blood pressure in preterm infants and to further evaluate the short and long-term effects of hypotension. Moreover, just as the etiology of brain damage in preterm newborns is multifactorial, so are the clinical factors that modify cerebral perfusion. Hypotensive infants are frequently treated with vasopressors, yet only two of the studies reporting an association between hypotension and developmental delay adequately controlled for treatment. In this study, most of the hypotensive infants received some treatment (volume expansion or vasopressor therapy) for hypotension. Use of vasopressors could have adverse effects on infants' neurodevelopmental outcome. Above all, we need to be better informed regarding the optimal timing and modes of intervention. Despite these limitations, our study has implications for researchers interested in preventing developmental delay in preterm infants. Specifically, our findings support the concept that early postnatal hypotension is an important risk factor for such delays.

CONCLUSION

Neurodevelopmental impairment at 12 months and 18 months was higher among preterm neonates with hypoten-

sion. Postnatal hypotension in preterm neonates was also associated with significant mortality and morbidity in early post-natal period.

RECOMMENDATIONS

Further multicenter studies including larger samples should be done for more appropriate findings.

ACKNOWLEDGEMENT

We would like to extend our gratitude to our study participants specially mothers for providing us with all required information. This study was coordinated by the Department of Neonatology, Bangabandhu Sheikh Mujb Medical University, Dhaka, Bangladesh with financial support from "Thesis Grant Committee", Bangabandhu Sheikh Mujib Medical University, Dhaka. We also like to thank the workforce in the health system for providing us with all required information and for providing support to the implementation process

Conflict of interest: NIL

Source of funding

"Thesis Grant Committee", Research and development, Bangabandhu Sheikh Mujib Medical University, Dhaka.

Individual author's contribution

All authors approved the manuscript and agreed with its submission. Mannan MA was the principal investigator, and in collaboration Shahidllah M, scale-up Study Team. Study Group was responsible for the conception, design, development and implementation of the research project. Wahab A in collaboration with Yasmin F prepared the first draft of the manuscript MA, Wahab A, Yasmin F, Hossain MA, Akter S, Moni SC, Jahan I, Chowdhury RM contributed to the implementation, data collection, analysis, learning and interpretation of data. All authors read and commented on the manuscript, and approved the final version.

REFERENCES

1. Gomella. T. 'Neonatology: management, procedures, on-call problems, diseases and drugs', 8th edn, 2013 McGraw-Hill Education, New York, (2013) p- 555-562.
2. Dionne. J., Flynn. J., Management of severe hypertension in the newborn. Archives of Disease in Childhood, 2017.102(12):1176-1179.
3. Matsushita. F., Krebs. V., de Carvalho. W., Neonatal Hypotension: What Is the Efficacy of Each Anti-Hypotensive Intervention? A Systematic Review. Current Treatment Options in Pediatrics, 2019. 5(4): 406-416.
4. Kent. A, Chaudhari. T. Determinants of Neonatal Blood Pressure. Current Hypertension Reports, 2013; 15(5): 426-432.
5. Joynt. C., Cheung. P., Treating Hypotension in Preterm Neonates with Vasoactive Medications. Frontiers in Pediatrics, 2018; 6 (5): 1-5.
6. Boode. W., Clinical monitoring of systemic hemodynamics in critically ill newborns. Early Human Development, 2010; 86(3): 137-141.
7. Bhupalam. P, Nalampati. S, Angiel. CJ, Gowthami. T, Narayana. G, Reddy. KS, et al. Influence of Low Birth Weight and Preterm Birth on Morbidity, Mortality and Medication Use among Neonates in Resource Limited Settings: A Prospective Observational Study. Int J Curr Res Rev. 2021;13.(22):80–5.
8. Alderliesten. T, Lemmers. PM, Van Haastert. IC. Hypotension in preterm neonates: low blood pressure alone does not affect neurodevelopmental outcome. J Pediatr, 2014;164 (5):986–91.
9. Lyu Y, Ye XY, Isayama T, Alvaro R, Nwaesei C, Barrington K, Lee SK, Shah PS; Canadian Neonatal Network Investigators. Admission Systolic Blood Pressure and Outcomes in Preterm Infants of ≤26 Weeks' Gestation. Am J Perinatol. 2017 Nov;34 (13):1271-1278.
10. Logan JW, O'Shea TM, Allred EN, Laughon MM, Bose CL, Dammann O, Batton DG, Engelke SC, Leviton A; ELGAN Study Investigators. Early postnatal hypotension and developmental delay at 24 months of age among extremely low gestational age newborns. Arch Dis Child Fetal Neonatal Ed. 2011 Sep;96(5): F321-8.