

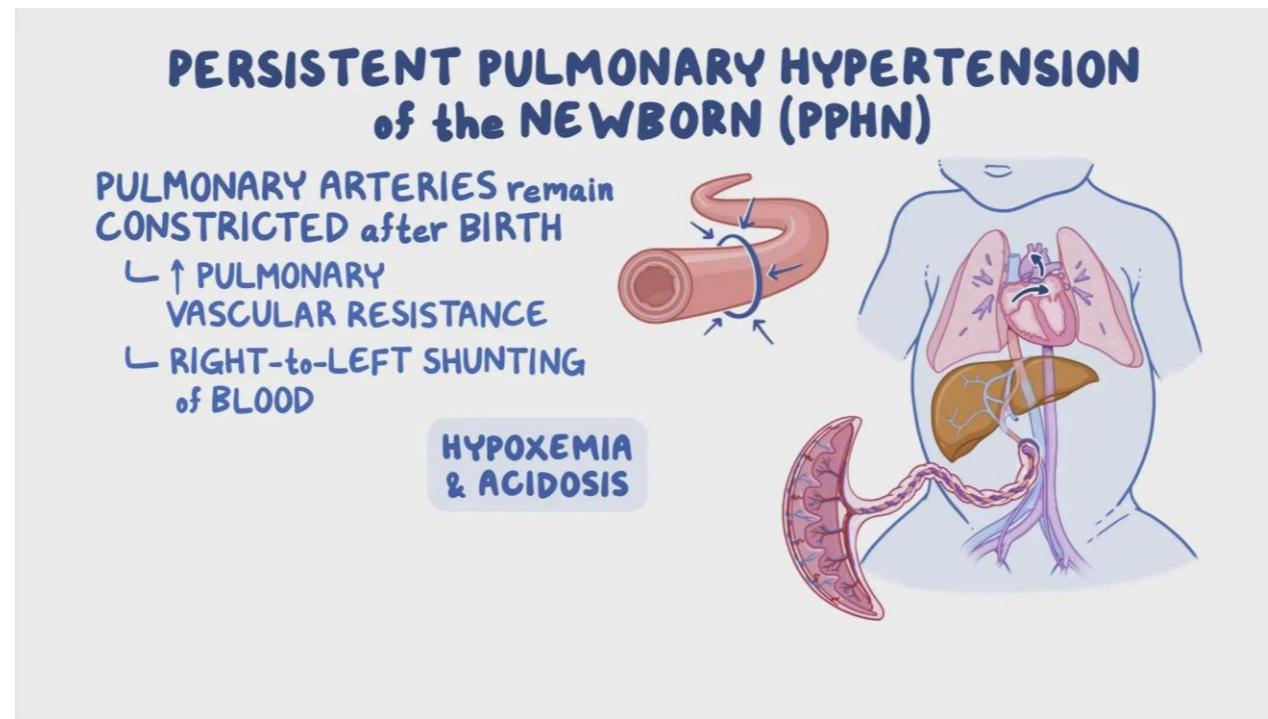
Persistent pulmonary hypertension of the newborn: clinical course, outcomes, and use of sildenafil

Dr Merlisa Kuama
Master in Medicine Child Health
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Outline

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Introduction



- Persistent pulmonary hypertension of the newborn (PPHN) is one of the most serious respiratory disease in the neonate.
- The incidence of PPHN is between 0.4 to 6.8 per 1000 live births. [1][2][10]

The ❤️ of this study



Literature Review

- PPHN remains a challenge to diagnose in low to middle income countries and current effective treatment are not always available.
- Despite Echocardiography (ECHO) remaining the gold standard for diagnosing PPHN other diagnostic approaches include simultaneous pre- and post-ductal oxygen saturation measurements, CXR, complete blood count and arterial blood gas analysis [2][3][4]
- Of these approaches, a more simple approach to diagnosing PPHN is pre ductal and post ductal saturations.

Literature Review (Cont.)

- A difference in oxygen saturation between pre-ductal (right upper limb) and post-ductal (either lower limb) measurements of $\geq 5-10\%$ is considered significant and suggestive of PPHN [6][11]
- A study in India showed that even in peripheral health centres with limited resources PPHN can be diagnosed with pulse oximetry (pre and post ductal SpO₂ difference of $>10\%$) along with clinical assessment. Around 61.5% were diagnosed with PPHN based on pulse oximetry alone before the first dose of sildenafil, which was confirmed by ECHO later in 75% of the cases.
- In PPHN, the pre-ductal saturation is typically higher than the post-ductal, while in some congenital heart defects, this pattern may be reversed or absent [13]

Literature Review (Cont.)

- There are now several alternative therapies available such as extracorporeal membrane oxygenation (ECMO), high frequency ventilation (HFV), surfactant and inhaled nitric oxide (iNO) [5][6]
- However all have also proven to be expensive and unavailable in many regions of the world.
- Despite these limitations studies have shown that sildenafil treatment can significantly improve oxygenation in neonates with PPHN. [8][9]
- A meta-analysis of randomised controlled trials demonstrated a steady improvement in oxygenation after the first dose of sildenafil, with potential for reducing mortality in these infants. [14]
- Study in India PPHN improved in 92.3% of the study population (24/26 cases), out of which 62.5% were diagnosed based on pulse oximetry alone before intervention. [17]

Aims

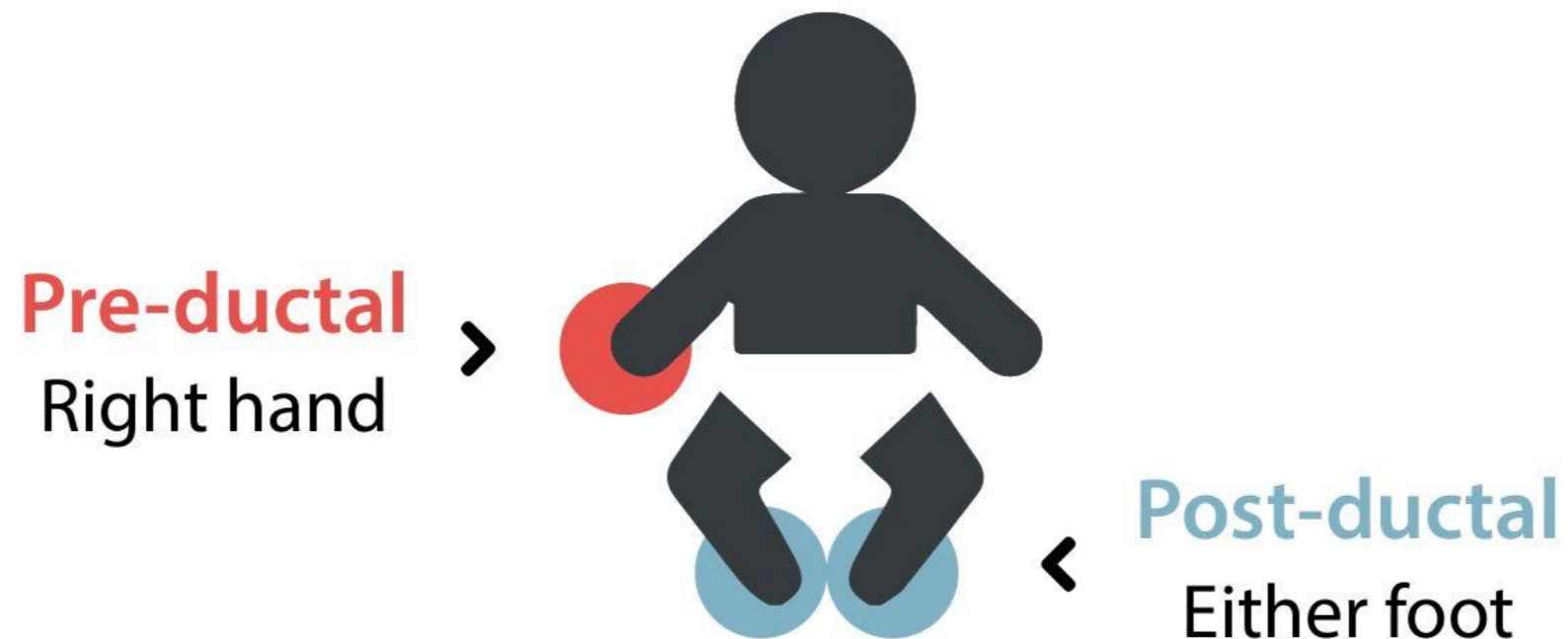
- To observe oxygen saturations and outcomes of sildenafil treatment in neonates with suspected PPHN at PMGH, SCN

Methodology

- Study Design: Observational Study
- Study Setting: Special Care Nursery at Port Moresby General Hospital
- Sample Size:
 - 42 neonates admitted to SCN
 - May - October (6 months) that fit study criteria
- Data Collection: Collection forms, Google forms
- Data Analysis: Microsoft Excel, descriptive statistics
- Sampling strategy: Researcher collected observations from neonates recruited

Methodology (Cont.)

- Inclusion Criteria:
 - Term or late term neonates (gestations > 35.5 weeks) with:
 - Hypoxaemia SpO₂ <90% at birth or cyanosis
 - A pulse oximetry oxygen saturation gradient >5-10%
 - Saturations not improving on single source oxygen
- Exclusion Criteria:
 - Preterm (gestations < 35.5 weeks)
 - Multiple congenital deformities



Respiratory Distress Score

Score	0	1	2
Respiratory Rate	<60	60 - 80	>80
Cyanosis	None	In Room Air or with 1L/min oxygen	With 2L/Min oxygen
Chest Recessions	None	Mild	Moderate Severe
Grunting	None	Audible with stethoscope	Audible without stethoscope
Air Entry	Clear	Decreased or crackles	Barely audible

Ethical Considerations

- Ethical Clearance received from Port Moresby General Hospital Ethics committee.
- Informed verbal consent: verbal consent was taken from mothers of participating neonates
- Confidentiality: patient information protected by using unique study codes, password security and limited sharing of data
- Safety: all infants where given treatment measures equally. No treatment needed was withheld at any time.

Results

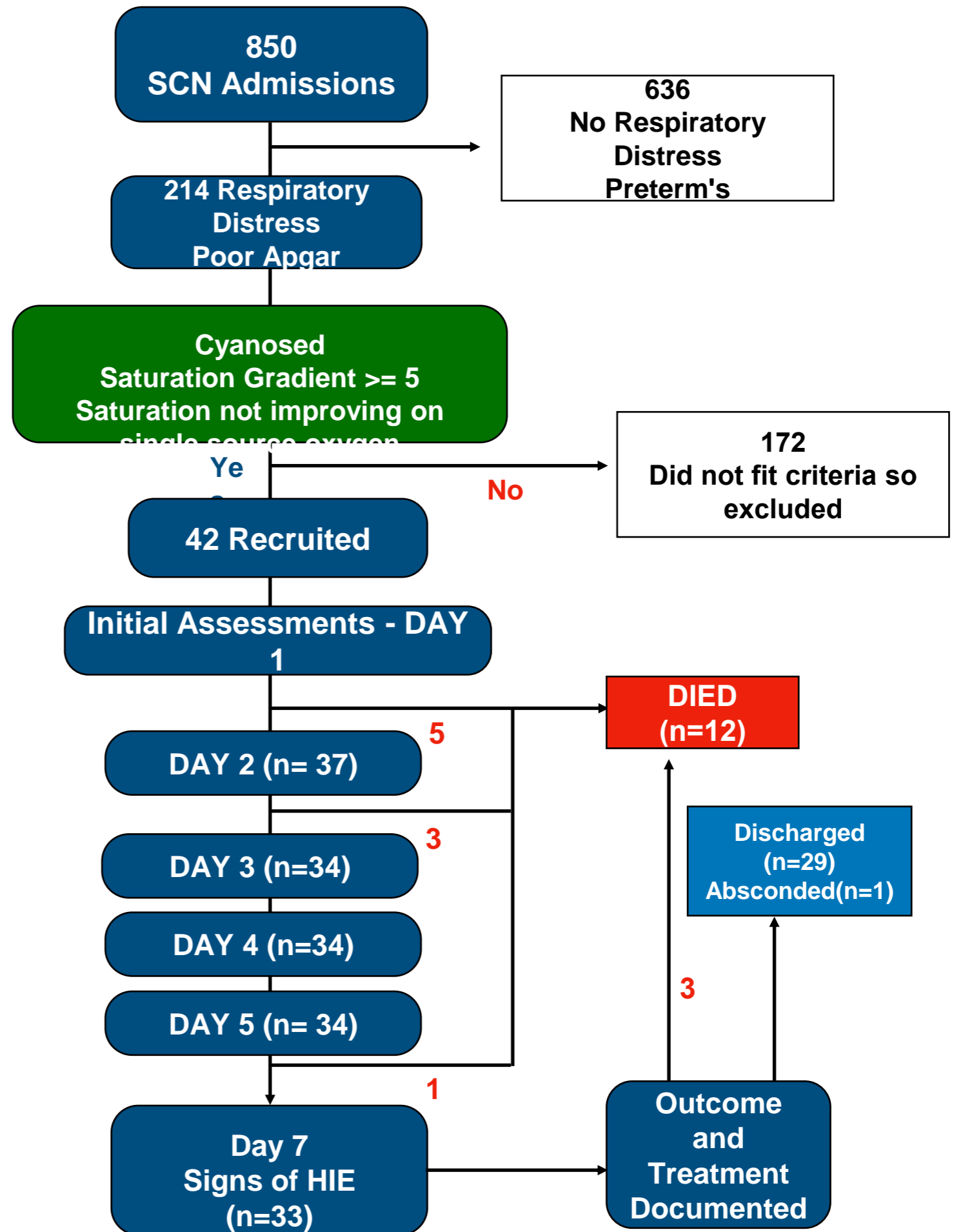


Table 1: Characteristics of neonates

Charateristics	n	%	Mean	\pm SD	Median	IQR
Gender (N=42)						
Male	24	57		-	-	-
Female	18	43		-	-	-
Gestational Age in weeks (N= 37)	-	-	39.1	1.5	-	-
Birthweight in grams (N=42)	-	-		-	3161.5	2802.5 - 3567.5
Mode of delivery (N=42)						
NVD	22	52.3		-	-	-
C/S	18	42.9		-	-	-
Vacuum	2	4.8		-	-	-

Table 2 - Neonatal clinical presentation

Clinical Presentation	n	%	Mean	± SD	Median	IQR
Respiratory Rate (breaths/min) (N=41)	-	-	-	-	83.7	68.5 - 99
Heart Rate (beats/min) (N=41)	-	-	-	-	153.7	148 - 164
Central Cyanosis (N=42)	8	19	-	-	-	-
Peripheral Cyanosis (N=42)	38	90	-	-	-	-
Grunting (N=42)	37	88	-	-	-	-
Nasal Flaring (N=42)	41	98	-	-	-	-
Intercostal Recessions (N=41)	39	95	-	-	-	-
Bilateral Crepitations (N=42)	33	79	-	-	-	-
Reduced Air Entry (N=42)	32	76	-	-	-	-
Loud P2 (N=42)	30	71	-	-	-	-
Pre-Duct Oxygen Saturation (In Room Air) (N=38)	-	-	77.9	19.3	-	-
Post-Duct Oxygen Saturation (in Room Air) (N=37)	-	-	66.9	18.5	-	-
Oxygen Saturation Gradient (N=37)	-	-	12.8	6.75	-	-
Oxygen Therapy Required (N=42)						
Single Source	28	67	-	-	-	-
Double Source	10	23	-	-	-	-
Ventilation	4	10	-	-	-	-

Table 3: Neonatal diagnoses

Diagnosis	n (N=42)	%	Died (N=12)	%	Survived (N=30)	%
Meconium Aspiration Syndrome (MAS)	15	33	3	7	12	26
Severe Birth Asphyxia (SBA)/MAS	10	24	6	14	4	10
Peunmonia (PNA)	4	10	0	0	4	10
Transient Tachypnea of the newborn (TTN)	3	7	0	0	3	7
Neonatal Sepsis (NNS)	3	7	0	0	3	7
SBA	2	5	1	2	1	2
Respiratory Distress Syndrome	2	5	2	5	0	0
Moderate Birth Asphyxia	3	2	0	0	3	2

Table 4: Investigations

Characteristics	N	%	Mean	± SD
Haemoglobin (g/dL) (n=25)	-	-	15.5	2.7
White Blood Cell Count (x10 ³ /μL) (n=25)	-	-	13.6	6.1
Platelet Count (x10 ³ /μL) (n=25)	-	-	224	117.7
Blood Culture (n=42)	Growth	9	21.4	-
	No Growth	18	42.9	-
	Not Performed	15	35.7	-
Chest Xray Findings	Normal	1	2.3	-
	Abnormal	34	81.0	-
	Not Done	7	16.7	-
Echocardiography Findings	Normal	2	4.8	-
	Abnormal	1	2.4	-
	Not Performed	39	92.8	-

Table 5: Treatment and Outcome

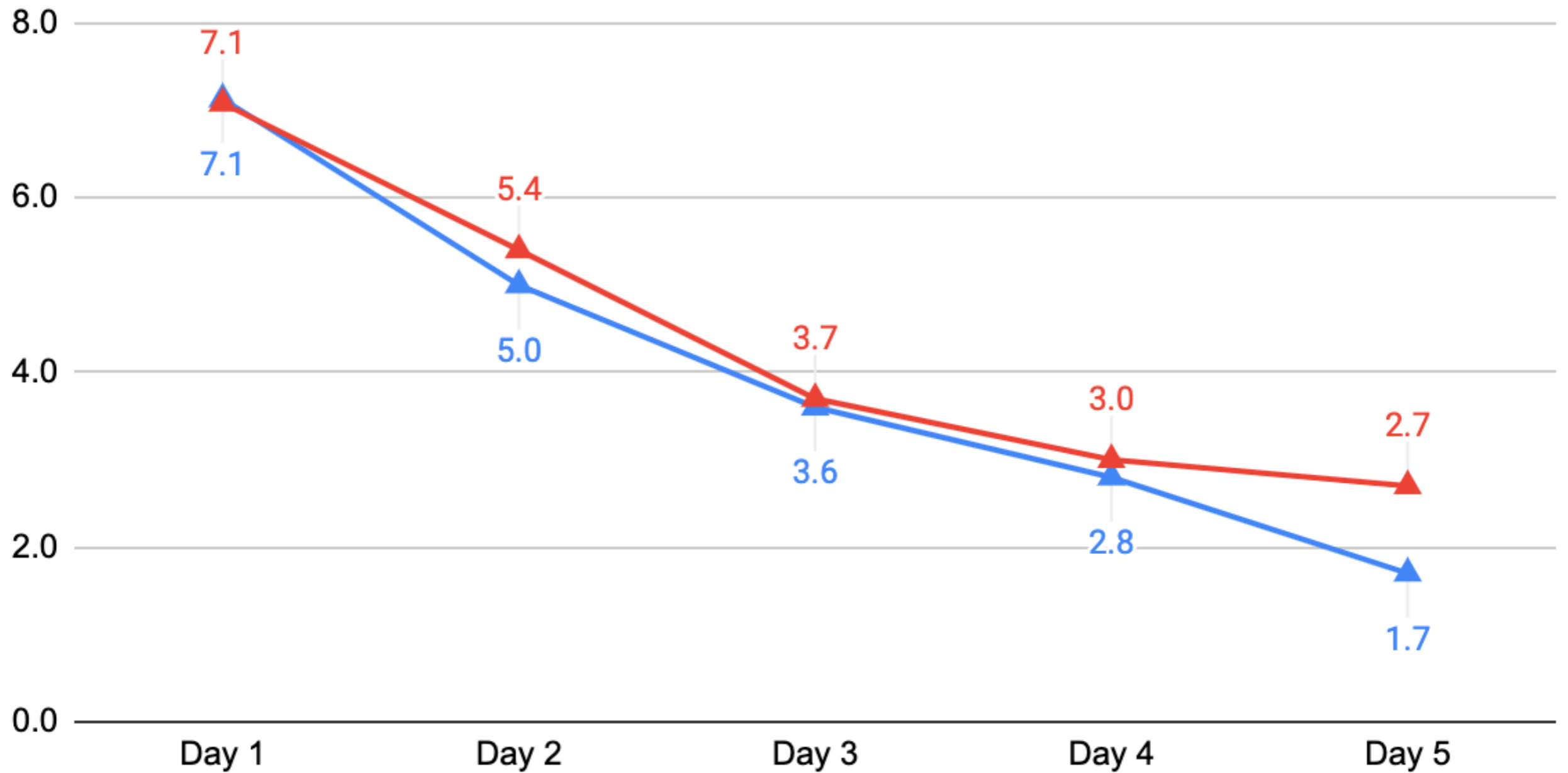
Treatment and Outcomes	n	%	Mean	± SD
Sildenafil dose (mg/kg)	-	-	1.08	0.3
Duration of Sildenafil treatment (days)	-	-	5.4	4.4
Total Sildenafil dose (mg/day)	-	-	4.3	1.2
Dose changed after 24 hours	7	16.7		
Days spend on oxygen	-	-	5.6	4.6
Length of hospital stay in days	-	-	7.7	6.5
Final outcome (N= 42)				
Died	12	29	-	-
Discharged	29	69	-	-
Absconded	1	2	-	-

Table 6: Improvement in clinical features after 24 hours of Sildenafil commenced

Characteristics	n (N=42)	%
Cyanosis	13	31.0
Tachypnoea	8	19.0
Tachycardia	14	33.3
Grunting	21	50.0
Intercostal recessions	10	23.8
Loud P2	2	4.8
Bilateral crepitation's	5	11.9
Reduced air entry	5	11.9

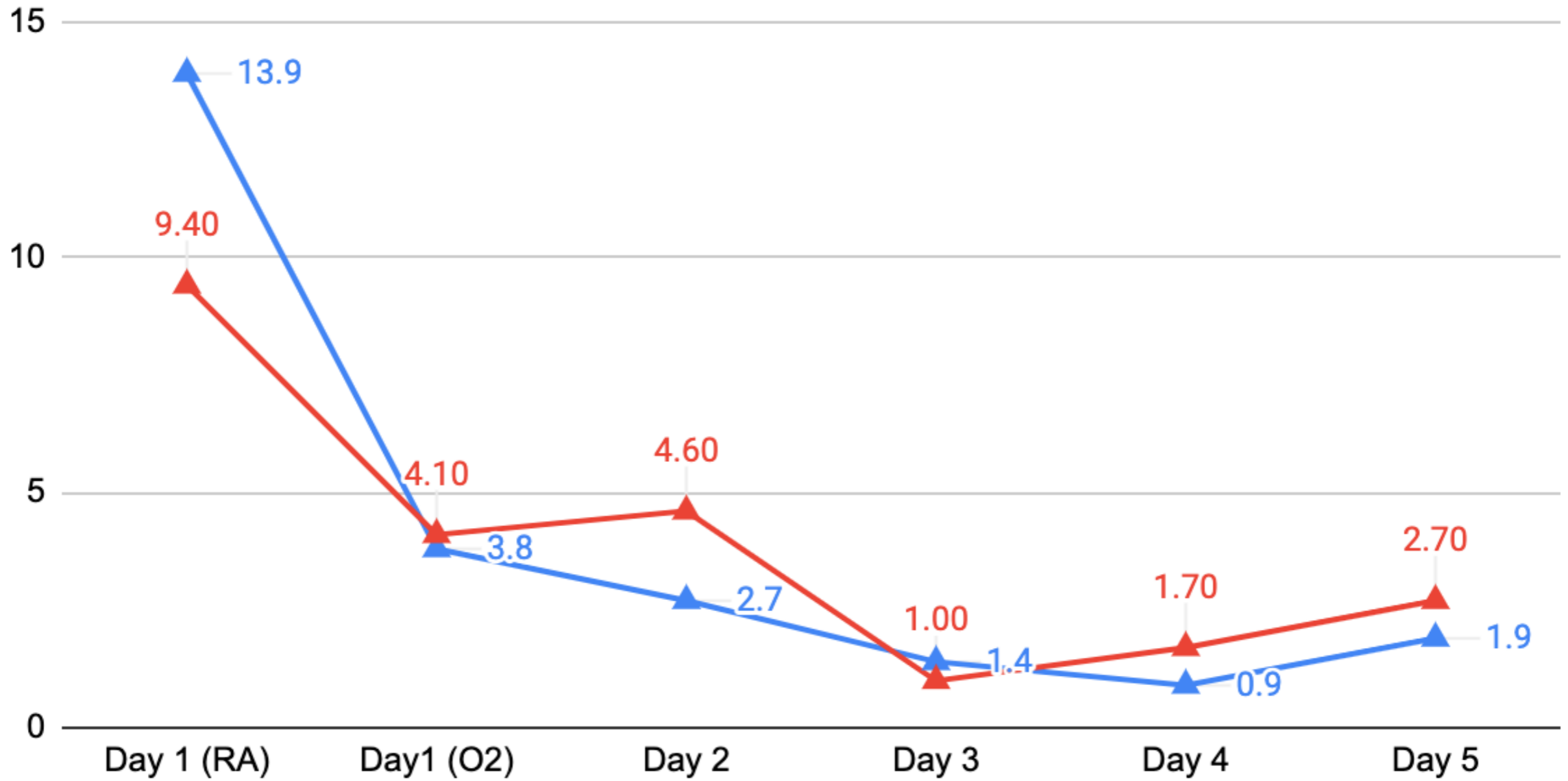
Graph 1: Respiratory distress score over 5 days

▲ Survived (n=30) ▲ Died (n =12)



Graph 2: Delta saturations over 5 days

▲ Survived (n=30) ▲ Died (n=12)



Discussion

Study Findings

- Out of 214 cases of respiratory distress, 42 neonates (19.6%) were diagnosed with PPHN, characterised by saturation difference of >5-10%
- The in-hospital mortality rate among these PPHN cases was 28.6%
- Similar mortality rates for PPHN have been reported in studies from Malaysia^[12]

Underlying Conditions and Mortality

- The majority of PPHN cases were associated with:
 - MAS: 15 cases (33%)
 - Both MAS and SBA: 10 cases (24%)
 - PNA: 4 cases (10%)
- Higher mortality was observed in neonates with both MAS and SBA (14%)
- A 9 year cohort study (2023) shows that SBA is a risk factor of death in neonates with MAS. The overall mortality for MAS was 7.8% which increased with SBA ^[18]

Discussion

MAS and PPHN Relationship

- Literature identifies a common triad: MAS, PPHN and Hypoxic Ischemic Encephalopathy (HIE):
 - MAS most common underlying diagnosis of PPHN 30 - 50% [15]
 - Infants with MAS - 15 - 20% Develop PPHN [16]

Improvement with Sildenafil Treatment

- Symptoms that improved with sildenafil treatment included grunting (50%), tachycardia (33%) and cyanosis (31%)
- Sildenafil also reduced respiratory distress scores and saturation differences suggesting potential benefits in improving outcomes
- Studies in Malaysia a meta study showed improvement in oxygenation after the first dose of sildenafil, with potential for reducing mortality in these infants. [12]

Discussion

Oxygen Therapy and Hospital Stay

- The mean duration of oxygen therapy was 5.6 days, with an average hospital stay of 7.7 days
- While sildenafil appeared to improve outcomes, further studies are needed to confirm its efficacy.

Safety and implications of sildenafil use

- No adverse side effects were observed with sildenafil during the study, supporting its safety at a dosage of 1 - 2 mg/kg QID consistent with existing literature
- A cochraine study (2017) that identified 5 studies showed improvement after first dose of sildenafil, no clinically important side effects seen and reduction in mortality ^[8]

Discussion

Safety and implications of sildenafil use

- This study has significant implications for neonatal care in resource limited settings:
 - Provided valuable data on PPHN incidence and risk factors, enabling targeted interventions
 - Evaluates sildenafil outcomes which could inform treatment protocols
 - Validates the use of pre- and post-ductal saturation measurements for diagnosing PPHN
- Limitations:
 - Limited recruitment of respiratory distressed neonates
 - No standard local guidelines for Sildenafil in PPHN
 - No Echo machine in SCN to diagnose PPHN on admission.
 - Small sample size

Recommendations

- Conduct More Research
 - Expand studies on sildenafil effectiveness and long-term outcomes in PPHN.
- Training on Early Identification
 - Implement training programs for prompt recognition of PPHN symptoms.
- Introduce Echocardiography in SCN
 - Acquire an echo machine for accurate PPHN diagnosis.
 - Train SCN staff on echo use for timely intervention.
- Develop PPHN Management Protocols
 - Standardise care with evidence-based protocols for treatment and monitoring.

Conclusion

- This prospective observational study addresses critical gaps in knowledge regarding PPHN management in resource-limited settings.
- Its findings could significantly impact clinical practice in similar environments, potentially improving outcomes for neonates with PPHN.
- Further research comparing sildenafil to other treatments and assessing long-term outcomes would be valuable additions to this important work.

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Thank You



