



## Clinical Profile and Outcome of Neonates with Respiratory Distress Within 24 Hours of Birth, Admitted to a Tertiary Care NICU: A Prospective Observational Study

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Received: May 10, 2026

Revised: May 25, 2026

Accepted: June 08, 2026

Published: June 18, 2026

### Abstract

**Background:** Respiratory distress is the most common cause of NICU admission and a major contributor to neonatal mortality. Identification of aetiology, severity, and risk factors within 24 hours of birth is critical for timely management. **Methods:** A prospective observational study was conducted over 12 months (November 2013–October 2014) at the NICU of Aditya Birla Memorial Hospital, Pune. Neonates with respiratory distress onset within 24 hours of birth were enrolled (n = 206). Clinical profile, aetiology, severity, respiratory support, and outcome were systematically recorded. **Results:** Of 424 NICU admissions, 206 (48.5%) had respiratory distress. Overall mortality was 5.82% (n = 12). Transient tachypnea of the newborn (TTN) was the commonest aetiology (63.1%), followed by respiratory distress syndrome (RDS; 22.8%), persistent pulmonary hypertension (PPHN; 6.3%), and birth asphyxia (4.4%). All deaths occurred exclusively in the severe distress group. Outborn status (p < 0.0001), hypothermia on admission (p < 0.01), and delivery room intubation (p < 0.0001) were significant predictors of mortality. All 32 CPAP-managed neonates survived. Antenatal steroids eliminated mortality in the <34-week gestation group. **Conclusion:** PPHN and birth asphyxia carry the highest mortality. Early NICU admission, CPAP availability, antenatal steroid administration, and prevention of hypothermia are key interventions for improving neonatal survival.

**Keywords:** Neonatal respiratory distress; NICU outcome; TTN; RDS; CPAP; PPHN; antenatal steroids; neonatal mortality



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### INTRODUCTION

Respiratory distress is among the most frequent reasons for neonatal intensive care unit (NICU) admission worldwide. The clinical syndrome encompasses tachypnea (respiratory rate  $\geq 60/\text{min}$ ), intercostal and subcostal retractions, nasal flaring, expiratory grunting, and cyanosis, arising from a diverse spectrum of pulmonary and extra-pulmonary aetiologies.[1] Birth weight, gestational age, and severity of compromise collectively determine the required level of care and largely govern outcome.[1]

Objective tools for grading distress include the Silverman–Anderson score for preterm neonates and Downe's score for term neonates; however, neither score identifies the underlying aetiology.[2] Over the past five decades, three interventions have dramatically altered the prognosis: (i) continuous positive airway pressure (CPAP), first described by Gregory et al in 1971;[3] (ii) exogenous surfactant replacement therapy;[4] and (iii) antenatal corticosteroids, whose meta-analysis by

Crowley et al demonstrated a 50–70% reduction in hyaline membrane disease (HMD).[5]

Indian studies spanning four decades report a wide variation in incidence (0.69–13.7%), aetiology, and case-fatality rates, reflecting differences in case definitions, gestational-age distributions, and healthcare resources.[6][7][8][9] The present study was designed to describe the demographic and clinical profile, aetiology, risk factors, need for respiratory support, and outcome of respiratory distress in neonates admitted to a tertiary care NICU within the first 24 hours of life.

### MATERIALS AND METHODS

This was a hospital-based prospective observational study conducted in the 28-bed tertiary NICU of Aditya Birla Memorial Hospital (ABMH), Pune, India. The unit provides combined Level II and Level III neonatal care and is equipped with CPAP devices, conventional and high-frequency oscillatory ventilators, inhaled nitric oxide delivery, pulse oximetry, portable radiography, 2D

echocardiography, and facilities for neonatal surgery. The study was conducted from November 2013 to October 2014 (12 months). Based on a reported incidence of 13.7% (Santosh S et al[9]), 95% confidence level, and 8% absolute precision, the minimum sample size was calculated as 71. The study enrolled 206 consecutive eligible neonates.

Neonates admitted to the NICU with respiratory rate  $\geq 60$  breaths/minute within the first 24 hours of birth were included, regardless of whether distress was present at admission or developed thereafter. Neonates admitted after 24 hours, those discharged against medical advice or transferred mid-treatment, and those whose guardians declined informed consent were excluded. Gestational age was assessed by the New Ballard Score.[10] Severity of distress was graded using Downe's score (term neonates) or the Silverman–Anderson score (preterm neonates)[2]: mild (score 1–3), moderate (4–6), or severe ( $>6$ ). All neonates underwent haemogram, chest radiograph, and arterial blood gas analysis. Blood

culture, cranial ultrasonography, and 2D echocardiography were performed as clinically indicated. Antenatal steroids were defined as two complete doses of betamethasone or dexamethasone administered  $\geq 12$  hours before delivery. Oxygen by hood, nasal CPAP, and invasive mechanical ventilation were provided per NICU standard protocols. Surfactant was administered intratracheally to eligible neonates with RDS. Nitric oxide was used as an adjunct in PPHN.

The study protocol was approved by the Institutional Ethics Committee of ABMH and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians prior to enrolment. Categorical variables were compared using Fisher's Exact Test (FET) or Chi-square test. Continuous variables are expressed as means with ranges. Z-tests were used for comparison of proportions. A two-tailed p-value  $<0.05$  was considered statistically significant.

## RESULTS

Of 424 neonates admitted to the NICU during the study period, 206 (48.5%) presented with respiratory distress within 24 hours of birth. Of these, 194 (94.17%) survived and 12 (5.82%) died.

### 3.1 Gender, Place of Birth, and Overall Outcome

The cohort comprised 121 males (58.7%) and 85 females (41.3%; M:F = 1.42:1). Of 206 neonates, 179 (86.9%) were inborn and 27 (13.1%) were outborn. Outborn neonates had a markedly higher mortality (33.33%) compared with inborn neonates (1.67%; FET  $<0.0001$ ). Gender did not significantly influence outcome (Table 1).

**Table 1: Association between gender, place of birth, and outcome**

| Parameter       | Category       | Survived (n=194) | Death (n=12) | p Value          |
|-----------------|----------------|------------------|--------------|------------------|
| Gender          | Male Female    | 113 81           | 8 4          | FET = 0.76       |
| Birth Place     | Inborn Outborn | 176 18           | 3 9          | FET $< 0.0001^*$ |
| Overall outcome | —              | 194 (94.2%)      | 12 (5.8%)    | —                |

FET – Fisher's Exact Test; \* statistically significant ( $p < 0.05$ )

### 3.2 Maternal and Perinatal Risk Factors

Significant antenatal history was identified in 27 mothers; diabetes mellitus was most frequent ( $n=12$ , 5.82%), followed by pre-eclampsia/eclampsia ( $n=5$ , 2.42%). Hypothermia on admission (7 neonates, 3.39%), significant maternal co-morbidity, and the need for delivery room intubation were strongly associated with death (Table 2). Notably, all neonates born to mothers with pregnancy-induced hypertension (PIH) survived despite carrying a significant Z-score ( $p < 0.0001$ ). Neonates admitted  $\geq 3$  hours after birth had a mortality of 38.46% versus 2.07% for those admitted within 3 hours (FET  $<0.0001$ ).

**Table 2: Severity of respiratory distress and outcome**

| Severity | Survived | Died | Total n (%) |
|----------|----------|------|-------------|
| Mild     | 157      | 0    | 157 (76.2%) |
| Moderate | 13       | 0    | 13 (6.3%)   |
| Severe   | 24       | 12   | 36 (17.5%)  |
| Total    | 194      | 12   | 206 (100%)  |

LR – Likelihood ratio;  $p < 0.0001$  (severe vs mild/moderate)

**Table 3: Association between perinatal risk factors and outcome**

| Risk Factor                              | Survived n (%) | Death n (%) | Total | Z Value | p Value  |
|------------------------------------------|----------------|-------------|-------|---------|----------|
| PIH                                      | 22 (11.34)     | 0 (0)       | 22    | 4.98    | <0.0001* |
| Significant maternal history             | 22 (11.34)     | 5 (41.67)   | 27    | 2.10    | <0.05*   |
| PROM (>24 h)                             | 39 (20.10)     | 1 (8.33)    | 40    | 1.39    | >0.05    |
| Hypothermia on admission                 | 2 (1.03)       | 5 (41.67)   | 7     | 2.85    | <0.01*   |
| Meconium-stained liquor                  | 19 (9.79)      | 2 (16.67)   | 21    | 0.63    | >0.05    |
| Delivery room resuscitation (intubation) | 15 (7.73)      | 11 (91.67)  | 26    | 10.23   | <0.0001* |

PIH – Pregnancy-induced hypertension; PROM – Premature rupture of membranes; \* statistically significant

### 3.3 Severity of Respiratory Distress and Outcome

At presentation, 157 (76.2%) neonates had mild, 13 (6.3%) moderate, and 36 (17.5%) severe respiratory distress. All 12 deaths occurred exclusively among neonates with severe respiratory distress (LR=56.90,  $p<0.0001$ ; Table 3 and Figure 4).

### 3.4 Aetiology and Outcome

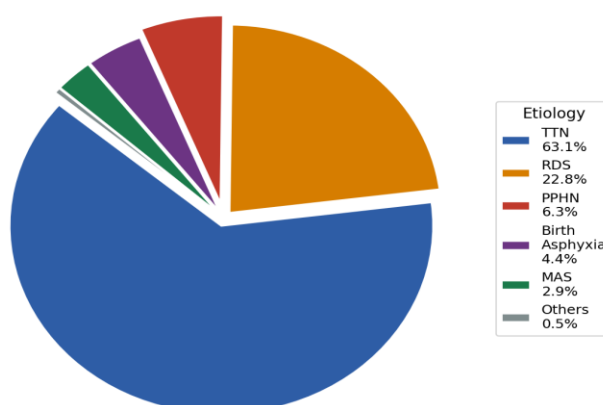
TTN was the most common aetiology (130/206; 63.1%) with zero mortality. RDS accounted for 22.8% with a case-fatality rate of 4.26% (2/47). PPHN was the leading cause of death: 7 of 13 affected neonates died (case fatality 53.85%;  $p<0.001$ ). Birth asphyxia (9 neonates; 4.4%) was significantly associated with death (4/9; 44.44%;  $p<0.05$ ). Six neonates had concurrent diagnoses, including three with both birth asphyxia and PPHN (all three died). Distribution of aetiologies is depicted in Figure 1 and case-fatality rates in Figure 2 (Table 4).

**Table 4: Aetiology of respiratory distress and its association with outcome**

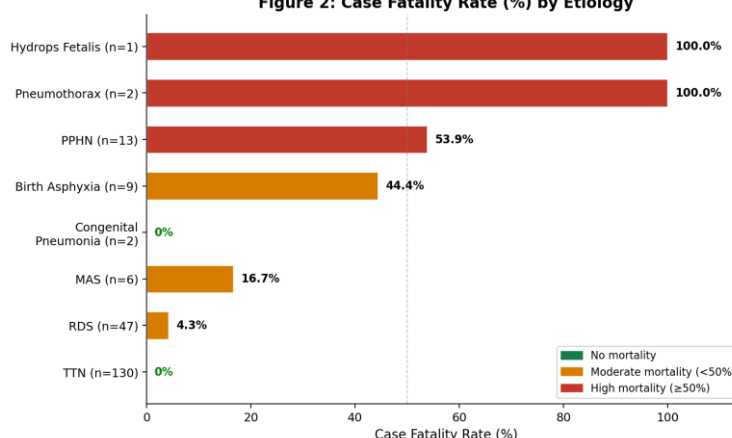
| Aetiology                                | Survived n (%) | Death n (%) | Total | Z Value | p Value  |
|------------------------------------------|----------------|-------------|-------|---------|----------|
| Transient Tachypnea of Newborn (TTN)     | 130 (67.01)    | 0           | 130   | 19.85   | <0.0001* |
| Respiratory Distress Syndrome (RDS)      | 45 (23.19)     | 2 (16.67)   | 47    | 0.58    | >0.05    |
| Persistent Pulmonary Hypertension (PPHN) | 6 (3.09)       | 7 (58.33)   | 13    | 3.87    | <0.001*  |
| Birth Asphyxia                           | 5 (2.58)       | 4 (33.33)   | 9     | 2.25    | <0.05*   |
| Meconium Aspiration Syndrome (MAS)       | 5 (2.58)       | 1 (8.33)    | 6     | 0.71    | >0.05    |
| Congenital Pneumonia                     | 2 (1.03)       | 0           | 2     | 1.42    | >0.05    |
| Congenital Heart Disease (CHD)           | 1 (0.51)       | 0           | 1     | 1.002   | N/A      |
| Pneumothorax                             | 0              | 2 (16.67)   | 2     | 1.55    | >0.05    |
| Hydrops Fetalis                          | 0              | 1 (8.33)    | 1     | 1.04    | >0.05    |
| Polycythemia                             | 1 (0.51)       | 0           | 1     | 1.002   | N/A      |

TTN – Transient tachypnea of newborn; RDS – Respiratory distress syndrome; PPHN – Persistent pulmonary hypertension of newborn; MAS – Meconium aspiration syndrome; \* statistically significant. Six neonates had more than one concurrent aetiology.

**Figure 1: Distribution of Etiologies of Neonatal Respiratory Distress (n = 206)**



**Figure 2: Case Fatality Rate (%) by Etiology**



### 3.5 Respiratory Support and Outcome

The majority of neonates (152/206; 73.79%) were managed with oxygen by hood alone, all of whom survived. Thirty-two neonates (15.53%) received CPAP, with a 100% survival rate and mean CPAP duration of 3.37 days. Thirty-seven neonates (17.96%) required mechanical ventilation; 25 (67.57%) survived, with a mean ventilation duration of 4.94 days. All 11 neonates who required immediate mechanical ventilation as the sole modality died (Table 5, Figure 3). The most common indication for mechanical ventilation was RDS (16/37; 43.2%).

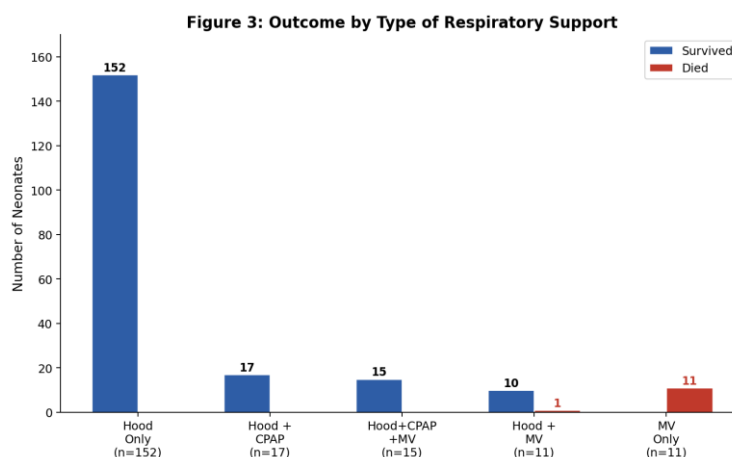
**Table 5: Type of respiratory support and outcome**

| Respiratory Support                  | Survived n (%)     | Death n (%)      | Total n (%)      |
|--------------------------------------|--------------------|------------------|------------------|
| Oxygen by Hood only                  | 152 (73.79)        | 0                | 152 (73.79)      |
| Hood + CPAP                          | 17 (8.25)          | 0                | 17 (8.25)        |
| Hood + CPAP + Mechanical Ventilation | 15 (7.28)          | 0                | 15 (7.28)        |
| Hood + Mechanical Ventilation        | 10 (4.85)          | 1 (0.51)         | 11 (5.34)        |
| Mechanical Ventilation only          | 0                  | 11 (5.34)        | 11 (5.34)        |
| <b>Total</b>                         | <b>194 (94.17)</b> | <b>12 (5.83)</b> | <b>206 (100)</b> |

CPAP – Continuous positive airway pressure; MV – Mechanical ventilation

### 3.6 Impact of Antenatal Steroids in <34 Weeks Gestational Age

Among the 32 neonates <34 weeks gestation, 10 received two complete antenatal steroid doses  $\geq 12$  hours before delivery and all 10 survived. Of the 22 who had incomplete or no steroid exposure, 4 (18.18%) died. The protective role of antenatal steroids was clinically evident (Table 6, Figure 5), consistent with prior randomised evidence.<sup>[11][5]</sup>



**Table 6: Effect of antenatal steroids on outcome in neonates <34 weeks gestational age**

| Antenatal Steroids                                      | Survived  | Died       | Total     |
|---------------------------------------------------------|-----------|------------|-----------|
| Received (2 complete doses $\geq 12$ h before delivery) | 10        | 0          | 10        |
| Not received / incomplete                               | 18        | 4 (18.18%) | 22        |
| <b>Total</b>                                            | <b>28</b> | <b>4</b>   | <b>32</b> |

*Antenatal steroids = 2 completed doses of betamethasone/dexamethasone given  $\geq 12$  h before delivery*

### 3.7 Gestational Age, Birth Weight, and Hospital Stay

Of 206 neonates, 96 (46.6%) were preterm (<37 weeks) and 110 (53.4%) were term. Mean birth weight was 2,509 g (range 650–4,220 g). Gestational age and birth weight categories did not independently achieve statistical significance for mortality ( $p > 0.05$  for both); however, ELBW (<1 kg) neonates had a mortality of 66.67%. Mean hospital stay was 10.11 days overall and 5.70 days for term neonates. Neonates with RDS had the longest stays (frequently >15 days), while TTN resolved within 1–5 days.

## DISCUSSION

The incidence of respiratory distress in our NICU (48.5% of NICU admissions) exceeded figures reported by Thomas et al[7] (8.1%), Alok Kumar and Vishnu Bhat[12] (6.7%), and Qian et al[13] (13.2%). This higher rate reflects the combined Level II/Level III care model, which admits even mildly symptomatic neonates, and the predominantly inborn population (86.9%).

Our overall mortality of 5.82% represents a substantial improvement over earlier Indian data: Khatua et al[6] reported 39%, Malhotra et al[14] 38%, Bhakoo et al[15] 49.3%, and Mathur et al[16] 32%. This improvement is attributable to a higher inborn rate, greater proportion of term neonates, routine surfactant use, antenatal steroid administration, trained NRP-certified resuscitation teams, and improved respiratory support. Ersch et al[17] documented a similar trend in Switzerland, with mortality declining from 15.5% to 3.5% over three decades.

TTN constituted 63.1% of all cases, higher than Bhakoo et al[15] (27.4%) and Alok Kumar and Vishnu Bhat[12] (42.7%). Zero mortality in TTN aligns with all contemporary studies.[12][14]

RDS (22.8%) accounted for only 4.26% of case fatalities. Historical Indian data reported RDS mortality of 57.1%[12] in the pre-surfactant era; the markedly improved outcome in our study is attributable to timely surfactant replacement and CPAP.[4][18]

PPHN emerged as the leading cause of death (7/13; 53.85%), underscoring its severity. Concurrent birth asphyxia with PPHN resulted in 100% mortality (3/3). MAS incidence was low (2.9%) compared with 9.5–12.5% in other Indian studies,[7][14][8] attributable to improved intrapartum monitoring, partogram use, and timely operative delivery for fetal distress.

CPAP achieved a 100% survival rate in our cohort, superior to Urs et al[5] (80%) and Malhotra et al[14] (50%). No pneumothorax occurred in any CPAP-managed neonate. These findings support CPAP as a safe, effective, and cost-appropriate primary mode of respiratory support, particularly relevant in resource-limited settings.[19-21]

The most actionable mortality predictors were outborn status (33.33% vs 1.67% inborn;  $p < 0.0001$ ) and

hypothermia on admission (5/7 died;  $p < 0.01$ ). Manji et al[4] similarly documented threefold higher mortality in hypothermic neonates. Time to admission was also critical: mortality below 3 hours was 2.07% versus 38.46% beyond 3 hours (FET  $< 0.0001$ ).

Antenatal steroids conferred complete protection against mortality in the  $< 34$ -week cohort (0/10 deaths vs 4/22), consistent with the Crowley meta-analysis[14] demonstrating 50–70% reduction in HMD and the data of Liggins and Howie.[17] Wider implementation of antenatal steroid protocols in preterm deliveries is strongly supported by our findings.

## CONCLUSION

TTN and RDS are the dominant aetiologies of neonatal respiratory distress presenting within 24 hours of birth. PPHN and birth asphyxia carry the highest case-fatality rates. Outborn status, hypothermia on admission, delayed NICU admission, and the need for delivery room intubation are the most significant independent predictors of mortality. Universal CPAP availability, antenatal steroid administration in preterm deliveries, prevention of neonatal cold stress during transport, and early NICU admission can substantially reduce mortality from neonatal respiratory distress.

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