

**Determining the Clinic-Etiological Profile of Respiratory Distress and its Outcome among Preterm Newborns**Priya Verma<sup>1</sup>, Gopal Shankar Sahni<sup>2</sup><sup>1</sup>Assistant Professor, Department Of Pediatrics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India<sup>2</sup>Associate professor & HOD, Department Of Pediatrics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

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Conflict of interest: Nil

**Abstract****Aim:** The aim of the present study was to determine causes of respiratory distress, pattern of respiratory modality used and its outcome among admitted preterm newborns.**Methods:** A retrospective descriptive study was conducted in the Department Of Pediatrics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India over a period of two years targeting all neonates admitted to neonatology department. A Total of 200 patients were admitted in NICU during the study.**Results:** Mean gestational age was 32.46±2.58 weeks. Most of the newborns (64%) belonged to the gestational age within 28 - <34 weeks category. Mean birth weight was 1665.43±585.58 g among them very low birth weight infants were 42%. Male out numbered female newborns (55% vs 45%). Total 12 (6%) infants had Apgar scores <7 at 5 minutes who required some degree of resuscitation just after birth. After admission 8 (4%) patients got single dose of surfactant. Most of the mother (66%) was multiparous and 51% of them did not receive even a single dose of antenatal corticosteroid. All of them were inborn and cesarean section was the mode of delivery for 80% of the enrolled neonates. Maternal hypertension and diabetes mellitus were present in 140 (70%) and 64 (32%) of mother respectively. Maternal risk factors for sepsis were present in 48 (24%) of infants admitted to the NICU.**Conclusion:** Respiratory distress syndrome is the commonest cause of respiratory distress. Two third of preterm newborns required respiratory support. Most common mode of respiratory support was non invasive mode in the form of supplemental oxygen, Heated humidified high flow nasal cannula and continuous positive airway pressure. Short term morbidities like nasal trauma, sepsis, septic shock, disseminated intravascular coagulation, necrotising enterocolitis and intraventricular haemorrhage were more common in newborns who required invasive respiratory support (p <0.05). Retinopathy of prematurity and mortality was significantly higher in invasive respiratory support group.**Keywords:** Neonates, Preterm, Mechanical ventilation, Non-invasive ventilationThis is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Preterm neonates often develop respiratory distress syndrome (RDS) due to a surfactant deficiency. [1] Incidence of RDS is inversely proportional to gestational age. It affects approximately 98% of neonates born at or before 24 weeks, while only a quarter of Very Low Birth Weight (VLBW) neonates develop RDS. [2] With advancement in the field of neonatology and usage of maternal antenatal steroids for fetal lung maturation, the incidence and severity of RDS have decreased by 34%. [3] Despite this, RDS remains a leading complication among preterm neonates. RDS presents early with difficulty in breathing, grunting and desaturation, which may lead to type 1 and type 2 respiratory failure and

ultimately developing multiorgan dysfunction if not treated optimally and timely. [1]

Treatment strategies for RDS include surfactant administration and respiratory support, including invasive and non-invasive ventilation. These respiratory support strategies have led to improved neonatal survival and outcomes. [4] Invasive ventilation may cause significant complications like atelectasis, pneumothorax and ventilator-associated pneumonia compared with non-invasive ventilation. There is an increasing trend to initiate non-invasive ventilation. [5,6] This is particularly true for low- and middle-income countries (LMIC) due to the

limited resources and expertise for invasive ventilation. [7]

Respiratory distress syndrome (RDS) in newborns is the most common cause of morbidity and mortality and is an indication for ventilation in preterm infants. [8] In recent years, the widespread implementation of nasal continuous positive airway pressure (CPAP) as the initial means of respiratory support for preterm infants has fundamentally changed respiratory management in the first hours of life. The universal use of CPAP has reduced the need for endotracheal intubation and mechanical ventilation (MV) [9] and their associated lung injuries. [10,11] The American Academy of Pediatrics [12] and the European Consensus Guidelines for the Management of RDS [13] recommended that the initial application of CPAP be considered as the optimal mode of respiratory support.

The aim of the present study was to determine causes of respiratory distress, pattern of respiratory modality used and its outcome among admitted preterm newborns.

#### Materials and Methods

A retrospective descriptive study was conducted in the Department Of Pediatrics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India over a period of two years targeting all neonates admitted to neonatology department. A Total of 200 patients were admitted in NICU during the study.

Ethical approval was taken from Ethical Review Committee of the institution. All inborn preterm neonates having gestational age of <37 weeks and admitted with respiratory distress were included in the study. Neonates with incomplete data and or lethal congenital anomalies were excluded from the study. Data were collected from the neonatal admission, discharge and death registers. The register contained each neonate's date of admission and discharge or death, sex, weight at admission or at birth, gestation age at birth, mode of delivery, duration of stay at the hospital, diagnosis and outcomes. The primary causes of admissions and deaths were defined as the underlying obstetric and neonatal factors or conditions, which resulted in the admission or death of the neonate. Standard definitions of the medical conditions were used for diagnosis. [14] All medical and nursing staff working at the neonatal unit was oriented on recording of the neonatal admission, discharge and death registers, clinical guidelines of diagnosis and compilation of monthly summaries for presentation at monthly perinatal mortality meetings. Extracted data included: mode of delivery, multiple gestations, use of antenatal corticosteroid, gestational diabetic mellitus (GDM), Pregnancy induced hypertension (PIH), risk factor for sepsis, sex of the baby,

gestational age (weeks), birth weight (g), APGAR score at 5th minutes, Silverman- Anderson score (SAS), neonatal resuscitation, surfactant administration, fetal growth at birth (SGA, AGA, LGA), respiratory distress, cause of respiratory distress, mode of respiratory support (NIV, MV) and days of hospitalization.

Neonates born at less than 37 completed weeks (less than 259 days) of gestation were termed as preterm and those having birth weight of < 2500 g were defined Low birth weight (LBW).<sup>14</sup> Newborns was defined small for gestational age (SGA) if the birth weight less than the 10th percentile. Resuscitation was defined as need for intermittent positive pressure ventilation and/or cardiac compression and/or drug administration in the neonatal stabilization period. Respiratory distress in newborn was labelled when a baby had one or more signs of increased work of breathing, such as tachypnea, nasal flaring, chest retractions, or grunting.<sup>8</sup> Severity of respiratory distress was categorized using Silverman-Anderson scoring system where Score  $\geq 4$  indicate clinical respiratory distress and score  $\geq 7$  indicate respiratory failure. [15]

Respiratory distress syndrome (RDS) was defined in neonates with increasing oxygen dependence during the first 24 h, typical radiological findings: like reduced air content, reticulo-granular pattern of the lungs, air bronchogram and/or white out lung. When newborns developed respiratory distress soon after birth and resolves within 18-24 hours of life with normal chest X-ray finding or show reduced translucency, infiltrates and hyperinflation of the lungs were labelled as Transient Tachypnea of newborn (TTN). Breathing pauses that last for > 20 seconds or for > 10 seconds if associated with bradycardia or oxygen desaturation was termed as apnea. Bronchopulmonary Dysplasia (BPD) was defined when a neonate was requiring oxygen at 36 weeks of post gestational age for babies born < 32 weeks of gestation or 28 days of age for neonates born  $\geq 32$  weeks of gestation or later. [15]

Maternal characteristics included as maternal age, maternal diseases like gestational and non-gestational diabetes mellitus, Pregnancy induced hypertension, infections and use of antenatal corticosteroids. Deliveries were categorized as vaginal or Cesarean Section (CS). The Data on respiratory support such as oxygen therapy administered through nasal-cannula, nasal continuous positive airways pressure (CPAP), heated humidified high flow nasal cannula (HHFNC) and mechanical ventilation (MV) was collected. When analyzing the data, for each neonate only the highest level of respiratory support was considered. The need for specific adjunctive therapy (surfactant Administration) and the short-term outcome including morbidities and in hospital mortality were recorded. Respiratory support was

divided into two groups as Invasive (Mechanical ventilation) and noninvasive which included supplemental oxygen through nasal cannula, head box, High flow nasal cannula and continuous positive airway pressure (CPAP). All the variables and mortality were compared between the two groups

Statistical analysis: Data entry and analysis was carried out by using the Statistical Package of Social

Science Software program (SPSS), version 22. Categorical variables were expressed in frequency and statistical analysis was done by Chi-Square test or Fisher exact test. Continuous variable was seen in mean  $\pm$  SD and statistical analysis was done by student t-test. P value  $<0.05$  was considered statistically significant.

## Results

**Table 1: Baseline neonatal characteristics in studied neonates**

Parameter	Value
Gestational age (weeks), Mean $\pm$ SD	32.46 $\pm$ 2.58
Gestational age category, n (%)	
<28 weeks	12 (6)
28-<34 weeks	128 (64)
34-<37 weeks	60 (30)
Birth weight (g), Mean $\pm$ SD	1665.43 $\pm$ 585.58
Birth weight category, n (%)	
<1000 g	20 (10)
1000-1499 g	84 (42)
1500-2499 g	80 (40)
$\geq$ 2500 g	16 (8)
Sex of the baby, n (%)	
Male	110 (55)
Female	90 (45)
Multiple birth, n (%)	44 (22)
Neonatal resuscitation, n (%)	12 (6)
APGAR score at 5th minute	
$\geq$ 7	188 (94)
<7	12 (6)
Silverman Anderson Score at randomization	
<4	28 (14)
4-7	172 (86)
>7	0
Surfactant administration, n (%)	8 (4)

Mean gestational age was 32.46 $\pm$ 2.58 weeks. Most of the newborns (64%) belonged to the gestational age within 28 - <34 weeks category. Mean birth weight was 1665.43 $\pm$ 585.58 g among them very low birth weight infants were 42%. Male out

numbered female newborns (55% vs 45%). Total 12 (6%) infants had Apgar scores  $<7$  at 5 minutes who required some degree of resuscitation just after birth. After admission 8 (4%) patients got single dose of surfactant.

**Table 2: Baseline maternal characteristics in studied group**

Parameter	Value
Consanguinity present, n (%)	4 (2)
Parity, n (%)	
Primipara	68 (34)
Multipara	132 (66)
Exposure to ACS, n (%)	
Complete	34 (17)
Incomplete	64 (32)
None	102 (51)
Mode of delivery, n (%)	
NVD	40 (20)
LUCS	160 (80)
GDM, n (%)	64 (32)
PIH, n (%)	140 (70)
Risk factors for sepsis, n (%)	48 (24)

Most of the mother (66%) was multiparous and 51% of them did not receive even a single dose of antenatal corticosteroid. All of them were inborn and cesarean section was the mode of delivery for 80% of the enrolled neonates. Maternal hypertension and

diabetes mellitus were present in 140 (70%) and 64 (32%) of mother respectively. Maternal risk factors for sepsis were present in 48 (24%) of infants admitted to the NICU.

**Table 3: Primary disease requiring respiratory support**

Parameter	Value
RDS, n (%)	102 (51)
Transient tachypnoea of newborn, n (%)	46 (23)
Congenital Pneumonia, n (%)	40 (20)
Perinatal asphyxia, n (%)	12 (6)
Meconium aspiration syndrome, n (%)	0

The respiratory distress syndrome (RDS) was the most common cause 102 (51%) following TTN 46 (23%), congenital pneumonia 40 (20%) and PNA 12 (6%).

**Table 4: Level of respiratory support**

Parameter	Value
Noninvasive support, n (%)	130 (65)
Invasive support, n (%)	70 (35)

Among total of 200 patients, 130 (65%) patients required NIV support including oxygen, CPAP or HFNC and 70 (35%) need Invasive support during the hospital course.

**Table 5: Associated mortality and morbidity of neonates who required respiratory support**

Parameters	NIV group (n=130)	IV group (n=70)	P value
PDA, n`	40	32	0.48
Sepsis, n	56	36	<0.001
Septic Shock, n	24	28	<0.001
DIC, n	8	24	<0.001
AKI, n	22	16	0.36
NEC, n	12	20	0.001
In-hospital mortality, n	12	52	<0.001

Among the associated mortality and morbidity, sepsis, septic shock, DIC, NEC and in-hospital mortality occurred significantly higher in the invasive support group (IV) in comparison to the NIV support group and the p-value were <0.05.

**Table 6: Complication of Respiratory support modality in preterm neonates**

Parameters	NIV group (n=130)	IV group (n=70)	P value
Nasal trauma, n	14	24	0.001
Pneumothorax, n	0	2	0.16
ROP, n	8	16	0.018
BPD, n	2	6	0.090
IVH, n	0	10	0.001

Among the complication of respiratory support only nasal trauma, sepsis, ROP and IVH occurred significantly higher in the MV support group in comparison to the NIV support group and the p-value were <0.05.

## Discussion

The first 28 days of life, defined as neonatal period is the most vulnerable time for a child's survival. Every year an estimated 4 million babies die in the

first 4 weeks of life [16] accounting for more than half of the under-five child deaths in most regions of the world. [17] Almost all (99%) neonatal deaths are happening in developing countries. [18] Neonatal mortality rate is one of the indicators for measuring the health status of a nation. The mortality and morbidity of preterm neonates are significantly higher than those of full-term neonates because preterm neonates are more prone to develop respiratory failure. [19] The functional immaturity

of their lung structure, can lead to impaired gas exchange and requires respiratory support. [20]

Mean gestational age was  $32.46 \pm 2.58$  weeks. Most of the newborns (64%) belonged to the gestational age within 28 - <34 weeks category. Mean birth weight was  $1665.43 \pm 585.58$  g among them very low birth weight infants were 42%. Male outnumbered female newborns (55% vs 45%). Total 12 (6%) infants had Apgar scores <7 at 5 minutes who required some degree of resuscitation just after birth. After admission 8 (4%) patients got single dose of surfactant. Nemr CN, et al. showed 100 cases with gestational age ranging from 27 to 40 weeks having mean of  $33.98 \pm 3.44$  weeks. Mean birth weight in our study was  $1631.44 \pm 578.57$ g which was comparable with the same study where mean birth weight was 1580 gm. [21] Male outnumbered female newborns (54.2% vs 45.8%). Similar finding was found by Nemr CH where sixty- three (63%) were boys and thirty-seven (37%) were girls and by Iqbal Q (60% males). [22]

Most of the mother (66%) was multiparous and 51% of them did not receive even a single dose of antenatal corticosteroid. All of them were inborn and cesarean section was the mode of delivery for 80% of the enrolled neonates. Maternal hypertension and diabetes mellitus were present in 140 (70%) and 64 (32%) of mother respectively. Maternal risk factors for sepsis were present in 48 (24%) of infants admitted to the NICU. In Lategan I, et al [23] 17.3% infants of < 34 weeks had optimal ANS, birth by Cesarean Section done in 60.3% of cases, maternal hypertension was present in 43.6% of mothers. The respiratory distress syndrome (RDS) was the most common cause 51 (51%) following TTN 23 (23%), congenital pneumonia 20 (20%) and PNA 6 (6%). Among total of 100 patients, 65 (65%) patients required NIV support including oxygen, CPAP or HFNC and 35 (35%) need Invasive support during the hospital course. Among the associated mortality and morbidity, sepsis, septic shock, DIC, NEC and in-hospital mortality occurred significantly higher in the invasive support group (IV) in comparison to the NIV support group and the p-value were <0.05. Among the complication of respiratory support only nasal trauma, sepsis, ROP and IVH occurred significantly higher in the MV support group in comparison to the NIV support group and the p- value were <0.05. Nemr CN, et al. showed 72% of the studied patients underwent CPAP, 14% underwent oxygen support by nasal cannula and 14% underwent mechanical ventilation. [21] The need of invasive support was less than our study as they utilize non-invasive respiratory support as most widely used modality and practiced different ways of delivering CPAP.

In the current study, non- invasive respiratory support was given by nasal cannula, head box, CPAP and invasive support by mechanical

ventilation. We used nasal CPAP with preterm neonates with recurrent apneas or early features of RDS. Those who had a failure of nasal CPAP therapy or had respiratory acidosis were ventilated. This is similar to the results of Iqbal Q, et al. in which all the preterm neonates with gestational age < 32 weeks or recurrent apnea or early features of RDS were given nasal CPAP therapy, and those who had a failure of nasal CPAP therapy were ventilated. [22] Judicious ventilator strategies, proper sedation, timely extubation and readily available X-ray and surgical facilities will help to control these problems. Mortality among sick neonates in NICU is high, but mortality among mechanically ventilated neonates is even higher. In this study, mortality in ventilated neonates was 60%, which is comparable to mortality by Hossain et al. 70.6 %. [24]

### Conclusion

Respiratory distress syndrome is the commonest cause of respiratory distress. Two third of preterm newborns required respiratory support. Most common mode of respiratory support was non invasive mode in the form of supplemental oxygen, Heated humidified high flow nasal cannula and continuous positive airway pressure. Short term morbidities like nasal trauma, sepsis, septic shock, disseminated intravascular coagulation, necrotising enterocolitis and intraventricular haemorrhage were more common in newborns who required invasive respiratory support ( $p < 0.05$ ). Retinopathy of prematurity and mortality was significantly higher in invasive respiratory support group.

### References

1. Yadav S, Lee B, Kamity R. Neonatal respiratory distress syndrome.
2. Ekhuagere OA, Okonkwo IR, Batra M, Hedstrom AB. Respiratory distress syndrome management in resource limited settings— Current evidence and opportunities in 2022. *Frontiers in pediatrics*. 2022 Jul 29;10:961509.
3. Roberts D. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev*. 2007;4.
4. Mahmoud RA, Roehr CC, Schmalisch G. Current methods of non-invasive ventilatory support for neonates. *Paediatr Respir Rev*. 2011 Sep;12(3):196-205.
5. Luo K, Huang Y, Xiong T, Tang J. High-flow nasal cannula versus continuous positive airway pressure in primary respiratory support for preterm infants: a systematic review and meta-analysis. *Frontiers in Pediatrics*. 2022 Nov 21;10:980024.
6. Wilkinson D, Andersen C, O'Donnell CP, De Paoli AG, Manley BJ. High flow nasal cannula for respiratory support in preterm infants.

- Cochrane Database of Systematic Reviews. 2016(2).
7. Miller JD, Carlo WA. Pulmonary complications of mechanical ventilation in neonates. *Clin Perinatol.* 2008 Mar;35(1):273-81, x-xi.
  8. Shao X-M, Ye H-M, Qiu X-S. Practice of neonatology (update 5). Beijing: People's Medical Publishing House; 2019. p. 855, 632, 1025. [Google Scholar]
  9. Robertson NR. Early nasal CPAP reduces the need for intubation in VLBW infants. *Eur J Pediatr.* 1998;157:438-440.
  10. Attar MA, Donn SM. Mechanisms of ventilator-induced lung injury in premature infants. *Semin Neonatol.* 2002;7:353-360.
  11. Apisarnthanarak A, Holzmann-Pazqal G, Hamvas A, Olsen MA, Fraser VJ. Ventilator-associated pneumonia in extremely preterm neonates in a neonatal intensive care unit. *Pediatrics.* 2003;112:1283-1289.
  12. Committee on Fetus and Newborn, American Academy of Pediatrics. Respiratory support in preterm infants at birth. *Pediatrics.* 2014;133(1):171-174.
  13. Sweet D, Carnielli V, Greisen G, Hallman M. European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants-2019 update. *Neonatology.* 2019;115(4):432-450.
  14. Gomella TL, Cunningham DM, Eyal FG, editors. *Neonatology: Management, Procedures, On-call Problems, Diseases and Drugs*, Eighth edition. New York. Mc Graw Hill. Lange; 2020.
  15. Hedstrom AB, Gove NE, Mayock DE, Batra M. Performance of the Silverman Andersen Respiratory Severity Score in predicting PCO2 and respiratory support in newborns: a prospective cohort study. *Journal of Perinatology.* 2018 May;38(5):505-11.
  16. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: when? Where? Why?. *The Lancet.* 2005 Mar 5;365(9462):891-900.
  17. Sweet LR, Keech C, Klein NP, Marshall HS, Tagbo BN, Quine D, Kaur P, Tikhonov I, Nisar MI, Kochhar S, Muñoz FM. Respiratory distress in the neonate: Case definition & guidelines for data collection, analysis, and presentation of maternal immunization safety data. *Vaccine.* 2017 Dec 12;35(48Part A):65-66.
  18. Ayaz A, Saleem S. Neonatal mortality and prevalence of practices for newborn care in a squatter settlement of Karachi, Pakistan: a cross-sectional study. *PLoS One.* 2010 Nov 1; 5(11):e13783.
  19. Hong H, Li XX, Li J, Zhang ZQ. High-flow nasal cannula versus nasal continuous positive airway pressure for respiratory support in preterm infants: a meta-analysis of randomized controlled trials. *The Journal of Maternal-Fetal & Neonatal Medicine.* 2021 Jan 17;34(2):259-66.
  20. Raju TN. Developmental physiology of late and moderate prematurity. In *Seminars in Fetal and Neonatal Medicine* 2012 Jun 1 (Vol. 17, No. 3, pp. 126-131). WB Saunders.
  21. Nemr CN, Bakheet MA, Hassan MA. Outcome of Neonatal Respiratory support Modalities in Sohag University Hospital. *The Egyptian Journal of Hospital Medicine.* 2021 Jan 1;82(4):778-84.
  22. Iqbal Q, Younus MM, Ahmed A, Ahmad I, Iqbal J, Charoo BA, Ali SW. Neonatal mechanical ventilation: Indications and outcome. *Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine.* 2015 Sep;19(9):523.
  23. Lategan I, Price C, Rhoda NR, Zar HJ, Tooke L. Respiratory interventions for preterm infants in LMICs: a prospective study from cape town, South Africa. *Frontiers in Global Women's Health.* 2022 Apr 6;3:817817.
  24. Hossain MM, Shirin M, Al Mamun MA, Hasan MN, Sahidullah M. Predictors of mortality in ventilated neonates in intensive care unit. *Bangladesh Journal of Child Health.* 2009;33(3):77-82.