International Journal of Contemporary Pediatrics
Pai DO et al. Int J Contemp Pediatr. 2026 Nov;13(11):2259-2266
https://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20263813

Original Research Article

Clinical spectrum and outcome determinants in persistent pulmonary hypertension of the newborn in a tertiary care centre: a cross-sectional study

Deepti Omkar Pai[1]*, Paramanand Andankar[2], Lavanya Peruri[2], Shakuntala Prabhu[1], Srinivas Lakshmivenkateshiah[3]

[1]Department of Pediatrics, Bai Jerbai Wadia Hospital for Children, Mumbai, Maharashtra, India
[2]Department of Pediatrics, Jupiter Hospital, Thane, Maharashtra, India
[3]Department of Cardiology, KIMS Hospital, Thane, India

Received: 07 September 2026
Accepted: 06 October 2026

***Correspondence:**
Dr. Deepti Omkar Pai,
E-mail: malhotradeepti9@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Persistent pulmonary hypertension of the newborn (PPHN) is a serious neonatal condition characterized by elevated pulmonary vascular resistance after birth, resulting in hypoxemia. It may be associated with perinatal risk factors such as birth asphyxia, meconium aspiration syndrome, respiratory distress syndrome, and sepsis. Early diagnosis and appropriate management are essential to improve neonatal outcomes. This study aims to assess the risk factors, clinical profile, treatment modalities, and outcomes in newborns with PPHN.
Methods: This cross-sectional study was conducted in the Level 3 neonatal unit in Western India, data of the neonates diagnosed to have PPHN on echocardiography admitted during the period from October 2019 till July 2021 were recorded. The normality of the continuous data was tested by Shapiro-Wilk test. The continuous variables were analysed by Mann-Whitney U test and Kruskal-Wallis test. Post-hoc Dunn's test is used to do pairwise comparisons. Categorical data is analysed using Fisher's Exact test. $P<0.05$ are accepted as indicative of statistical significance.
Results: Total 36 neonates were included in the study with incidence of 8.2 per 1000 live births with mortality of 27.8% with better survival in inborn neonates. Resuscitation at birth in neonates correlated with the severity of PPHN. ABG parameters showing metabolic and respiratory acidosis, hypoxemia and poor oxygenation indices were associated with mortality. On Echocardiography, parameters like right to left shunt across PDA/PFO, right ventricular dysfunction and septal position deviated to left were associated with mortality. Requirement of surfactant, multiple inotropes, HFOV and iNO were independently associated with mortality.
Conclusions: PPHN is a disease with significant mortality and long-term morbidity which can be prevented with timely intervention, targeted Echocardiography, monitoring of parameters and requires multiple modalities of treatment.

Keywords: Persistent pulmonary hypertension in neonates, Echocardiography, Right ventricular systolic pressure, High frequency oscillatory ventilation, inhaled nitric oxide

INTRODUCTION

Persistent pulmonary hypertension of the newborn (PPHN) results when there is circulatory dysadaptation leading to hypoxemic respiratory failure.[1] PPHN is a syndrome characterized by sustained elevation of pulmonary vascular resistance and is associated with normal or low systemic vascular resistance. This leads to right-to-left shunting of blood through foramen ovale (PFO) and ductus arteriosus (PDA) and prevents the

increase in pulmonary blood flow (PBF), essential for extrauterine oxygenation and survival.[2] The incidence of PPHN as reported from 6 Asian countries ranges from 1.2-4.6 and worldwide as high as 5.4 per 1000 live births, being highest in term and late preterm infants.[1,3] However the prevalence obtained from 43 studies across different countries, showed higher prevalence particularly in Asia ranging from 0.12- 8.1%.[3] Despite advances in perinatal and neonatal cardiorespiratory care, PPHN is still one of the main causes of neonatal morbidity and mortality, with a worldwide mortality rate of 3–57.9% with highest rate in Asian countries.[3,4] Pathophysiology of PPHN is attributed to maladaptation, maldevelopment and underdevelopment of normal pulmonary vasculature.[1] There are various maternal and neonatal risk factors associated with PPHN like cesarean birth, large for gestational age babies, late preterm or post term birth, sepsis and meconium stained liquor and maternal medications like non-steroidal anti- inflammatory drugs.[4,5] Conventional as well as advanced neonatal care can help in treating PPHN although some modalities not being easily available in developing countries contributes to higher morbidity and mortality.[6] Improved outcome is attributed to gentle ventilation strategies and lung recruitment, inhaled nitric oxide(iNO) and surfactant therapy. Refractory cases of PPHN can have requirement for extracorporeal membrane oxygenation (ECMO).[7-9] iNO is well proven for treating PPHN, however 30-40% are non-responsive to iNO.[9,10] As there is a scarcity of data about PPHN from developing countries, better understanding of pathophysiology may enlighten targeted and more effective therapies. For insight, we have conducted a cross-sectional study to review the profile of PPHN in a tertiary neonatal unit in Western India.

The objectives of the study is clinical and demographic profile of neonates diagnosed with PPHN on 2D Echocardiography/CD; Identifying the risk factors, response to treatment modalities and the factors affecting severity; Correlating the outcome with clinical and echocardiographic findings.

METHODS

Study design and study population

This is a Cross-sectional study conducted in a Level 3 Neonatal Intensive Care Unit in Western India. All neonates above 35 complete weeks of gestation admitted in NICU or referred from outside hospital within the first 48 hours diagnosed with PPHN on 2D Echocardiography/CD (2D-echo) after taking informed consent were included in the study. There were 36 PPHN cases admitted during the study period out of which 24 were referred from outside hospital. With universal sampling size and 95% confidence interval minimum sample size required was 32 (calculated by using EPI Software). Neonates with congenital diaphragmatic hernia, structural heart disease and upper airway obstruction like choanal atresia were excluded.

Data collection

PPHN was categorised as mild, moderate and severe based on either of the 2D-echo parameters -1) Direction of shunt across PDA/PFO (if present)- mild- left to right, moderate- bidirectional and severe- right to left, 2) Right ventricular systolic pressure (RVSP) (measured by TR jet velocity)- mild- 40-50, moderate- 50-70 and severe- >70, 3) interventricular septal position- mild- bulging to right, moderate- flat and severe- bulging to left.[3,11] Data pertaining to patient's and maternal details (gestational age, mode of delivery, preexisting illness/illness during pregnancy, drug intake, etc.), investigations (arterial blood gas, CXR), clinical condition and treatment details (APGAR score, type of ventilation, duration of ventilation, types of drugs), duration of NICU stay and Outcome (discharged/expired) were recorded.

ABG analysis done on a blood gas analyser machine. ABG was done at admission in NICU and parameters like PH, PO2, PCO2, P/F ratio (PaO2/FiO2), Oxygenation Index (OI) ([MAP X FiO2]/PaO2 X 100) and lactates were recorded. Serial ABGs done within 24 hours of admission, between 48-72 hours, 72 hours –7 days and beyond 14 days of life were recorded. APGAR and modified Downe's score were calculated for the inborn neonates after delivery. Various treatment modalities were offered to the neonates depending on the severity. Neonates having respiratory distress were given oxygen support or ventilatory support (noninvasive/invasive) including HFOV if not responding to conventional ventilation. They were also offered various pulmonary vasodilators like sildenafil and iNO, initiated if OI>15 and 25 respectively and bosentan in non-responders to dual therapy.

Neonates with hypotension were also initiated on inotropic support- dobutamine, adrenaline, noradrenaline, vasopressin and milrinone determined by cardiac contractility. Vasoinotropic score was calculated, VIS=Dobutamine dose + (10X milrinone dose-mcg/kg/min) + (100X adrenaline/noradrenaline dose-mcg/kg/min) + (10000X vasopressin dose-U/kg/min). Few neonates were given steroids in view of raised inflammatory markers. Outcome was noted by the improvement/deterioration seen on ABG indices, duration of ventilator days, oxygen support and ICU stay and was compared between the survivors and non survivors.

Statistical analysis

Statistical software used are IBM SPSS Version 2025 and Microsoft Office Excel 2013.

Statistical tests

Continuous data has been expressed as median (Interquartile range). The categorical data is summarised as frequencies and percentages. The normality of the

continuous data was tested by Shapiro-Wilk test. The continuous variables have been analysed by Mann-Whitney U test and Kruskal-Wallis test. Post-hoc Dunn's test is used to do pairwise comparisons. Categorical data is analysed using Fisher's Exact test. P<0.05 are accepted as indicative of statistical significance.

RESULTS

During the study period, total 47 neonates were diagnosed with PPHN out of which 36 were included and 11 were excluded from the study- 8 had congenital anomalies like structural heart disease, congenital diaphragmatic hernia and 4 were discharged against medical advice. 12 (33.3%) were born in the study centre while the majority were referred from outside hospital (66.7%). Over the period, the incidence of PPHN among inborn babies were 8.2 per 1000 live births and total incidence in NICU-42 per 1000 admissions.

Demographic details, risk factors, clinical profile and investigations were recorded as shown in Table 1. 63.9% were term neonates and 38.9% were late preterms among which 27.8% were small for gestational age. There was no sex predilection noted (M: F-1:1.4). 55.8% mothers did not have any comorbidities, however the remaining had hypothyroidism/PIH. Also, the majority had normal amniotic fluid index (72.2%) and normal anomaly scans. Intranatally, around 50% neonates had signs of fetal distress; out of which 47% cases had meconium-stained liquor, 27.8% cases had abnormal NST and Doppler, 23.5% cases had meconium-stained liquor with abnormal NST and 1.7% had cord prolapse. 80.6% of the neonates were delivered by c-section and remaining by normal vaginal delivery and there was history of premature rupture of membranes in 16.7% neonates.

Table 1: Demographic profile, risk factors, clinical profile and treatment modalities offered to neonates with persistent pulmonary hypertension.

Characteristics	Number	Frequency
Late preterm	13	36.1
Term	23	63.9
Male	15	41.7
Female	21	58.3
Low birth weight	14	38.9
SGA	10	27.8
Antenatal and perinatal risk factors		
Maternal comorbidities	16	44.5
Abnormal anomaly scan	1	2.8
Antenatal steroids	4	11.1
Oligo /polyhydramnios	10	17.8
PROM	6	16.7
Fetal distress	18	50.0
C- section	29	80.6
Not cried at birth	13	36.1
Clinical profile		
Tachypnoea/ respiratory distress	27	75.0
No/ reduced efforts	9	25.0
Modified Downe's score >7 (n=8)	1	12.5
Sepsis	6	16.7
Co-existing conditions	8	22.2
Modified Downe score (n = 8) ≤6	7	87.5
Apgar score <5 at 1 min (n=13)	10	76.9
Apgar score <5 at 5 mins (n=8)	3	37.5
Investigations (n=35)		
Metabolic/respiratory acidosis	20	55.6
Alkalosis	3	8.3
Hypoxemia	14	40.0
Hypercarbia	5	14.3
Abnormal P/F (n=33)	8	24.2
Abnormal OI (n=19)	14	73.7
Raised lactate	31	88.6
Abnormal chest X-ray (n=36)	13	36.1

SGA- Small for Gestational Age, PROM- Premature Rupture of Membranes, OI- Oxygenation Index

In the postnatal period, 36.1% neonates did not cry immediately after birth and required resuscitation and 75% neonates were observed to have tachypnea and respiratory distress while rest had poor respiratory efforts. Modified Downe's score and Apgar scores (>5 mins) were available only for inborn neonates who did not get intubated at birth (n=8) and hence correlation of the scores with outcomes/ severity could not be compared. During the course, 16.7% neonates developed sepsis and 22.2% neonates had other co-morbidities like hypoxic ischemic encephalopathy, intraventricular hemorrhage and pneumothorax.

Investigations like ABG were analysed- 55.6% cases had metabolic/respiratory acidosis, increased OI in 73.7% and increased lactates in 88.6%. Abnormal chest x-ray findings like decreased vascular markings or bilateral homogenous opacities were noted in 36.1% neonates.

2D echo not only helped in establishing the diagnosis but was also used for categorising PPHN into mild (5.6%), moderate (25%) and severe (69.4%) (Table 2). In neonates with cardiac shunt across PDA/PFO (n=27), 81% severe cases had either right to left/bidirectional shunt and all severe cases had flat/left bulging inter-ventricular septal position which was the most consistent finding in severe PPHN (p=0.00009) (Figure 1 and 2). In ABG correlation with severity, neonates with severe PPHN had more acidosis, hypoxemia and poor oxygenation indices with higher CO2 levels, however the difference was not statistically significant. Lactates were paradoxically higher in mild cases as compared to severe/moderate cases because of the heterogeneity of the population, most of them being severe cases. On regression analysis, it was noted that all the neonates having severe PPHN required respiratory support at birth (p=0.015). Also, neonates with severe PPHN required invasive ventilation during the stay (p=0.005) and for prolonged duration with a median of 7 days (p=0.036) along with multiple inotropes and higher vasoactive-inotropic score with median of 10 (p=0.002). Pulmonary vasodilators like sildenafil was given in 21 neonates in which 16 had severe and 5 had moderate PPHN and 3 severe cases received bosentan. Also, 8 cases of severe PPHN required iNO while none of mild/moderate cases required iNO which was significant (p-0.05). 48% of severe cases based on Xray and clinical findings.

Table 2: Comparison of parameters among mild, moderate and severe cases of Persistent Pulmonary Hypertension of newborn.

Findings	Pulmonary artery hypertension			P value
	Mild (2)	Moderate (9)	Severe (25)	
2-D Echo				
Right to left shunt~	0 (0)	0 (0)	6 (28.6)	0.061
Left to right shunt~	0 (0)	4 (80.0)	4 (19.0)	
Bidirectional shunt~	1 (100)	1 (20.0)	11 (52.4)	
Ventricular Dysfunction	1 (50)	0 (0)	6 (24)	0.278
Flat/ left bulging interventricular septum	0 (0)	5 (55.6)	25 (100)	0.00009*
RVSP (n=12)	1 (8.3)	3 (25)	8 (66.6)	0.275
Arterial blood gas				
pH (n=35)	7.36 (7.34-7.38)	7.32 (7.32-7.41)	7.29 (7.18-7.36)	0.446
pO_2 (n=35)	125.1 (109-141.2)	181.5 (136.1-241.8)	78.9 (34.6-211.2)	0.304`
pCO_2 (n=35)	31.5 (30.8-32.1)	36.2 (30.1-40.2)	37.0 (32.7-41.4)	0.756
P/F Ratio (n=33)	342 (165-519)	302.0 (241.8-365.0)	78.9 (32.1-255.0)	0.184`
OI (n=19)	-	4.5 (4 -5.6)	9.3(4.5-30)	0.254^
Lactate (n=35)	6.8 (5.9-7.6)	2.3 (1.8-2.7)	4.9 (3.1-7.4)	0.045*
Received CPR at birth	0 (0)	0 (0)	3(12)	1.000
Respiratory support at birth	1 (50)	7 (77.8)	25 (100)	0.015*
Respiratory support in NICU				
Oxygen	1 (50)	3 (33.3)	2 (8)	0.005*
High flow nasal catheter	0 (0)	2 (22.2)	0 (0)	
Non-invasive ventilation	1 (50)	1 (11.1)	3 (12)	
Invasive ventilation	0 (0)	3 (33.3)	20 (80)	
HFOV	0 (0)	0 (0)	8 (32)	0.144
Inotrope/Vasoactive received				
Single	0 (0)	4 (44.4)	11 (44)	0.043*
Multiple	0 (0)	0 (0)	11 (44)	
Vasoactive-inotropic score (Median IQR)	0 (0-0)	0 (0-10)	10 (10-70)	0.002*

Continued.

Findings	Pulmonary artery hypertension			P value
	Mild (2)	Moderate (9)	Severe (25)	
Pulmonary vasodilators				
Sildenafil	0 (0)	5 (55.6)	16 (64)	0.255
iNO	0 (0)	0 (0)	8 (32)	0.05*
Bosentan	0 (0)	0 (0)	3 (12)	0.622
Others				
Surfactant	0 (0)	1 (11.1)	12 (48)	0.089
Steroids	0 (0)	0 (0)	5 (20)	0.478
Duration of respiratory support	4.5 (3-6)	6 (4-9)	5 (0-14)	0.781
Duration of ventilator support	2 (0-4)	0 (0-5)	7 (2-12)	0.036*
Duration of ICU stay	8.5 (4-13)	9 (6-14)	12 (6-17)	0.702

#Fisher Exact test used. `Kruskal-wallis test used. ^ Mann-Whitney U test used. * Significant at 0.05 level. ~On 2D Echo, 27 neonates had shunt present across PDA/PFO.

Various factors were compared in relation to the outcome in PPHN as shown in Table 3. Kaplan–Meier survival analysis demonstrated higher survival probability among inborn neonates (91.7%) compared to outborn neonates (62.5%) and this difference was statistically significant (p=0.046). Outcome was not affected by the gestational age and birth weight. However, females and small for gestational age neonates had poor outcomes though not statistically significant. Outcome was not affected by the maternal comorbidities or abnormal antenatal scan. Out of 10 neonates who died, 8 neonates had signs of fetal distress prior to delivery, however statistically significant correlation could not be obtained. Neonatal factors like delayed cry at birth, tone disturbances, respiratory distress, sepsis or other coexisting conditions did not affect the outcome. Significant mortality was noted in neonates having metabolic/respiratory acidosis (p=0.0002), hypoxemia (p=0.0005) and hypercarbia (p=0.031) on ABG. Interestingly, neonates who were ventilated, statistical significance was also noted with non survivors having low P/F ratio and OI (p=0.001 and p=0.0002 respectively). The majority of the neonates with normal chest x-ray survived as compared to the neonates with abnormal chest x-ray (p=0.00007). According to 2D Echo, severe PPHN was noted in non survivors as compared to survivors which included parameters like right to left/bidirectional shunt across PDA/PFO, ventricular dysfunction and flat/ left bulging inter-ventricular septal with significant p=0.045, p=0.039 and p=0.003 respectively.

Table 3: Comparison of demographic and clinical profile, investigations and treatment modalities between survivors and non survivors.

Risk factors	Outcome		P value
	Survival (26)	Death (10)	
Inborn	11 (91.7)	1 (8.3)	0.046*
Outborn	15 (62.5)	9 (37.5)	
Preterm	9 (69.2)	4 (30.8)	1.000
Male	17 (81)	4 (19)	0.260
Female	9 (60)	6 (40)	
Low birth weight	10 (71.4)	4 (28.6)	1.000
SGA	6 (60)	4 (40)	0.413
Maternal comorbidities	11 (68.8)	5 (31.3)	0.722
Abnormal anomaly scan	0 (0)	1 (100)	0.278
Antenatal steroids	1 (25)	3 (75)	0.057
Oligohydramnios	5 (71.4)	2 (28.6)	0.307
Polyhydramnios	1 (33.3)	2 (66.7)	
PROM	5 (83.3)	1 (16.7)	0.655
Fetal distress	10 (55.6)	8 (44.4)	0.060
C section	19 (65.5)	10 (34.5)	0.155
Not cried immediately after birth	10 (76.9)	3 (23.1)	
Hypotonia	8 (57.1)	6 (42.9)	0.140
Tachypnoea/ respiratory distress	20 (74.1)	7 (25.9)	0.686
No breathing/ Decreased efforts	6 (66.7)	3 (33.3)	
Sepsis	4 (66.7)	2 (33.3)	1.000
Coexisting condition	4 (50)	4 (50)	0.179

Continued.

Risk factors	Outcome		P value
	Survival (26)	Death (10)	
Investigation			
pH (n=35)	7.361 (7.309 – 7.423)	7.181 (7.151 – 7.320)	0.0002^*
pO_2 (n=35)	101.5 (66.3 – 207.2)	34.6 (28.4 – 70.8)	0.0005^*
pCO_2 (n=35)	32.1 (27.9 – 37.6)	37.2 (36.4 – 53.1)	0.031^*
P/F Ratio (n=33)	165 (85.2 – 345)	34.6 (29.5 – 84.0)	0.001^*
OI (n=19)	4.5 (3.3 – 6.1)	30 (13.2 – 39)	0.0002^*
Lactate (n=35)	3.98 (2.94 – 5.06)	5.42 (3.12 – 11.06)	0.113^
Abnormal chest X-ray	4 (30.8)	9 (69.2)	0.00007^*
Severity of pulmonary artery hypertension			
Mild	2 (100)	0 (0)	0.043*
Moderate	9 (100)	0 (0)	
Severe	15 (60)	10 (40)	
Direction of shunt (PDA or PFO) (n=27)			
Right to left	1 (16.7)	5 (83.3)	0.045*
Left to right	6 (75.0)	2 (25.0)	
Bidirectional	10 (76.9)	3 (23.1)	
Ventricular function			
Left ventricular dysfunction	1 (100)	0 (0)	0.039*
Right ventricular dysfunction	2 (33.3)	4 (66.7)	
Interventricular septum (IVS)			
Flat	17 (85)	3 (15)	0.003*
Bulging to the right	6 (100)	0 (0)	
Received CPR at birth	2 (66.6)	1 (33.3)	0.636
Respiratory support at birth	23 (69.7)	10 (30.3)	0.612
Respiratory support in NICU			
Oxygen	6 (100)	0 (0)	0.053
High flow nasal catheter	2 (100)	0 (0)	
Non-invasive ventilation	5 (100)	0 (0)	
Invasive ventilation	13 (56.5)	10 (43.5)	
HFOV	1 (12.5)	7 (87.5)	0.0001*
Inotrope received			
Single	14 (87.5)	2 (12.5)	0.0001*
Multiple	3 (27.2)	8 (72.7)	
Vasoactive-inotropic score (Median IQR)	10 (0 – 10)	74 (50 – 120)	0.000007^*
Pulmonary vasodilators			
Sildenafil	12 (57.1)	9 (42.9)	0.024*
iNO	2 (25)	6 (75)	0.002*
Bosentan	0 (0)	3 (100)	0.017*
Others			
Surfactant	5 (38.5)	8 (61.5)	0.001*
Steroids	1 (20)	4 (80)	0.015*
Duration of ventilator free days	5.5 (4-9)	0 (0 – 0)	<0.0005^*
Duration of ICU stay	13 (8 – 17)	4 (2 – 12)	0.010^*

#Fisher Exact test used. ^Mann-Whitney U test used. *Significance level is 0.05.

Also, all the neonates who did not require inotropic support survived (p=0.035) while the neonates who died were offered multiple treatment modalities– all of them required inotropic support and 8 of them required multiple inotropes (p=0.0001), 8 of them were given surfactant (p=0.001), 8 of them were started on HFOV (p=0.0001), and most of them were given pulmonary vasodilators like sildenafil, iNO and bosentan which were statistically significant as compared to neonates who survived. Median vaso-inotropic score was 10 (IQR-0-10) in survivors and 74 (IQR- 54-120) in non survivors. Neonates who survived had more ventilator free days and more days of ICU stay as compared to neonates who did not survive with significant p<0.0005 and p<0.010 respectively.

DISCUSSION

In our study we attempted to evaluate the profile of neonates diagnosed with PPHN. PPHN is a complex clinical syndrome with a worldwide estimated incidence of 2-4 per 1000 live-births (maximum 5.4 per 1000 live-births).[1,3] Incidence in our hospital- 8.2 per 1000 live and incidence in NICU admission- 42 per 1000 NICU admissions. Mortality in PPHN across different countries ranged between 3-57.9% with highest in Malaysia 57.9% and lowest in USA 3%.[3] In this study, mortality was 27.8 %, however there was a difference noted between the inborn (8.3%) and outborn (37.5%) neonates. Interestingly, the survival curve for inborn neonates showed a significantly softened decline indicating reduced mortality risk probably due to early stabilisation and immediate NICU care. In a study, Steurer et al reported that neonates with <37 weeks of gestation and small for gestational age had higher mortality in PPHN likewise in our study also, mortality amongst small for gestational age neonates was higher though not statistically significant.[7]

There was no significant association noted between maternal comorbidities during pregnancy and the severity/outcome of PPHN. Though oligohydramnios leads to pulmonary hypoplasia increases the risk for PPHN as reported by Olivia Williams et al but we did not observe any such significant association.[8] Also among neonates who died, the majority (80%) had signs of fetal distress prior to delivery, though not statically significant. Similarly, a study conducted by Abdel Hakeem Abdel Mohsen et al showed that meconium-stained liquor increased the risk for PPHN and perinatal asphyxia increased mortality risk.[5]

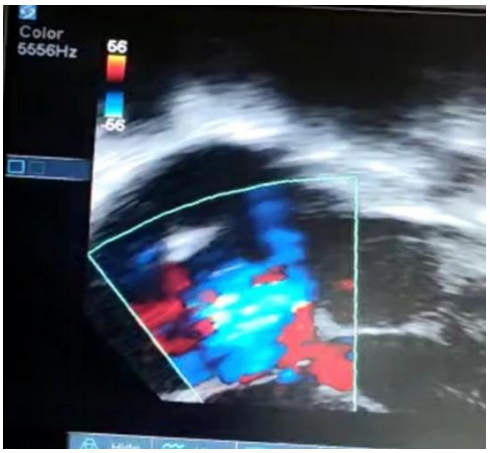


Figure 1: 2D Echo demonstrating right to left shunt across PDA.

A study conducted by Bah et al in Malaysia demonstrated that APGAR ≤5 at 5 mins was associated with increased mortality in PPHN but in our study APGAR scores could not be correlated.[12] Though, we noticed that neonates who required resuscitation at birth were found to have severe PPHN. According to 2D echo parameters, mortality in the neonates was correlating with right to left shunting across PDA/PFO, right ventricular dysfunction and inter-ventricular septal bulge to the left (Figure 1 and 2). Also, Malowitz et al demonstrated that right ventricular dysfunction and a predominant right-to-left shunt across the PDA, were associated with poor outcomes.[11]

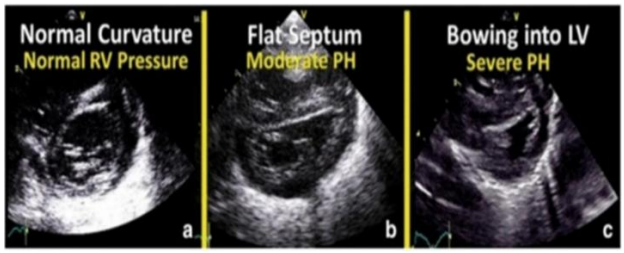


Figure 2 (a-c): 2D Echo demonstrating Interventricular septal position varying according to severity of PPHN.

Serial ABG parameters and oxygenation indices were evaluated from the time of admission till discharge/death and it was noted that metabolic and respiratory acidosis was more in severe cases and correlated with mortality. Worse hypoxemia levels at admission and higher OI were predictive of poor outcomes. Similarly, Pakhathirathien et al demonstrated that an OI score of 41 and higher vaso-inotropic score at 72 hours showed accuracy in predicting mortality.[13]

Neonates with severe PPHN despite being offered multiple treatment modalities including HFOV had poor outcome and high vaso-inotropic score significantly predicted mortality probably due to the severe disease itself. Pulmonary vasodilators like sildenafil, iNO, bosentan and milrinone were used and response was studied by monitoring serial oxygenation parameters but no significant improvement was noted in non survivors probably due to the severe disease itself. Although, in inborn neonates survival rates were better and improvement was noted in the oxygen indices after the treatment. In a meta-analysis, Kelly et al noted that sildenafil reduces mortality and improves oxygenation.[14,15] According to the studies, an acceptable indication for treatment with iNO would be an OI>15-25 with echocardiographic evidence of PPHN or a higher OI with or without evidence of right-to-left shunt and in this study, iNO was used only in severe cases with OI >25.[8] Median duration of ventilator support and ICU days were more for neonates with severe PPHN suggesting requirement of prolonged intensive care. Also, median duration of ICU stay in survivors was more than the non survivors possibly reflecting early death in non survivors.

Strengths

This was a single centre study which demonstrated various parameters associated with PPHN including

antenatal and postnatal risk factors, clinical condition, investigations, different treatment modalities and their association with the outcome. Very few studies including all the parameters have been conducted.

Limitations

As this study was done in a tertiary care referral centre and majority neonates were outborn but were referred within 48 hours of birth. Hence, this could explain more severe PPHN in our cohort. The sample size of the study was small. Follow up of PPHN neonates for chronic lung disease could not be done in the study.

CONCLUSION

In conclusion, PPHN is associated with significant morbidity and mortality. Early diagnosis, prompt echocardiographic evaluation and timely initiation of appropriate therapeutic interventions with serial monitoring are essential for improving survival. Inborn neonates demonstrated better outcomes, highlighting the importance of early stabilization, targeted echocardiography and access to specialized neonatal care. Poor prognostication markers included requirement of resuscitation at birth, abnormal arterial blood gas parameters (metabolic/respiratory acidosis and poor oxygenation indices), requirement for advanced ventilator and inotropic support and echocardiography findings like right to left shunt across PDA/PFO, right ventricular dysfunction and septal deviation to left.

ACKNOWLEDGEMENTS

The authors sincerely thank the Cardiology Team and Neonatal Intensive Care Unit Team for the support and assistance.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sardar S, Pal S, Mishra R. A retrospective study on the profile of persistent pulmonary hypertension of newborn in a tertiary care unit of Eastern India. J Clin Neonatol. 2020;9(1):18-26.
2. Lakshminrusimha S, Keszler M. Persistent pulmonary hypertension of the newborn. Neo Reviews. 2015;16(12):e680-92.
3. Huang Y, Yang T, Liang X, Chen Y, Zhou P, Yu Z, et al. Global, regional and national trends in the burden of persistent pulmonary hypertension of the newborn and essentials of its management from 1993 to 2023: a scoping review. Front Pediatr. 2025;13:1502385.
4. Arshad MS, Adnan M, Anwar-Ul-Haq HM, Zulqarnain A. Postnatal causes and severity of persistent pulmonary hypertension of newborn. Pak J Med Sci. 2021;37(5):1387-91.
5. Mohsen AH, Amin AS. Risk factors and outcomes of persistent pulmonary hypertension of the newborn in the neonatal intensive care unit of Al-Minya University Hospital in Egypt. J Clin Neonatol. 2013;2 (2):78-82.
6. Nakwan N, Jain S, Kumar K, Hosono S, Hammoud M, Elsayed YY, et al. An Asian multicenter retrospective study on persistent pulmonary hypertension of the newborn: incidence, etiology, diagnosis, treatment and outcome. J Matern Fetal Neonatal Med. 2020;33(12):2032-7.
7. Bendapudi P, Rao GG, Greenough A. Diagnosis and management of persistent pulmonary hypertension of the newborn. Paediatr Respir Rev. 2015;16(3):157-61.
8. Nair J, Lakshminrusimha S. Update on PPHN: mechanisms and treatment. Semin Perinatol. 2014;38(2):78-91.
9. Martinho S, Adão R, Leite-Moreira AF, Brás-Silva C. Persistent pulmonary hypertension of the newborn: pathophysiological mechanisms and novel therapeutic approaches. Front Pediatr. 2020;8:342.
10. Pedersen J, Hedegaard ER, Simonsen U, Krüger M, Infanger M, Grimm D. Current and future treatments for persistent pulmonary hypertension in the newborn. Basic Clin Pharmacol Toxicol. 2018;123(4):392-406.
11. Malowitz JR, Forsha DE, Smith PB, Cotten CM, Barker PC, Tatum GH. Right ventricular echocardiographic indices predict poor outcomes in infants with persistent pulmonary hypertension of the newborn. Eur Heart J Cardiovasc Imaging. 2015;16(11):1224-31.
12. Mat Bah MN, Tan RYH, Razak H, Sapian MH, Abdullah N, Alias EY. Survival and associated risk factors for mortality among infants with persistent pulmonary hypertension of the newborn in Malaysia. J Perinatol. 2021;41(4):786-93.
13. Pakhathirathien P, Maneenil G, Thatrimontrichai A, Dissaneevate S, Praditaukrit M. Mortality prediction in newborns with persistent pulmonary hypertension: a comparison of four illness severity scores. Pediatr Pulmonol. 2025;60:e27484.
14. Kelly LE, Ohlsson A, Shah PS. Sildenafil for pulmonary hypertension in neonates. Cochrane Database Syst Rev. 2017;(8):CD005494.
15. Vargas-Origel A, Gómez-Rodríguez G, Aldana-Valenzuela C, Vela-Huerta MM, Alarcón-Santos SB, Amador-Licona N. The use of sildenafil in persistent pulmonary hypertension of the newborn. Am J Perinatol. 2010;27(3):225-30.

Cite this article as: Pai DO, Andankar P, Peruri L, Prabhu S, Lakshmivenkateshiah S. Clinical spectrum and outcome determinants in persistent pulmonary hypertension of the newborn in a tertiary care centre: a cross-sectional study. Int J Contemp Pediatr 2026;13:2259-66.