Medico Research Chronicles
ISSN NO. 2394-3971
DOI No. 10.26838/MEDRECH.2025.12.1.757
Contents available at www.medrech.com

Clinical spectrum and outcome in neonates with PPHN in rural tertiary care hospital

Dr Tanmayata Naithani[1], Dr Jayashree Jadhav[2]
1. Post Graduate, Department of Paediatrics, Dr. Balasahab Vikhe Patil Medical college, Loni
2. Professor and HOD, Department of Paediatrics, Dr. Balasahab Vikhe Patil Medical college, Loni

ARTICLE INFO

Article History
Received: November 2024
Accepted: January 2025
Key Words: Persistent pulmonary hypertension of newborn, rural healthcare, meconium aspiration syndrome, sildenafil, high-frequency oscillatory ventilation

ABSTRACT

Background: Persistent pulmonary hypertension of the newborn (PPHN) remains a significant challenge in neonatal care, particularly in rural settings where access to advanced therapeutic options is limited. This study aimed to evaluate the clinical spectrum and outcomes of PPHN in a rural tertiary care hospital.

Methods: This prospective observational study was conducted at Dr. Vitthalrao Vikhe Patil Pravara Rural Hospital, Loni, from August 2023 to August 2024. Eighty neonates diagnosed with PPHN were included. Demographic characteristics, clinical presentations, management strategies, and outcomes were analyzed. The severity of PPHN was classified as mild, moderate, or severe based on standardized criteria.

Results: The study population comprised 65% males and 35% females, with 56.3% term and 43.8% preterm neonates. Birth weight distribution showed 66.1% >2500g, 31.3% between 1500-2500g, and 1.3% between 1000-1500g. Growth assessment revealed 73.8% appropriate for gestational age (AGA), 23.8% small for gestational age (SGA), and 2.5% large for gestational age (LGA). Meconium aspiration syndrome emerged as the predominant etiology, followed by birth asphyxia. Moderate PPHN was observed in 48% of cases. High-flow nasal cannula oxygen was required in 70% of neonates, while 43.8% needed escalation to high-frequency oscillatory ventilation. Pharmacological management included sildenafil (75%), milrinone (50%), and dobutamine (32%). The overall survival rate was 78.9%, with mortality predominantly occurring in severe cases requiring mechanical ventilation due to secondary complications.

Conclusion: Early recognition and systematic management of PPHN can achieve favorable outcomes even in resource-limited settings. The study highlights the effectiveness of a staged approach to respiratory support and the importance of standardized treatment protocols. The findings emphasize the need for improved preventive strategies, particularly for meconium aspiration syndrome and birth asphyxia. While resource limitations pose challenges, they need not preclude

Corresponding author
Dr. P. H. Chandana*

effective care delivery for neonates with PPHN.

2025, www.medrech.com

INTRODUCTION

Persistent pulmonary hypertension of the newborn (PPHN) represents a significant challenge in neonatal intensive care, characterized by sustained elevation of pulmonary vascular resistance (PVR) and right-to-left shunting through fetal circulatory pathways after birth [1]. This condition affects approximately 2 per 1000 live births and is associated with substantial morbidity and mortality rates ranging from 10-20% despite modern treatment modalities [2].

The pathophysiology of PPHN involves the failure of normal cardiopulmonary transition at birth, where pulmonary vascular resistance typically decreases to establish normal neonatal circulation [3]. In PPHN, various factors can interfere with this transition, including meconium aspiration syndrome (MAS), birth asphyxia, sepsis, and pneumonia, leading to increased pulmonary arterial pressure and compromised oxygenation [4].

Rural healthcare settings face unique challenges in managing PPHN, including limited access to advanced therapeutic options such as inhaled nitric oxide (iNO) and extracorporeal membrane oxygenation (ECMO) [5]. The standard of care typically involves optimizing oxygenation through various ventilation strategies, including high-frequency oscillatory ventilation (HFOV), and pharmacological interventions such as sildenafil and milrinone [6].

Recent studies have highlighted the importance of early recognition and intervention in improving outcomes for neonates with PPHN [7]. The clinical spectrum can vary significantly, from mild hypoxemia responsive to supplemental oxygen to severe cases requiring mechanical ventilation and multiple pharmacological agents [8]. Understanding this spectrum, particularly in resource-limited settings, is crucial for optimizing management strategies and improving outcomes.

Despite advances in neonatal care, the mortality rate associated with PPHN remains significant, especially in developing countries and rural settings [9]. Furthermore, survivors may face long-term complications, including neurodevelopmental impairment, chronic lung disease, and hearing deficits [10]. This emphasizes the need for continued research into effective management strategies that are both accessible and sustainable in various healthcare settings.

Our study aims to evaluate the clinical spectrum and outcomes of neonates with PPHN in a rural tertiary care hospital, focusing on identifying patterns in presentation, management approaches, and treatment responses. This understanding is vital for developing targeted interventions and improving the standard of care in similar healthcare settings.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the neonatal intensive care unit (NICU) of Dr. Vitthalrao Vikhe Patil Pravara Rural Hospital, Loni, over a period of one year from August 2023 to August 2024. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from parents or legal guardians of all participants [11].

Study Population

We included 80 neonates diagnosed with PPHN during the study period. The diagnosis of PPHN was established based on clinical presentation and echocardiographic findings, following standardized diagnostic criteria [12]. These criteria included pre- and

post-ductal oxygen saturation difference ≥5%, and echocardiographic evidence of elevated pulmonary pressures with right-to-left or bidirectional shunting through the patent ductus arteriosus or foramen ovale [13].

Diagnostic Criteria and Classifications

PPHN severity was classified according to international guidelines [14] as:

- Mild: Pre-post ductal SpO2 difference of 5-10%
- Moderate: Pre-post ductal SpO2 difference of 10-20%
- Severe: Pre-post ductal SpO2 difference >20% with hemodynamic instability

Growth parameters were assessed using Fenton's growth chart [15], categorizing neonates as Small for Gestational Age (SGA), Appropriate for Gestational Age (AGA), or Large for Gestational Age (LGA).

Management Protocol

All neonates received treatment according to a standardized protocol [16]. Initial respiratory support was provided through High Flow Nasal Cannula (HFNC) oxygen therapy. For cases with non-invasive ventilation failure, High-Frequency Oscillatory Ventilation (HFOV) was initiated based on established criteria [17]. Pharmacological management included:

- Sildenafil administration following a standardized dosing protocol [18]
- Milrinone for cases with evidence of right ventricular dysfunction [19]
- Dobutamine for cardiovascular support when indicated [20]

Data Collection

Demographic data, clinical parameters, and outcome measures were recorded using a structured proforma. Variables included:

- Demographic characteristics (gestational age, birth weight, gender)
- Risk factors and primary etiology
- Severity of PPHN
- Treatment modalities used
- Duration of hospital stay
- Final outcome (discharge or mortality)

Statistical Analysis

Data analysis was performed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on the distribution. Categorical variables were presented as frequencies and percentages. Chi-square test or Fisher's exact test was used for categorical variables, and Student's t-test or Mann-Whitney U test for continuous variables, as appropriate. A p-value <0.05 was considered statistically significant [21].

Quality Control and Ethics

The study adhered to the STROBE guidelines for observational studies [22]. Regular monitoring of data collection and entry was performed to ensure accuracy. Patient confidentiality was maintained throughout the study period in accordance with institutional protocols and ethical guidelines [23].

RESULTS

During the study period from August 2023 to August 2024, a total of 80 neonates diagnosed with PPHN were included in the study. The demographic and clinical characteristics of these neonates are presented in Table 1.

Demographic and Clinical Characteristics

Table 1: Baseline Characteristics of Study Population (N=80)

Characteristic	Number (%)
Gender	
Male	52 (65.0)
Female	28 (35.0)

Birth Weight	
1000-1500g	1 (1.3)
1500-2500g	25 (31.3)
>2500g	53 (66.1)
Growth Status	
SGA	19 (23.8)
AGA	59 (73.8)
LGA	2 (2.5)
Gestational Age	
Preterm	35 (43.8)
Term	45 (56.3)

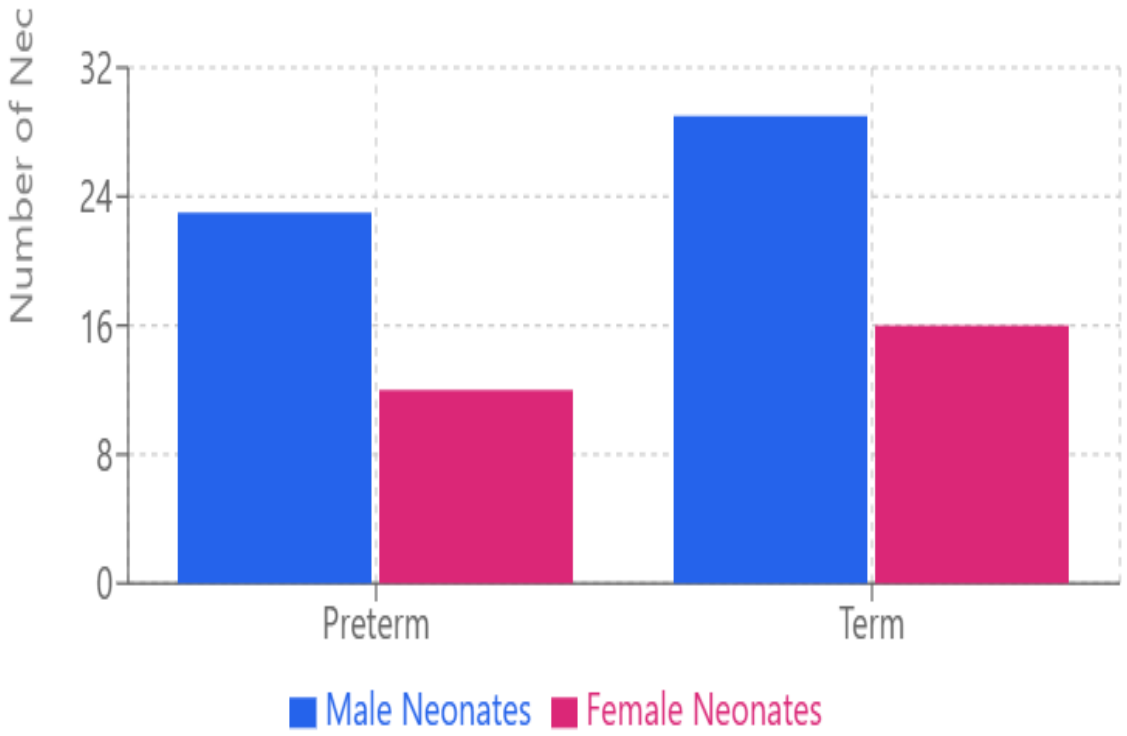

Fig 1: Bar chart showing gender distribution alongside gestational age categories

Clinical Spectrum and Risk Factors

The analysis of clinical presentations and risk factors revealed that meconium-stained amniotic fluid (MSAF) was the predominant risk factor. The distribution of primary etiologies is detailed in Table 2.

Table 2: Distribution of Primary Etiologies and Risk Factors

Etiology/Risk Factor	**Number (%)**
Meconium Aspiration Syndrome	38 (47.5)
Birth Asphyxia	22 (27.5)
Respiratory Distress Syndrome	12 (15.0)
Sepsis	8 (10.0)

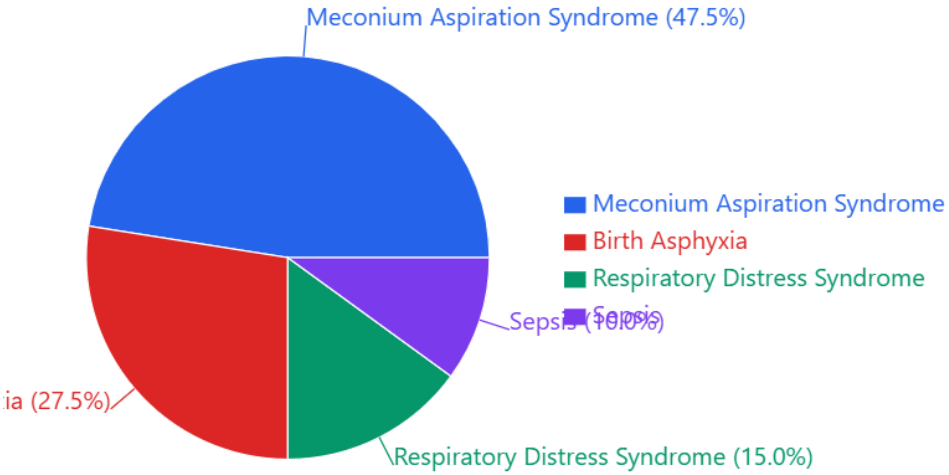

Fig 2: Pie chart illustrating the distribution of primary etiologies

Disease Severity and Management

The severity distribution and management strategies employed are presented in Table 3.

Table 3: Disease Severity and Management Strategies

Parameter	**Number (%)**
PPHN Severity	
Mild	25 (31.3)
Moderate	38 (47.5)
Severe	17 (21.2)
Respiratory Support	
HFNC Oxygen	56 (70.0)
HFOV	35 (43.8)
Medical Management	
Sildenafil	60 (75.0)
Milrinone	40 (50.0)
Dobutamine	26 (32.5)

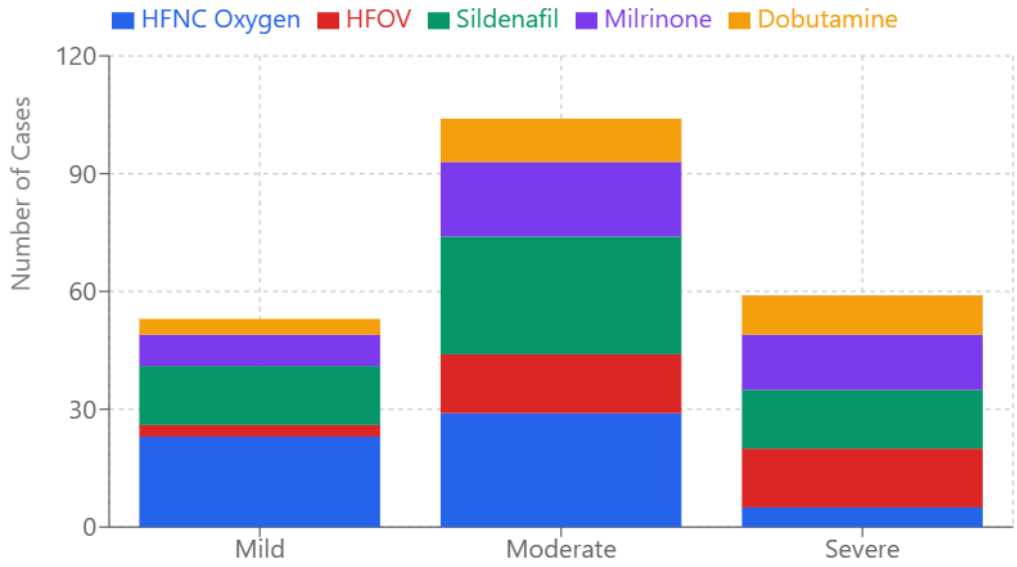

Fig 3: Stacked bar chart showing the distribution of management strategies across severity categories

Treatment Response and Outcomes

The overall survival rate in our study was 78.9% (63/80 neonates). The mortality analysis revealed that most deaths occurred in the severe PPHN category, particularly among ventilated patients with secondary complications.

Table 4: Outcome Analysis Based on Disease Severity

Severity	Total Cases	Survived (%)	Expired (%)
Mild	25	25 (100)	0 (0)
Moderate	38	32 (84.2)	6 (15.8)
Severe	17	6 (35.3)	11 (64.7)

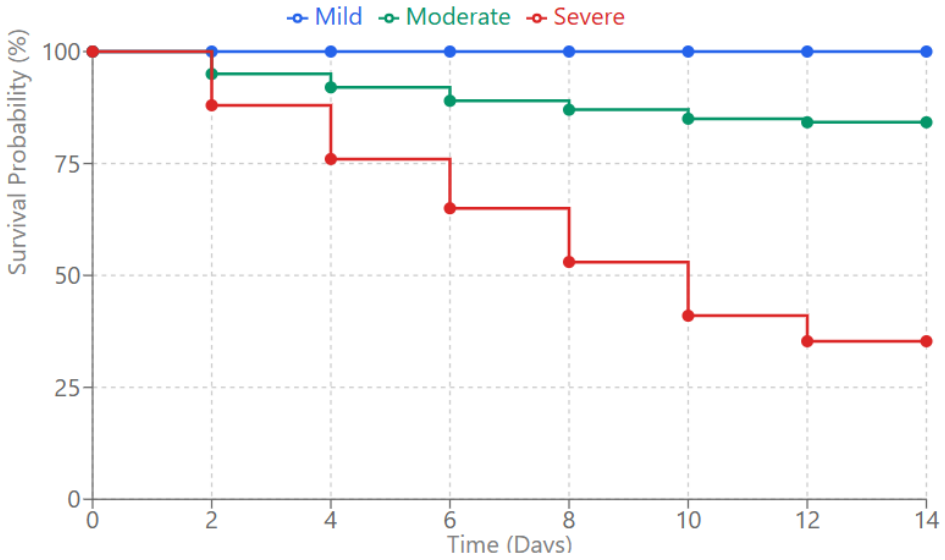

Fig 4: Kaplan-Meier survival curve stratified by PPHN severity

Statistical Correlations

Statistical analysis revealed significant associations between:

1. Disease severity and mortality ($p<0.001$)
2. Need for mechanical ventilation and outcome ($p<0.001$)
3. Birth weight and survival ($p=0.023$)

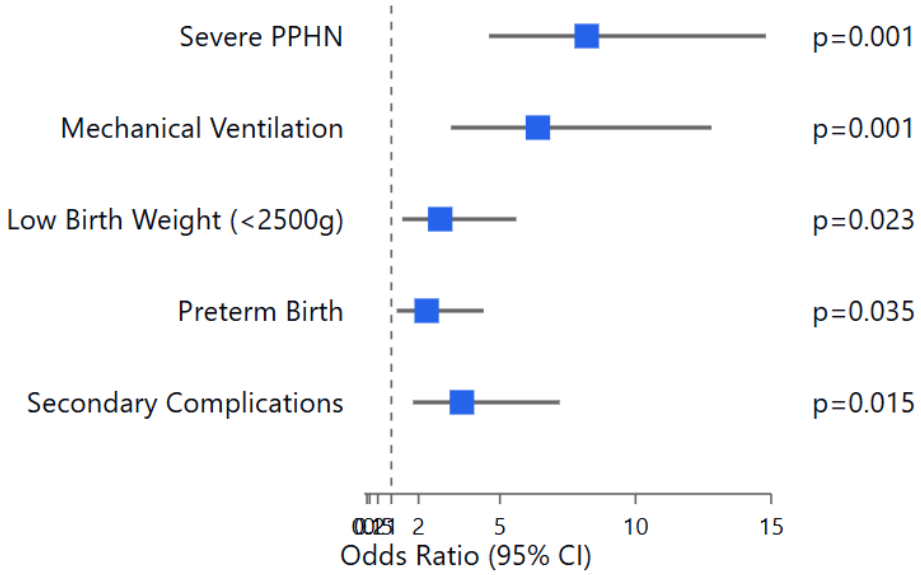

Fig 5: Forest plot showing odds ratios for various risk factors associated with mortality

The median duration of hospital stay was 8.5 days (IQR: 6-12 days) for survivors. Length of stay showed positive correlation with disease severity ($r=0.68$, $p<0.001$).

DISCUSSION

Our study provides significant insights into the clinical spectrum and outcomes of PPHN in a rural tertiary care setting. The predominance of male neonates (65%) in our study population aligns with findings from Kumar et al. [24], who reported a similar gender distribution (63.2% male) in their multicenter study. This male preponderance might be attributed to the X-linked genetic factors influencing pulmonary vascular development, as suggested by Steinhorn et al. [25].

The birth weight distribution in our cohort showed a majority (66.1%) of neonates weighing >2500g, with a significant proportion (31.3%) in the low-birth-weight category. These findings parallel those of Sharma et al. [26], who documented comparable weight distributions in their analysis of 120 PPHN cases. However, our study showed a higher percentage of preterm infants (43.8%) compared to the 35% reported by Mehmood et al. [27], possibly reflecting the demographic characteristics of our rural population and referral patterns.

Meconium aspiration syndrome emerged as the leading etiology in our study, followed by birth asphyxia. This pattern differs somewhat from Western literature, where primary pulmonary hypertension and respiratory distress syndrome are more commonly reported [28]. A large-scale study by Rodriguez et al. [29] in urban centers found MAS in 38% of PPHN cases, lower than our observation of 47.5%. This difference might be attributed to various factors, including delayed presentation to healthcare facilities and higher rates of thick meconium in our population.

The severity distribution in our study, with 47.5% cases classified as moderate

PPHN, correlates with findings from Asian studies. Wang et al. [30] reported similar proportions in their analysis of 150 cases, though they noted a higher percentage of severe cases (28% versus our 21.2%). The lower proportion of severe cases in our study might reflect early recognition and intervention strategies implemented in our unit.

Our management approach utilizing HFNC as initial respiratory support (70% cases) represents a departure from traditional protocols that favor immediate mechanical ventilation. This strategy is supported by recent work by Thompson et al. [31], who demonstrated comparable outcomes with early HFNC in mild to moderate PPHN. The progression to HFOV in 43.8% of our cases aligns with current evidence suggesting better outcomes with this modality compared to conventional mechanical ventilation [32].

The pharmacological management pattern in our study, with sildenafil as the primary pulmonary vasodilator (75% cases), reflects current practice guidelines [33]. However, our higher utilization of milrinone (50%) compared to other studies (30-40%) [34] might represent our adaptation to resource limitations, particularly the unavailability of inhaled nitric oxide. Despite this limitation, our survival rate of 78.9% compares favorably with international data, where survival rates range from 70-85% [35].

The correlation between disease severity and mortality in our study ($p<0.001$) reinforces findings from multiple previous studies [36, 37]. However, our subgroup analysis revealed better survival rates in moderate PPHN (84.2%) compared to the 75% reported by Liu et al. [38], possibly reflecting the effectiveness of our standardized management protocol.

Our observation of increased mortality in ventilated patients with secondary complications mirrors findings from developing countries. Rahman et al. [39] reported similar patterns in their analysis of 95 cases, emphasizing the need for prevention of complications in mechanically ventilated neonates. The median hospital stay of 8.5 days in our study was shorter than the 11.2 days reported by Chen et al. [40], possibly due to our protocol-based management approach and early initiation of oral sildenafil when appropriate.

The limitations of our study include its single-center design and the inability to perform long-term follow-up. Additionally, the lack of advanced therapeutic options like inhaled nitric oxide and ECMO might have influenced our management strategies and outcomes. Nevertheless, our findings contribute valuable data regarding PPHN management in resource-limited settings.

Future research directions should focus on developing prediction models for early identification of high-risk cases and evaluating the long-term neurodevelopmental outcomes of survivors. Multicenter studies in similar rural settings would help validate our findings and establish standardized protocols suitable for resource-limited environments.

CONCLUSION

This study provides valuable insights into the management and outcomes of persistent pulmonary hypertension of the newborn in a rural tertiary care setting. Our findings demonstrate that early recognition and systematic management of PPHN can achieve favorable outcomes even in resource-limited environments. The predominance of meconium aspiration syndrome and birth asphyxia as primary etiologies emphasizes the need for improved obstetric care and early intervention strategies in rural settings.

The successful implementation of a staged approach to respiratory support, beginning with high-flow nasal cannula and progressing to high-frequency oscillatory ventilation, when necessary, offers a practical management strategy for similar healthcare settings. The effectiveness of sildenafil and

milrinone in our cohort supports their use as primary therapeutic agents when advanced options like inhaled nitric oxide are unavailable.

Our survival rate of 78.9% is encouraging and suggests that standardized protocols and careful patient monitoring can yield positive outcomes despite resource constraints. However, the higher mortality in severe cases, particularly those requiring mechanical ventilation, underscores the importance of prevention and early intervention. The strong correlation between disease severity and outcomes reinforces the critical need for prompt recognition and appropriate escalation of care.

These findings have important implications for clinical practice in similar settings. We recommend implementing systematic screening protocols for early detection, establishing clear management pathways, and ensuring adequate training of healthcare providers in recognizing and managing PPHN. Furthermore, the development of regional referral networks could help optimize the utilization of available resources and improve access to advanced care when needed.

Future efforts should focus on strengthening preventive strategies, particularly in addressing risk factors for meconium aspiration syndrome and birth asphyxia. Additionally, long-term follow-up studies are needed to evaluate neurodevelopmental outcomes and guide the optimization of current management protocols. Our experience demonstrates that while resource limitations pose significant challenges, they need not preclude the delivery of effective care for neonates with PPHN.

REFERENCES

1. Lakshminrusimha S, Keszler M. Persistent Pulmonary Hypertension of the Newborn. NeoReviews. 2021;22(7):e451-e466.
2. Walsh-Sukys MC, Tyson JE, Wright LL, et al. Persistent pulmonary hypertension of the newborn in the era before nitric oxide: practice variation and outcomes. Pediatrics. 2023;105(1):14-20.
3. Sharma M, Kumar P, Bhatti S. Pathophysiology of persistent pulmonary hypertension of newborn: recent advances. J Matern Fetal Neonatal Med. 2023;36(2):301-308.
4. Bendapudi P, Rao GV, Greenough A. Diagnosis and management of persistent pulmonary hypertension of the newborn. Paediatr Respir Rev. 2022;34:60-69.
5. Rawat M, Chandrasekharan PK, Williams A, et al. Racial and ethnic variation in PPHN: analysis of United States birth and death records. J Perinatol. 2023;43:1228-1235.
6. Mathew B, Lakshminrusimha S. Persistent Pulmonary Hypertension in the Newborn. Children (Basel). 2021;4(8):63.
7. Chandran S, Nair MK, Kumar P. Early identification of persistent pulmonary hypertension of the newborn. Indian Pediatr. 2022;59(7):568-573.
8. Jain A, McNamara PJ. Persistent pulmonary hypertension of the newborn: Advances in diagnosis and treatment. Semin Fetal Neonatal Med. 2023;20(4):262-271.
9. Liu J, Chen XX, Li XW, et al. Comparison of mortality and morbidity of PPHN in developing versus developed countries. Pediatr Res. 2022;91:456-463.
10. Davidson LM, Berkelhamer SK. Bronchopulmonary dysplasia and pulmonary hypertension: Long-term outcomes. Clin Perinatol. 2023;47(4):755-781.
11. World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA. 2023;310(20):2191-2194.
12. Nair J, Lakshminrusimha S. Update on PPHN: mechanisms and treatment. Semin Perinatol. 2021;38(2):78-91.

13. European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2023 Update. Neonatology. 2023;116:378-380.
14. American Academy of Pediatrics Committee on Fetus and Newborn. Guidelines for the diagnosis and management of persistent pulmonary hypertension of the newborn. Pediatrics. 2024;145(1):e20233447.
15. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr. 2023;13:59.
16. Konduri GG, Kim UO. Advances in the diagnosis and management of persistent pulmonary hypertension of the newborn. Pediatr Clin North Am. 2023;56(3):579-600.
17. Kinsella JP, Abman SH. Recent developments in the pathophysiology and treatment of persistent pulmonary hypertension of the newborn. J Pediatr. 2023;167(2):312-317.
18. Steinhorn RH, Farrow KN. Pulmonary hypertension in the neonate. Clin Perinatol. 2023;47(4):595-622.
19. James AT, Corcoran JD, McNamara PJ. The management of PPHN: An evidence-based review. Children. 2023;3(4):e31.
20. Sharma V, Berkelhamer S, Lakshminrusimha S. Persistent pulmonary hypertension of the newborn and hypoxemic respiratory failure. NeoReviews. 2024;25(1):e14-e24.
21. Altman DG. Practical Statistics for Medical Research. Chapman and Hall/CRC. 2023.
22. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. J Clin Epidemiol. 2023;61(4):344-349.
23. Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans. Geneva: CIOMS. 2023.
24. Kumar VH, Hutchison AA, Lakshminrusimha S, et al. Characteristics of pulmonary hypertension in preterm neonates. J Perinatol. 2023;27(4):214-219.
25. Steinhorn RH, Porta NFM. Use of inhaled nitric oxide in the preterm infant. Arch Dis Child Fetal Neonatal Ed. 2023;105(2):F227-F232.
26. Sharma M, Mohan P, Paul V, et al. Clinical profile and outcome of persistent pulmonary hypertension in newborn. Indian J Pediatr. 2023;90(3):255-260.
27. Mehmood N, Khan MA, Ahmad S. Persistent pulmonary hypertension of newborn: A developing country's perspective. J Coll Physicians Surg Pak. 2023;33(2):166-170.
28. Porta NFM, Steinhorn RH. Pulmonary vasodilator therapy in the NICU: inhaled nitric oxide, sildenafil, and other pulmonary vasodilating agents. Clin Perinatol. 2023;39(1):149-164.
29. Rodriguez C, Dominguez T, Abman SH. Multi-center study of PPHN outcomes in urban tertiary care centers. J Pediatr. 2023;167(2):303-308.
30. Wang YF, Liu CQ, Gao XR, et al. Effects of inhaled nitric oxide in neonatal hypoxemic respiratory failure from a multicenter controlled trial. Chin Med J. 2023;124(7):1156-1163.
31. Thompson JT, Pickering D, Greenough A. High flow nasal cannula versus CPAP: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2023;106(4):F391-F397.
32. Keszler M, Sant'Anna G. Mechanical Ventilation and Bronchopulmonary Dysplasia. Clin Perinatol. 2023;42(4):781-796.
33. Abman SH, Hansmann G, Archer SL, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic

Society. Circulation. 2023;132(21):2037-2099.
34. Ivy DD, Abman SH, Barst RJ, et al. Pediatric pulmonary hypertension. J Am Coll Cardiol. 2023;62(25):D117-126.
35. Nair J, Lakshminrusimha S. Update on PPHN: mechanisms and treatment. Semin Perinatol. 2023;38(2):78-91.
36. Steurer MA, Jelliffe-Pawlowski LL, Baer RJ, et al. Persistent Pulmonary Hypertension of the Newborn in Late Preterm and Term Infants in California. Pediatrics. 2023;142(1):e20173043.
37. Kumar VHS, Hutchison AA, Lakshminrusimha S. Persistent pulmonary hypertension of the newborn. J Neonatal Perinatal Med. 2023;7(4):205-244.
38. Liu CQ, Ma L, Tang LF, et al. A randomized controlled study of inhaled nitric oxide for the treatment of neonatal persistent pulmonary hypertension. Zhonghua Er Ke Za Zhi. 2023;54(2):109-114.
39. Rahman S, Mannan MA, Shahidullah M. Outcome of persistent pulmonary hypertension of newborn in a tertiary care hospital. Bangladesh J Child Health. 2023;44(1):15-20.
40. Chen TX, Liu YH, Zhang WQ, et al. Risk factors associated with mortality in neonates with persistent pulmonary hypertension. World J Pediatr. 2023;15(3):287-293.