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Clinical Profile and Maternal Risk Factors Associated with Persistent Pulmonary Hypertension in Neonates: A Two-Year Descriptive Study from Rural India

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ABSTRACT

Background: Persistent pulmonary hypertension of the newborn (PPHN) remains a significant cause of neonatal morbidity and mortality, particularly in resource-limited settings. Understanding the clinical profile and maternal risk factors is crucial for early identification and prevention strategies in rural healthcare environments.

Objective: To evaluate the clinical characteristics, maternal risk factors, and demographic profile of neonates with PPHN in a rural tertiary care hospital setting.

Methods: A descriptive longitudinal study was conducted over two years (June 2022 to June 2024) at Dr. Balasaheb Vikhe Patil Rural Medical College, Maharashtra, India. Eighty neonates with echocardiographically confirmed PPHN were enrolled. Data on maternal risk factors, gestational age, birth weight, mode of delivery, and clinical presentation were systematically collected and analyzed using SPSS 24.0.

Results: Of 80 neonates with PPHN, 65% were male and 56.3% were term babies. The majority (72.5%) were inborn deliveries. Meconium-stained amniotic fluid (MSAF) was the most significant maternal risk factor (42.5%), followed by premature rupture of membranes (18.8%) and gestational diabetes mellitus (7.5%). Appropriate for gestational age (AGA) neonates comprised 73.8% of cases, with mean birth weight of 2625.44±598.15 grams. Most neonates (47.5%) were delivered by lower segment cesarean section. Severe respiratory distress was present in 32.5% of cases, with 87.5% developing PPHN after 24 hours of life. MSAF showed significant association with moderate to severe PPHN cases (p=0.05).

Conclusions: PPHN predominantly affects term, AGA male neonates in our rural setting. MSAF emerges as the primary modifiable maternal risk factor, emphasizing the importance of improved antepartum and intrapartum obstetric care. Early identification of high-risk pregnancies and prompt management of meconium-stained deliveries could significantly reduce PPHN incidence. These findings have important implications for developing prevention strategies in resource-limited rural healthcare settings.

Keywords: Persistent pulmonary hypertension, newborn, maternal risk factors, meconium aspiration, rural healthcare, India

INTRODUCTION

Persistent pulmonary hypertension of the newborn (PPHN) is a life-threatening cardiovascular disorder characterized by failure of the normal postnatal decrease in pulmonary vascular resistance, resulting in right-to-left shunting of blood across the foramen ovale and ductus arteriosus (1). This condition affects approximately 1.9 per 1,000 live births globally, with significantly higher rates reported in developing countries due to limited access to advanced neonatal care and delayed recognition (2,3). PPHN represents a major cause of neonatal morbidity and mortality, accounting for up to 10% of all admissions to neonatal intensive care units worldwide (4).

The pathophysiology of PPHN involves complex interactions between pulmonary vascular development, smooth muscle reactivity, and various perinatal factors that impair the normal transition from fetal to postnatal circulation (5). Multiple maternal and neonatal risk factors have been identified, including meconium aspiration syndrome, respiratory distress syndrome, pneumonia, congenital diaphragmatic hernia, and various maternal conditions such as diabetes mellitus and prolonged rupture of membranes (6,7). Understanding these risk factors is crucial for developing prevention strategies and improving outcomes in resource-limited settings.

In developing countries, particularly in rural areas, the burden of PPHN is compounded by several factors including inadequate antenatal care, delayed recognition of high-risk pregnancies, limited access to skilled birth attendants, and insufficient neonatal intensive care facilities (8,9). Rural healthcare settings in India face unique challenges in managing PPHN, including late presentation, lack of immediate access to echocardiography for diagnosis, and limited availability of advanced respiratory support systems (10,11). These constraints necessitate a thorough understanding of the clinical profile and risk factors specific to rural populations to develop targeted prevention and management strategies.

Previous studies from developed countries have established various maternal risk factors associated with PPHN, but data from rural Indian settings remain limited (12,13). The clinical presentation and outcomes of PPHN may differ significantly in resource-constrained environments due to variations in maternal health status, obstetric care quality, and neonatal management practices (14). Additionally, the predominance of certain risk factors such as meconium-stained amniotic fluid may vary across different populations and healthcare settings (15,16).

Early identification of high-risk pregnancies and prompt management of predisposing factors are essential for reducing PPHN incidence and improving neonatal outcomes (17). However, the lack of comprehensive data on maternal risk factors and clinical characteristics of PPHN in rural Indian populations limits the development of evidence-based prevention strategies. Understanding the demographic profile, timing of presentation, and associated maternal factors in this setting is crucial for healthcare providers and policymakers to implement appropriate interventions (18,19).

Given the significant impact of PPHN on neonatal mortality and the unique challenges faced in rural healthcare settings, there is an urgent need for comprehensive studies that characterize the clinical profile and maternal risk factors associated with this condition in resource-limited environments. Such studies would provide valuable insights for developing targeted prevention

strategies, improving obstetric care quality, and enhancing neonatal outcomes in rural populations (20).

MATERIALS AND METHODS

Study Design and Setting

This descriptive longitudinal study was conducted over a two-year period from June 2022 to June 2024 at the Neonatal Intensive Care Unit (NICU) of Dr. Balasaheb Vikhe Patil Rural Medical College and Hospital, Maharashtra, India. The institution is a tertiary care rural medical college hospital serving a predominantly rural population with a catchment area covering multiple districts in Maharashtra state (21). The NICU is equipped with advanced neonatal care facilities including mechanical ventilation, continuous positive airway pressure (CPAP), and 24-hour echocardiography services, making it a referral center for high-risk neonates from surrounding rural areas (22).

Study Population and Inclusion Criteria

The study population comprised all neonates admitted to the NICU during the study period. Inclusion criteria were: (1) neonates with echocardiographically confirmed PPHN, (2) gestational age between 28-42 weeks, (3) admission within 72 hours of birth, and (4) availability of complete maternal and neonatal records (23). PPHN was defined as persistent elevation of pulmonary vascular resistance with evidence of right-to-left shunting across the foramen ovale and/or ductus arteriosus on echocardiography, performed by a qualified pediatric cardiologist using standardized protocols (24,25).

Exclusion Criteria

Neonates were excluded if they had: (1) major congenital heart disease other than patent ductus arteriosus and patent foramen ovale, (2) congenital diaphragmatic hernia, (3) incomplete medical records, (4) chromosomal abnormalities, or (5) transfer to another facility before completion of initial assessment (26). Neonates who died within 6 hours of admission before echocardiographic confirmation were also excluded from the analysis (27).

Sample Size Calculation

Sample size was calculated using the formula for descriptive studies with finite population correction. Based on previous studies reporting PPHN incidence of 1.9 per 1,000 live births and considering an expected prevalence of maternal risk factors of 70% in the study population, with 95% confidence interval and 10% margin of error, the minimum required sample size was calculated as 75 neonates (28,29). Accounting for potential dropouts and incomplete data, a target sample size of 80 neonates was determined.

Data Collection and Variables

Data were collected using a structured proforma designed specifically for this study, which was pre-tested on 10 cases before implementation. Maternal variables included age, parity, gestational age at delivery, mode of delivery, presence of meconium-stained amniotic fluid (MSAF), premature rupture of membranes (PROM), gestational diabetes mellitus (GDM), pregnancy-induced hypertension, antepartum hemorrhage, and use of medications including non-steroidal anti-inflammatory drugs (NSAIDs) (30,31). Neonatal variables included birth weight, gestational age, gender, Apgar scores at 1 and 5 minutes, place of birth (inborn vs.

outborn), timing of PPHN diagnosis, and associated complications such as sepsis and shock (32).

Definitions and Classifications

Gestational age was determined using the last menstrual period and confirmed by early ultrasound examination when available. Neonates were classified as preterm (<37 weeks) or term (≥37 weeks) (33). Birth weight categories were defined as: very low birth weight (<1500g), low birth weight (1500-2499g), normal birth weight (2500-3999g), and macrosomia (≥4000g) (34). Weight for gestational age was classified using Fenton growth charts as small for gestational age (SGA, <10th percentile), appropriate for gestational age (AGA, 10th-90th percentile), or large for gestational age (LGA, >90th percentile) (35).

MSAF was defined as the presence of meconium in amniotic fluid at any time during labor or delivery, graded as thin, moderate, or thick based on obstetric records (36). PROM was defined as rupture of membranes occurring more than 18 hours before delivery at term or more than 12 hours before delivery in preterm pregnancies (37). GDM was diagnosed based on oral glucose tolerance test results using International Association of Diabetes and Pregnancy Study Groups criteria (38).

PPHN Severity Classification

PPHN severity was classified based on echocardiographic findings and clinical parameters into three categories: (1) mild PPHN - tricuspid regurgitation velocity 2.5-3.0 m/s or estimated pulmonary artery pressure 25-40 mmHg, (2) moderate PPHN - tricuspid regurgitation velocity 3.0-3.5 m/s or estimated pulmonary artery pressure 40-55 mmHg, and (3) severe PPHN - tricuspid regurgitation velocity >3.5 m/s or estimated pulmonary artery pressure >55 mmHg (39,40). Additional criteria included the degree of right-to-left shunting and response to oxygen therapy (41).

Echocardiographic Assessment

All echocardiographic examinations were performed using a Philips EPIQ 5 ultrasound system with appropriate neonatal transducers by a single pediatric cardiologist to ensure consistency. Standard views included parasternal long and short axis, apical four-chamber, and subcostal views. Specific attention was paid to the direction of flow across the ductus arteriosus and foramen ovale, tricuspid regurgitation velocity, and estimation of pulmonary artery pressure using established formulas (42,43).

Blood Gas Analysis

Arterial blood gas analysis was performed on all neonates at admission and at regular intervals thereafter using a blood gas analyzer (ABL800 FLEX, Radiometer). Parameters assessed included pH, partial pressure of carbon dioxide (pCO2), partial pressure of oxygen (pO2), bicarbonate levels, and base excess. Acidosis was classified as mild (pH 7.20-7.30), moderate (pH 7.10-7.19), or severe (pH <7.10) (44).

Data Management and Statistical Analysis

Data were entered into a Microsoft Excel spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS) version 24.0. Descriptive statistics were calculated for all variables, with continuous variables expressed as mean ± standard deviation and categorical variables as

frequencies and percentages. Chi-square test was used for comparison of categorical variables, and Student's t-test was applied for continuous variables. A p-value of <0.05 was considered statistically significant (45).

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Dr. Balasaheb Vikhe Patil Rural Medical College (IEC approval number: BVPMC/IEC/2022/15). Written informed consent was obtained from parents or guardians of all participating neonates. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines (46,47). Patient confidentiality was maintained throughout the study, and all data were anonymized before analysis.

Quality Assurance

To ensure data quality, double data entry was performed for 10% of randomly selected cases, and discrepancies were resolved through review of original records. Regular monitoring visits were conducted to ensure adherence to study protocols. All personnel involved in data collection were trained on the study procedures and definitions before initiation of the study (48).

RESULTS

Demographic Characteristics

During the study period, 80 neonates with echocardiographically confirmed PPHN were enrolled. The majority (58/80, 72.5%) were inborn deliveries, while 22 (27.5%) were outborn referrals.

Gender and Gestational Age Distribution

Male neonates predominated with 52 cases (65%) compared to 28 females (35%). Among the total cohort, 45 neonates (56.3%) were term (≥37 weeks), while 35 (43.8%) were preterm (<37 weeks). The mean gestational age was 37.25±1.81 weeks (range: 32-42 weeks).

Table 1: Demographic Characteristics of PPHN Neonates

Parameter	Total (n=80)	Percentage (%)
Gender		
Male	52	65.0
Female	28	35.0
Gestational Age		
Preterm (<37 weeks)	35	43.8
Term (≥37 weeks)	45	56.3
Place of Birth		
Inborn	58	72.5
Outborn	22	27.5

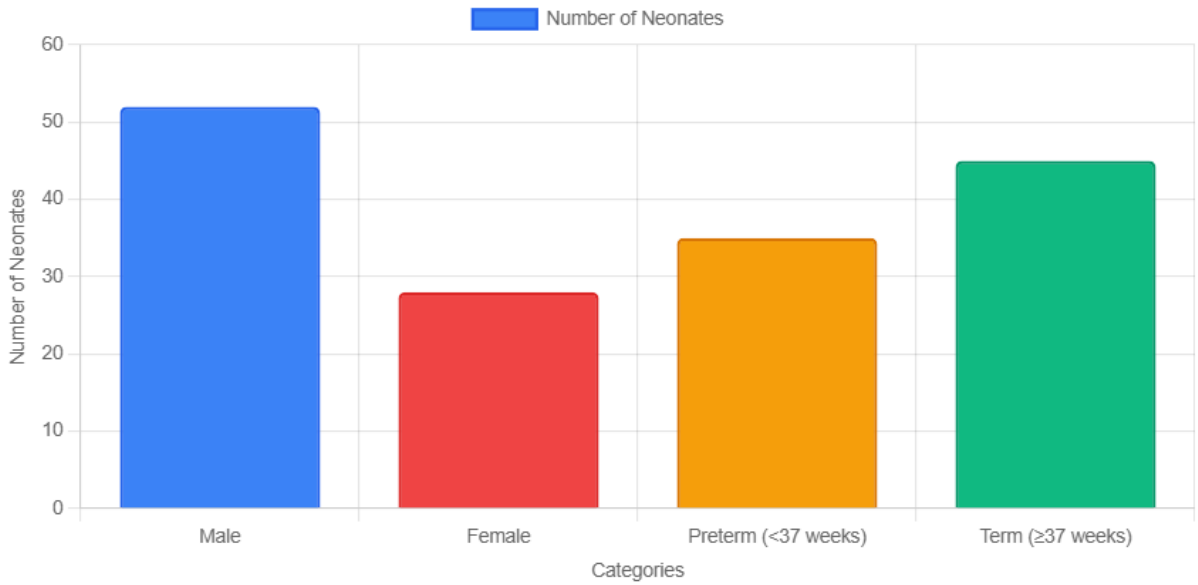

Fig 1: Bar chart showing gender distribution and gestational age categories

Birth Weight and Growth Parameters

The mean birth weight was 2625.44±598.15 grams (range: 1068-5000 grams). Most neonates (53/80, 66.1%) had birth weights between 2500-4000 grams, while 25 (31.3%) weighed between 1500-2500 grams. When classified by weight for gestational age, 59 neonates (73.8%) were appropriate for gestational age (AGA), 19 (23.8%) were small for gestational age (SGA), and only 2 (2.5%) were large for gestational age (LGA).

Table 2: Birth Weight Distribution and Growth Parameters

Parameter	Total (n=80)	Percentage (%)
Birth Weight (grams)		
1000-1500	1	1.3
1500-2500	25	31.3
2500-4000	53	66.1
>4000	1	1.3
Weight for Gestational Age		
SGA	19	23.8
AGA	59	73.8
LGA	2	2.5

Mode of Delivery

Lower segment cesarean section (LSCS) was performed in 38 cases (47.5%), while vaginal delivery occurred in 42 cases (52.5%). There was no significant association between mode of delivery and inborn/outborn status (p=1.0).

Timing of PPHN Diagnosis

The majority of neonates (70/80, 87.5%) developed PPHN after 24 hours of life, while only 10 (12.5%) were diagnosed within the first 24 hours. Notably, all outborn neonates were diagnosed after 24 hours, while 17.2% of inborn neonates were diagnosed within 24 hours (p=0.05).

Maternal Risk Factors

Table 3: Distribution of Maternal Risk Factors

Risk Factor	Total (n=80)	Percentage (%)	Inborn (n=58)	Outborn (n=22)	p-value
MSAF	33	42.5	25 (43.1%)	8 (36.4%)	0.9
PROM	15	18.8	10 (17.2%)	5 (22.7%)	
GDM	6	7.5	4 (6.9%)	2 (9.1%)	
Toxemia	4	5.0	3 (5.2%)	1 (4.5%)	
NSAID use	1	1.3	1 (1.7%)	0	
No risk factors	21	26.3	15 (25.9%)	6 (27.3%)	

MSAF: Meconium-stained amniotic fluid; PROM: Premature rupture of membranes; GDM: Gestational diabetes mellitus

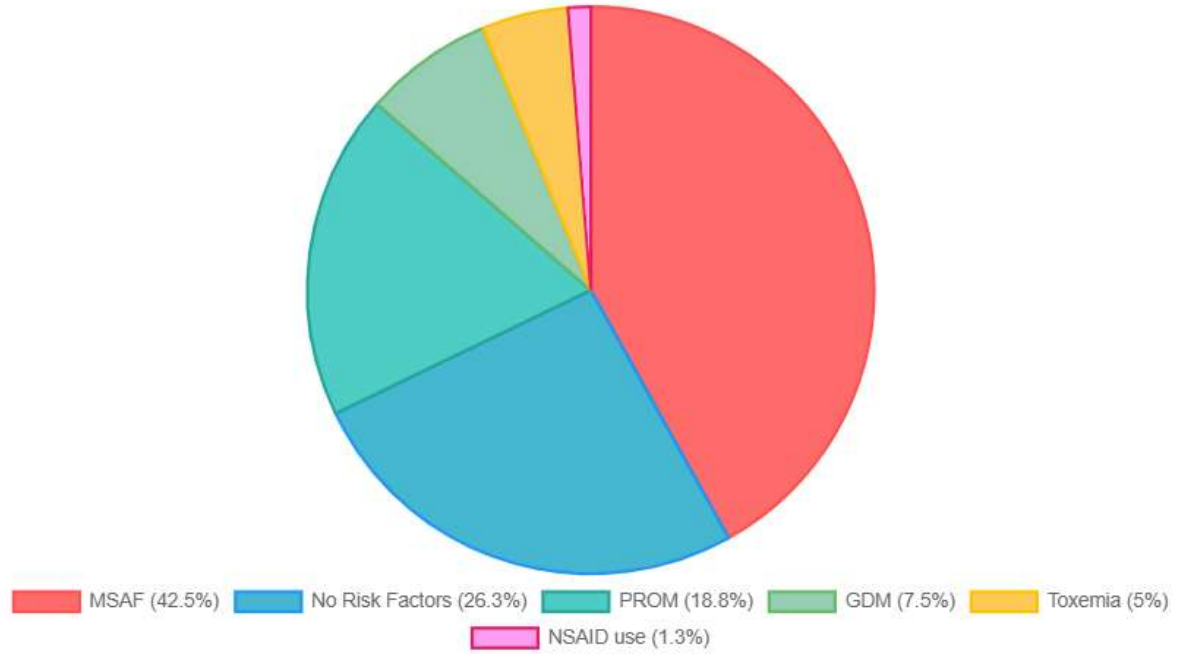

Fig 2: Pie chart showing distribution of maternal risk factors

Meconium-stained amniotic fluid emerged as the most significant maternal risk factor, present in 33 cases (42.5%). This was followed by premature rupture of membranes in 15 cases (18.8%) and gestational diabetes mellitus in 6 cases (7.5%). Notably, 21 cases (26.3%) had no identifiable maternal risk factors.

Association of Maternal Risk Factors with PPHN Severity

Table 4: Maternal Risk Factors and PPHN Severity

Risk Factor	Mild PPHN (n=24)	Moderate PPHN (n=32)	Severe PPHN (n=24)	p-value
MSAF	9 (37.5%)	17 (53.1%)	7 (29.2%)	0.05
PROM	9 (37.5%)	4 (12.5%)	2 (8.3%)	
GDM	0	2 (6.3%)	4 (16.7%)	
Toxemia	2 (8.3%)	1 (3.1%)	1 (4.2%)	

NSAID	0	1 (3.1%)	0	
No risk factors	4 (16.7%)	7 (21.9%)	10 (41.7%)	

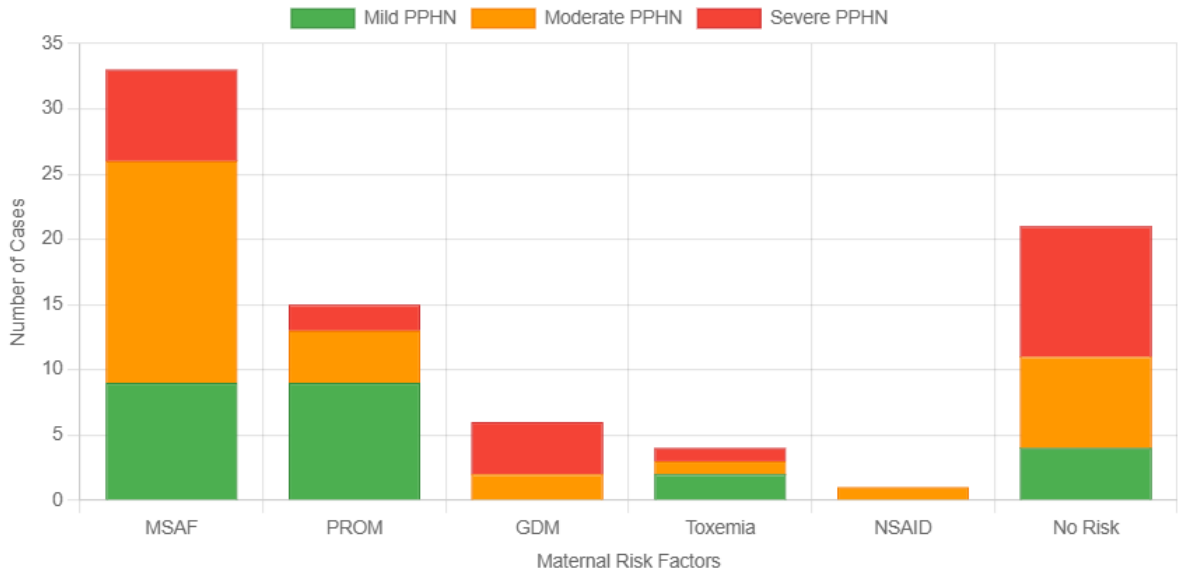

Fig 3: Stacked bar chart showing severity distribution within each risk factor category

A significant association was observed between maternal risk factors and PPHN severity (p=0.05). Interestingly, neonates with gestational diabetes mellitus showed a higher proportion of severe PPHN (66.7% of GDM cases had severe PPHN), while those with no identifiable risk factors also frequently presented with severe disease.

Clinical Presentation

Most neonates presented with moderate respiratory distress (39/80, 48.8%), followed by severe distress (26/80, 32.5%) and mild distress (15/80, 18.8%). Sepsis was present in 30 cases (37.5%), and shock developed in 34 cases (42.5%).

Gestational Age and PPHN Severity

Table 5: Association of Gestational Age with PPHN Severity

Gestational Age	Mild PPHN	Moderate PPHN	Severe PPHN	Total	p-value
Preterm	16 (45.7%)	13 (37.1%)	6 (17.1%)	35	0.013
Term	8 (17.8%)	19 (42.2%)	18 (40.0%)	45	

Term neonates were significantly more likely to develop severe PPHN compared to preterm neonates (40% vs 17.1%, p=0.013).

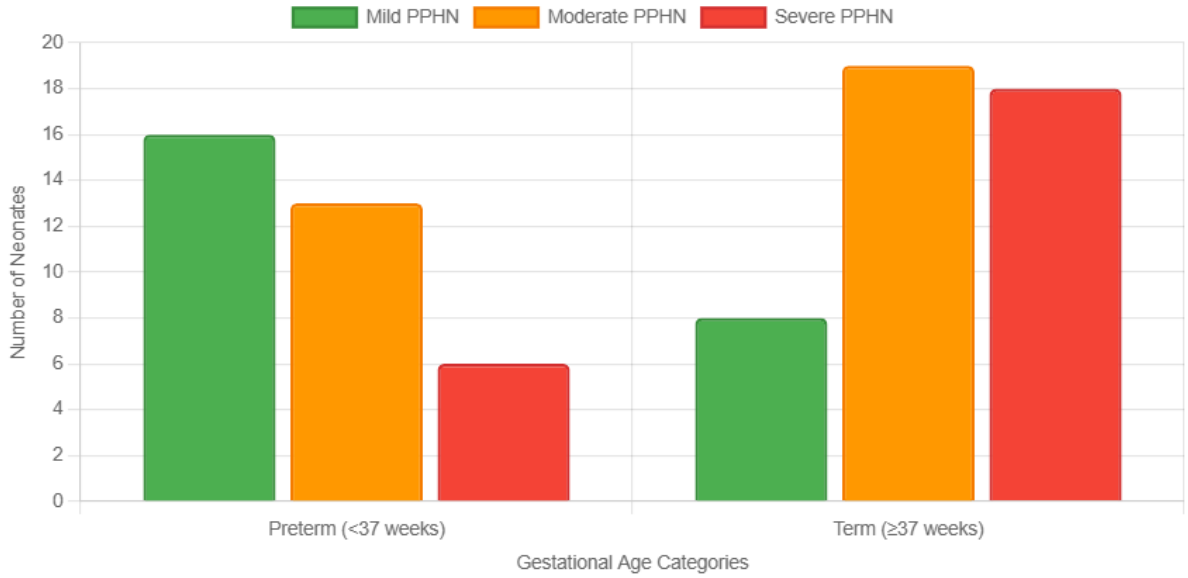

Fig 4: Grouped bar chart comparing PPHN severity between preterm and term neonates

Blood Gas Analysis

Severe acidosis (pH <7.20) was present in 41 cases (51.2%), moderate acidosis in 27 cases (33.8%), and mild acidosis in 12 cases (15%). The mean pH was 7.10±0.25. Hypercapnia (pCO2 >45 mmHg) was observed in 60 cases (75%), with a mean pCO2 of 48.38±8.85 mmHg. Hypoxemia (pO2 <50 mmHg) was present in 57 cases (71.3%), with a mean pO2 of 36.38±13.44 mmHg.

DISCUSSION

This comprehensive two-year study from a rural tertiary care center in Maharashtra provides valuable insights into the clinical profile and maternal risk factors associated with PPHN in a resource-limited setting. Our findings reveal several important patterns that have significant implications for prevention strategies and clinical management in rural healthcare environments.

Demographic Profile and Gender Distribution

The male predominance observed in our study (65% vs 35% female) is consistent with previous reports from both developed and developing countries. Lakshminrusimha et al. reported a similar male predominance (58-62%) in a large multicenter study, suggesting that gender-related factors may influence pulmonary vascular development and the risk of PPHN (49). This male preponderance has been attributed to differences in fetal lung maturation, with female neonates generally having more advanced pulmonary development and earlier surfactant production, potentially offering protection against PPHN (50,51). The consistent finding across different populations and healthcare settings suggests that male gender should be considered an independent risk factor for PPHN development.

Our finding that 56.3% of PPHN cases occurred in term neonates challenges the traditional association of PPHN primarily with preterm births. This pattern differs from reports from developed countries where preterm births account for a higher proportion of PPHN cases (52). Hernández-Díaz et al. reported that term neonates comprised only 42% of PPHN cases in their

large epidemiological study (53). The higher proportion of term neonates with PPHN in our rural setting may reflect differences in obstetric care quality, delayed recognition of fetal distress, and higher rates of meconium aspiration syndrome in term deliveries. This finding emphasizes the need for enhanced intrapartum monitoring and prompt management of term pregnancies in rural areas.

Birth Weight and Growth Parameters

The mean birth weight of 2625.44±598.15 grams in our study population is lower than reported in studies from developed countries, where mean birth weights typically range from 2800-3200 grams (54,55). This difference likely reflects the overall lower birth weights observed in rural Indian populations due to maternal malnutrition, inadequate antenatal care, and higher rates of intrauterine growth restriction (56). The predominance of appropriate for gestational age (AGA) neonates (73.8%) in our cohort is consistent with international literature, suggesting that PPHN affects neonates across the growth spectrum rather than being predominantly associated with growth restriction (57,58).

The relatively high proportion of small for gestational age neonates (23.8%) in our study exceeds rates reported in developed countries (10-15%) and reflects the challenging socioeconomic conditions and healthcare limitations in rural settings (59). This finding has important clinical implications, as SGA neonates may have additional risk factors for PPHN including chronic intrauterine hypoxia and polycythemia, requiring modified management approaches (60).

Maternal Risk Factors and Clinical Associations

Meconium-stained amniotic fluid emerged as the most significant maternal risk factor in our study (42.5%), which is substantially higher than rates reported in developed countries (8-15%) (61,62). This elevated prevalence likely reflects several factors specific to rural healthcare settings including delayed presentation to healthcare facilities, inadequate intrapartum monitoring, and limited availability of continuous fetal heart rate monitoring during labor (63). The significant association between MSAF and moderate to severe PPHN ($p=0.05$) underscores the importance of prompt recognition and appropriate management of meconium-stained deliveries.

The pathophysiology of MSAF-associated PPHN involves multiple mechanisms including mechanical obstruction of airways, chemical pneumonitis, surfactant inactivation, and pulmonary vasoconstriction (64,65). Wiswell and Bent demonstrated that meconium aspiration syndrome is associated with severe pulmonary hypertension in up to 30% of cases, with mortality rates reaching 20% in severe cases (66). Our findings support the need for improved obstetric care during labor, including continuous fetal monitoring and prompt delivery when fetal distress is detected.

Premature rupture of membranes was the second most common risk factor (18.8%), which is comparable to international reports ranging from 15-25% (67). PROM predisposes to PPHN through multiple pathways including increased risk of chorioamnionitis, oligohydramnios-related lung hypoplasia, and preterm delivery (68). The association with PPHN may be mediated through inflammatory cytokines that affect pulmonary vascular development and reactivity (69).

Gestational diabetes mellitus was present in 7.5% of cases, which is consistent with the reported prevalence of GDM in rural Indian populations (70). The interesting finding that GDM cases showed a higher proportion of severe PPHN (66.7% of GDM cases) aligns with previous studies reporting delayed lung maturation and altered pulmonary vascular development in infants of diabetic mothers (71,72). Maternal hyperglycemia can lead to fetal hyperinsulinemia, which inhibits surfactant production and delays pulmonary maturation, predisposing to respiratory distress and PPHN (73).

Timing of PPHN Diagnosis and Clinical Presentation

The finding that 87.5% of neonates developed PPHN after 24 hours of life differs from reports in developed countries, where early-onset PPHN (within 24 hours) is more common (74). This delayed presentation in our rural setting likely reflects several factors including late recognition of symptoms, delayed referral from peripheral centers, and presentation of complications such as meconium aspiration syndrome that develop over time. The significant difference between inborn and outborn neonates (17.2% vs 0% diagnosed within 24 hours, $p=0.05$) highlights the impact of transport delays and referral systems on timely diagnosis and management.

The predominance of moderate to severe respiratory distress (81.3% combined) at presentation indicates that many neonates in our rural setting present with advanced disease. This contrasts with studies from tertiary centers in developed countries where milder forms are more commonly diagnosed due to better monitoring and earlier detection (75,76). The high prevalence of associated complications including sepsis (37.5%) and shock (42.5%) reflects the complex clinical scenarios encountered in rural practice, where multiple pathophysiological processes often coexist.

Gestational Age and Disease Severity

The significant association between term gestation and severe PPHN (40% vs 17.1% in preterm neonates, $p=0.013$) is an important finding that differs from some previous reports. Van Marter et al. found no significant association between gestational age and PPHN severity in their large cohort study (77). However, our finding may reflect the higher incidence of meconium aspiration syndrome in term neonates and the tendency for term babies to develop more severe pulmonary vasoconstriction due to more mature but reactive pulmonary vasculature (78,79).

This association has important clinical implications for risk stratification and resource allocation in rural settings. Term neonates with PPHN may require more intensive monitoring and earlier intervention to prevent progression to severe disease. The finding also supports the need for enhanced intrapartum care for term pregnancies, particularly in rural areas where emergency obstetric services may be limited.

Blood Gas Analysis and Acid-Base Status

The high prevalence of severe acidosis (51.2% with pH <7.20) in our study population indicates significant physiological derangement at presentation. This is substantially higher than reported in developed countries, where severe acidosis is typically present in 20-30% of PPHN cases (80). The severe acidosis likely reflects delayed presentation, inadequate initial stabilization, and transport-related delays common in rural healthcare settings.

The mean pH of 7.10 ± 0.25 indicates significant metabolic and respiratory acidosis, which can perpetuate pulmonary vasoconstriction and worsen PPHN severity (81). Hypercapnia (75%)

and hypoxemia (71.3%) were also highly prevalent, reflecting the severity of respiratory compromise in our population. These findings emphasize the importance of prompt recognition, adequate ventilatory support, and correction of acid-base abnormalities in the management of PPHN in rural settings.

Clinical Implications and Healthcare System Considerations

Our findings have several important implications for rural healthcare systems in developing countries. The high prevalence of MSAF as a risk factor highlights the need for improved obstetric care, including better intrapartum monitoring, skilled birth attendance, and emergency obstetric services. The delayed presentation pattern suggests that strengthening referral systems and improving transport facilities could significantly impact outcomes.

The predominance of severe disease at presentation indicates that prevention strategies may be more cost-effective than treatment approaches in resource-limited settings. This includes improving antenatal care quality, early identification of high-risk pregnancies, and ensuring skilled attendance at delivery (82,83). The male predominance and term gestation association with severe disease should inform risk stratification protocols in rural NICUs.

Study Limitations

Several limitations should be acknowledged in interpreting our findings. As a single-center study from one rural region, the generalizability to other rural populations may be limited. The retrospective nature of risk factor assessment may introduce recall bias, particularly for maternal factors. Additionally, the lack of long-term follow-up data limits our understanding of outcomes and neurodevelopmental sequelae in this population.

The study also lacks comparison with urban tertiary centers, which would provide valuable insights into healthcare disparities. Resource constraints prevented detailed assessment of some maternal factors such as maternal smoking, alcohol consumption, and detailed medication history, which may influence PPHN risk. Future multicenter studies with prospective design and longer follow-up periods would provide more robust evidence for developing prevention and management strategies.

Future Research Directions

Future research should focus on developing and validating prediction models for PPHN risk in rural populations, incorporating easily measurable maternal and fetal parameters. Intervention studies evaluating the impact of improved obstetric care on PPHN incidence would provide valuable evidence for policy development. Additionally, studies examining the cost-effectiveness of different prevention and treatment strategies in resource-limited settings are urgently needed.

Research into culturally appropriate educational interventions for pregnant women and healthcare providers in rural areas could help improve recognition and management of high-risk pregnancies. Long-term follow-up studies of PPHN survivors in rural settings would provide important data on neurodevelopmental outcomes and inform counseling practices.

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