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Original Article

Paediatrics Section

Clinical Profile, Risk Factors and Outcomes of Neonates with Respiratory Distress at a Rural Tertiary Care Setting, Tamil Nadu, India: A Prospective Cohort Study

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ABSTRACT

Introduction: Neonatal Respiratory Distress (RD) is one of the leading causes of Neonatal Intensive Care Unit (NICU) admissions and contributes significantly to neonatal morbidity and mortality, particularly in resource-limited rural settings. Early identification of aetiological factors and timely respiratory support are crucial for improving outcomes.

Aim: To study the clinical profile, associated risk factors, and outcomes of neonates admitted with RD in a rural tertiary care centre.

Materials and Methods: The present hospital-based prospective cohort study was conducted in the NICU of Government Villupuram Medical College, Tamil Nadu, India between April 2020 and March 2021. A total of 120 neonates presenting with RD were included. Demographic data, perinatal risk factors, clinical presentation, aetiology, severity scores, respiratory support requirements, and outcomes were recorded and analysed. Statistical analysis was performed using the chi-square test to assess the association between risk factors and adverse outcomes. A p-value <0.05 was considered statistically significant.

Results: Among the 120 neonates, 72 (60%) were male and 62 (51.7%) were preterm. Low-birth-weight was observed in 66 (55%) neonates. Caesarean section was the predominant mode of delivery, accounting for 74 (61.7%) deliveries. The most common aetiology was Transient Tachypnoea of the Newborn (TTN) in 38 (31.7%) neonates, followed by RD Syndrome (RDS) in 34 (28.3%), birth asphyxia in 22 (18.3%), and meconium aspiration syndrome in 14 (11.7%). Among term neonates, moderate to severe RD was seen in 38 (65.5%) neonates. Mechanical ventilation was required in 30 (25%), while 46 (38.3%) were managed with Continuous Positive Airway Pressure (CPAP). The overall survival rate was 92 (76.7%), with a mortality rate of 16 (13.3%). Prematurity, severe RD, sepsis and requirement of mechanical ventilation were significantly associated with adverse outcomes (p <0.05).

Conclusion: Neonatal RD remains a major contributor to morbidity and mortality in rural tertiary care settings, with TTN being the most common cause. Strengthening antenatal care, early CPAP initiation, and strict infection-control practices may improve survival outcomes.

Keywords: Antenatal care, Birth asphyxia, Neonatal morbidity, Positive pressure respiration, Premature infants

INTRODUCTION

The RD is one of the most common causes of NICU admission and remains a major contributor to neonatal morbidity and mortality worldwide [1]. It affects approximately 7-8% of all live births, with a higher incidence among preterm and low-birth-weight neonates [2,3]. In India, RD contributes substantially to neonatal morbidity, particularly in tertiary care hospitals where it accounts for nearly one-fourth of NICU admissions [4,5]. Despite advances in neonatal intensive care, respiratory disorders continue to pose a significant challenge, especially in resource-limited settings where delayed diagnosis and limited access to advanced respiratory support adversely influence outcomes. Early recognition and timely intervention are therefore essential to improve neonatal survival and reduce complications.

Neonatal RD is clinically characterised by tachypnoea (respiratory rate >60/min), chest retractions, nasal flaring, grunting, and cyanosis [5]. If not identified and managed promptly, it may progress to respiratory failure, hypoxaemia, multi organ dysfunction, and death [6,7]. The aetiology of neonatal RD is diverse and varies according to gestational age, maternal risk factors, and perinatal events. Common pulmonary causes include TTN, RDS, Meconium Aspiration Syndrome (MAS), neonatal pneumonia, and air leak syndromes [5]. Non-pulmonary causes such as birth asphyxia, congenital heart disease, neonatal sepsis, metabolic disorders, and congenital anomalies may also present with RD [2,8].

The TTN is the most common cause of RD in term and late-preterm neonates and results from delayed clearance of fetal lung fluid [2,3]. RDS predominantly affects preterm neonates because of surfactant deficiency and remains an important cause of neonatal mortalitydespite advances in antenatal corticosteroid therapy and surfactant replacement [9]. MAS is commonly observed in term or post-term neonates with meconium-stained amniotic fluid, whereas neonatal pneumonia and sepsis continue to be major causes of RD in developing countries [6].

Previous studies have identified TTN and RDS as the predominant aetiologies of neonatal RD, with prematurity, low-birth-weight, male sex, caesarean delivery, meconium-stained liquor, and low APGAR scores as important risk factors [10-15]. Adverse outcomes are more frequently observed in neonates with severe respiratory distress, neonatal sepsis, and those requiring invasive mechanical ventilation [10,12]. However, most available evidence has been generated from urban tertiary care centres, while data from rural healthcare settings remain scarce [2,3].

Therefore, the present study was undertaken to evaluate the clinical profile, associated risk factors, aetiological spectrum, respiratory support requirements, and outcomes of neonates with RD admitted to the NICU of a rural tertiary care centre. The findings are expected to provide region-specific evidence that may facilitate early identification of high-risk neonates, optimise resource utilisation, and improve neonatal care in similar healthcare settings. Hence, the present study aimed to describe the demographic and perinatal characteristics of neonates presenting with RD , to identify aetiological factors and clinical severity patterns associated with neonatal RD and to assess respiratory support requirements and clinical outcomes among affected neonates.

MATERIALS AND METHODS

The present study was a hospital-based prospective cohort study conducted in the NICU of Government Villupuram Medical College in Tamil Nadu, India. The study was carried out over a one-year period from April 2020 to March 2021. The study was approved by the Institutional Ethics Committee of Chengalpattu Medical College, Chengalpattu (IEC Registration No: ECR/774/INST/TN/2015). Written informed consent was obtained from the parents or guardians of all enrolled neonates. Confidentiality of patient information was maintained throughout the study.

Inclusion criteria: The study included term and preterm neonates aged 28 days or less who were admitted to the NICU and exhibited clinical signs of RD either at the time of admission or during their hospital stay. Both inborn and outborn neonates were eligible for inclusion.

Exclusion criteria: Neonates with major congenital anomalies incompatible with life, neonates with isolated congenital heart disease without respiratory involvement, neonates who were discharged against medical advice before completion of the evaluation and those readmitted with RD were excluded.

Definition of Respiratory Distress (RD) [2]: RD was defined by the presence of one or more of the following clinical features: tachypnoea (respiratory rate >60/min), chest retractions (subcostal, intercostal, or suprasternal), nasal flaring, and grunting.

Sample size calculation: The sample size was calculated based on the expected proportion of neonatal RD among NICU admissions. Assuming a prevalence of approximately 30% from previous study [8], with 95% confidence level and 8% absolute precision, the minimum required sample size was calculated as 126 using the formula $n=Z^2pq/d^2$. Due to feasibility constraints and the Coronavirus Disease of 2019 (COVID-19) pandemic period, a total of 120 neonates were enrolled using consecutive sampling during the study period.

Study Procedure

Data collection: Data were collected using a pre-designed, structured proforma. Maternal and perinatal details recorded included antenatal complications (such as diabetes mellitus, hypertension, and infections), antenatal steroid administration, mode of delivery, duration of rupture of membranes, and presence of meconium-stained liquor. Neonatal characteristics documented were gestational age (assessed using the New Ballard score), birth weight, gender, place of delivery (inborn/outborn), APGAR (Appearance, Pulse, Grimace, Activity, Respiration) score and cry at birth.

Clinical assessment: All neonates were clinically assessed at admission and monitored periodically thereafter. Severity of RD was assessed using Downes' score for term neonates and Silverman-Andersen score for preterm neonates. Downes' score includes five clinical parameters-respiratory rate, cyanosis, air entry, grunting, and retractions-each scored from 0 to 2, with a maximum score of 10; a score of <4 indicates mild, 4-6 moderate, and >6 severe RD. The Silverman-Andersen score assesses upper chest movement, lower chest retractions, xiphoid retractions, nasal flaring, and expiratory grunting, each graded from 0 to 2 (maximum score 10), with higher scores indicating increasing severity of RD [16,17].

Investigations were performed as clinically indicated and included complete blood count, sepsis screen C-Reactive Protein (CRP), micro-Erythrocyte Sedimentation Rate (ESR), immature-to-total neutrophil ratio), blood culture, chest X-ray, arterial blood gas analysis, blood glucose, and serum electrolytes. Echocardiography was performed in cases where congenital heart disease was suspected.

Based on clinical features, laboratory investigations, and radiological findings, neonates were classified etiologically as:

- **Transient Tachypnoea of the Newborn (TTN):** RD occurring shortly after birth due to delayed clearance of fetal lung fluid, typically presenting with tachypnoea and characteristic chest X-ray findings of prominent pulmonary vascular markings and fluid in the interlobar fissures [18].
- **Respiratory Distress Syndrome (RDS):** RD occurring primarily in preterm neonates due to surfactant deficiency, characterised by increasing oxygen requirement and a chest radiograph showing diffuse reticulogranular ("ground-glass") appearance with air bronchograms [6].
- **Meconium Aspiration Syndrome (MAS):** RD in a neonate born through meconium-stained amniotic fluid with compatible clinical and radiological findings not otherwise explained [19].
- **Birth asphyxia:** Failure to initiate and sustain breathing at birth, diagnosed based on perinatal history, low APGAR scores, need for resuscitation, and/or evidence of hypoxic-ischemic encephalopathy [20].
- **Neonatal Pneumonia/Sepsis:** RD associated with clinical signs of infection and supported by laboratory evidence such as positive sepsis screen, elevated inflammatory markers, blood culture positivity, or radiological findings suggestive of pneumonia [21,22].

Management Protocol: All neonates were managed according to standard NICU protocols, which included thermoneutral care, oxygen therapy via hood or nasal prongs, CPAP for moderate RD, mechanical ventilation for severe respiratory failure, surfactant therapy for neonates diagnosed with RDS, antibiotic therapy when sepsis was suspected or confirmed, and supportive care including fluid and electrolyte management.

Outcome measures: The primary outcome measured was clinical outcome at discharge, categorised as improved and discharged, referred to a higher centre, or death. Secondary outcomes included the requirement and duration of respiratory support and the association between risk factors and adverse outcomes.

STATISTICAL ANALYSIS

Data were entered and analysed using Statistical Package for the Social Sciences (SPSS) software version 18.0. Categorical variables were expressed as frequency and percentage. Associations between risk factors and clinical outcomes were analysed using

the chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

Among the 120 neonates with RD, 62 (51.7%) were preterm and 58 (48.3%) were term. There was a male predominance, with 72 (60%) males. Low-birth-weight (<2.5 kg) was observed in 66 (55%) neonates. The most common mode of delivery was Lower Segment Caesarean Section (LSCS), accounting for 74 (61.7%) cases, and 88 (73.3%) neonates were inborn. A total of 84 (70%) neonates cried at birth, while 36 (30%) required resuscitative support [Table/Fig-1].

Variable	Category	n (%)
Gestational age	Preterm (<37 weeks)	62 (51.7)
	Term (>37 weeks)	58 (48.3)
Gender	Male	72 (60.0)
	Female	48 (40.0)
Birth weight	<2.5 kg	66 (55.0)
	>2.5 kg	54 (45.0)
Mode of delivery	Vaginal	46 (38.3)
	LSCS	74 (61.7)
Place of delivery	Inborn	88 (73.3)
	Outborn	32 (26.7)
Cried at birth	Yes	84 (70.0)
	No	36 (30.0)

[Table/Fig-1]: Demographic and perinatal characteristics of neonates with Respiratory Distress (RD) (N=120).

Meconium-stained liquor is the most frequent risk factor observed in 28 (23.3%) neonates followed by, Premature rupture of membranes (>24 hours) was noted in 22 (18.3%) cases. Maternal co-morbidities included hypertension in 18 (15%) and diabetes mellitus in 14 (11.7%) mothers. Only 48 (40%) mothers received antenatal steroids, while 72 (60%) did not receive steroid prophylaxis [Table/Fig-2].

Risk factors	n (%)
Meconium-stained liquor	28 (23.3)
Premature rupture of membranes	22 (18.3)
Maternal diabetes	14 (11.7)
Maternal hypertension	18 (15.0)
Antenatal steroid received	48 (40.0)
No antenatal steroids	72 (60.0)

[Table/Fig-2]: Maternal risk factors associated with Respiratory Distress (RD) (N=120).

Prematurity was the most common neonatal risk factor associated with RD, observed in 62 (51.7%) neonates, followed by birth asphyxia in 22 (18.3%) cases [Table/Fig-3].

Risk factors	n (%)
Prematurity	62 (51.7)
Birth asphyxia	22 (18.3)

[Table/Fig-3]: Neonatal risk factors presented in Respiratory Distress (RD) (N=120).

The most common aetiology of RD was TTN, observed in 38 (31.7%) neonates, followed by RDS in 34 (28.3%), other causes included birth asphyxia in 22 (18.3%), meconium aspiration syndrome in 14 (11.7%), and neonatal pneumonia/sepsis in 12 (10%) [Table/Fig-4].

Variable	Category	n (%)
Aetiology	Transient Tachypnoea of Newborn (TTN)	38 (31.7)
	Respiratory Distress Syndrome (RDS)	34 (28.3)
	Birth asphyxia	22 (18.3)
	Meconium aspiration syndrome (MAS)	14 (11.7)
	Neonatal pneumonia/ sepsis	12 (10.0)

[Table/Fig-4]: Aetiology of Respiratory Distress (RD) (N=120).

Among term neonates (n=58), moderate RD was the most common severity, observed in 22 (37.9%) neonates, followed by severe RD in 16 (27.6%) and mild RD in 20 (34.5%) neonates, as assessed using the Downes' score [Table/Fig-5a].

Severity	n (%)
Mild	20 (34.5)
Moderate	22 (37.9)
Severe	16 (27.6)

[Table/Fig-5a]: Clinical severity of Respiratory Distress (RD) among term neonates (Downes' score, n=58).

Among preterm neonates (n=62), moderate RD was the most common severity, observed in 24 (38.7%) neonates, followed by mild RD in 22 (35.5%) and severe RD in 16 (25.8%) neonates, as assessed using the Silverman-Andersen score [Table/Fig-5b].

Severity	n (%)
Mild	22 (35.5)
Moderate	24 (38.7)
Severe	16 (25.8)

[Table/Fig-5b]: Clinical severity of Respiratory Distress (RD) among preterm neonates (Silverman-Andersen score, n=62).

The CPAP was the most commonly used respiratory support modality, administered to 46 (38.3%) neonates, followed by supplemental oxygen in 44 (36.7%) cases, while 30 (25.0%) neonates required mechanical ventilation. Among ventilated neonates (n=30), 7 (23.3%) received ventilation for less than 24 hours, 10 (33.3%) for 24-72 hours, and 13 (43.3%) for more than 72 hours. Surfactant therapy was administered to 30 (25.0%) neonates, of whom 22 (73.3%) received a single dose and 8 (26.7%) required multiple doses [Table/Fig-6].

Variables	Category	n (%)
Respiratory support	Supplemental oxygen only	44 (36.7)
	CPAP	46 (38.3)
	Mechanical ventilation	30 (25.0)
Duration of ventilation (n=30)	<24 hours	7 (23.3)
	24-72 hours	10 (33.3)
	>72 hours	13 (43.3)
Surfactant therapy	Given	30 (25.0)
	Not given	90 (75.0)
Surfactant doses (n=30)	Single dose	22 (73.3)
	Multiple doses	8 (26.7)

[Table/Fig-6]: Respiratory support and treatment modalities.

Overall clinical outcomes showed that 92 (76.7%) neonates improved and were discharged, 12 (10%) were referred, and 16 (13.3%) died [Table/Fig-7].

A total of 16 (13.3%) neonates died during the study period. Mortality was highest among neonates with RDS (8/34, 23.5%), followed by birth asphyxia (4/22, 18.2%) and neonatal sepsis/pneumonia (2/12,

16.7%), while no deaths were observed among neonates with TTN [Table/Fig-8].

Outcomes	n (%)
Improved and discharged	92 (76.7)
Referred	12 (10.0)
Mortality	16 (13.3)

[Table/Fig-7]: Clinical outcomes (N=120).

Diagnosis	Total cases (n)	Deaths n (%)
Transient Tachypnoea of the Newborn (TTN)	38	0
Respiratory Distress Syndrome (RDS)	34	8 (23.5)
Birth asphyxia	22	4 (18.2)
Meconium aspiration syndrome (MAS)	14	2 (14.3)
Neonatal sepsis/ pneumonia	12	2 (16.7)
Total	120	16 (13.3)

[Table/Fig-8]: Distribution of deaths according to diagnosis.

Mean birth weight, gestational age, and APGAR scores were significantly lower among non survivors compared to survivors, indicating that prematurity and low-birth-weight were associated with adverse outcomes, as shown in [Table/Fig-9].

Variables	Survivors (n=104) Mean±SD	Non survivors (n=16) Mean±SD	p-value
Birth weight (kg)	2.41±0.49	1.98±0.42	0.001
Gestational age (weeks)	36.4±2.3	33.8±2.6	0.002
APGAR score at 1 minute	6.9±0.7	5.8±0.9	<0.001
APGAR score at 5 minutes	7.9±0.6	6.6±0.8	<0.001

[Table/Fig-9]: Comparison of continuous variables between survivors and non survivors.

DISCUSSION

The present study evaluated the clinical profile, risk factors, aetiological spectrum, respiratory support requirements, and outcomes of neonates admitted with RD in a rural tertiary care centre. The key findings include a higher burden among preterm and low-birth-weight neonates, predominance of TTN, significant association of severe RD and sepsis with adverse outcomes, and a mortality rate of 13.3%.

Neonatal RD remains one of the most common causes of NICU admission and contributes significantly to neonatal morbidity and mortality, particularly in resource-limited and rural settings. This prospective cohort study provides insight into the clinical profile, aetiological spectrum, risk factors, respiratory support requirements, and outcomes of neonates with RD in a rural tertiary care centre, and the findings are discussed in comparison with previously published studies.

RDS was predominantly observed among preterm neonates, consistent with the pathophysiology of surfactant deficiency, as also reported by Bajad M et al., [22] and Nagendra K et al., [6]. In the present study, preterm neonates constituted 51.7% of cases, highlighting prematurity as a major contributor to RD. This observation is comparable to findings by Woldeyes D et al., who reported a higher incidence of RD among preterm neonates (57%) admitted during the early neonatal period [10]. RDS was predominantly observed among preterm neonates, consistent with the pathophysiology of surfactant deficiency [21]. Similar observations were made by Bajad M et al., where prematurity was identified as a significant predisposing factor for neonatal respiratory morbidity [22]. A male predominance (60%) was observed in this study, consistent with reports from Sahoo MR et al., [12] and Lamichhane A et al., who documented male proportions of 64% and 69%, respectively [1]. This male preponderance has been attributed to delayed pulmonary maturity and hormonal influences affecting surfactant production in male neonates. Low-birth-weight was observed in 55% of neonates, reinforcing the association between reduced birth weight and respiratory compromise. Kommawar A et al., also reported a high proportion of low-birth-weight neonates (70.25%) among cases with RD [23].

The majority of neonates in the present study were delivered by lower segment caesarean section (61.7%), aligning with observations from Sahoo MR et al., who reported LSCS rates of 56% [12]. The absence of thoracic compression and delayed lung fluid clearance in caesarean deliveries may explain the increased risk of RD, particularly TTN [24].

Prematurity emerged as the most common risk factor (51.7%), followed by birth asphyxia (28.3%) and meconium-stained liquor (23.3%). These findings are comparable to those of Wang Y et al., who also reported prematurity and perinatal hypoxia as leading risk factors [25]. Prolonged rupture of membranes was observed in 18.3% of cases, similar to findings by Chandini P and Kumari BS who identified PROM as a significant contributor to neonatal RD due to increased risk of infection and pneumonia [26].

Only 40% of mothers received antenatal steroids, which is lower than expected for a tertiary care setting. This finding is concerning, as antenatal steroid administration has been shown to significantly reduce the incidence and severity of RDS. Ramya et al., demonstrated lower rates of RDS and improved neonatal outcomes among steroid exposed preterm infants, emphasising the need for improved antenatal care practices [27].

The most common aetiology identified was TTN (31.7%), followed by RDS (28.3%). This aetiological distribution closely mirrors findings from Sodawat R et al., [28], and Pawar S and Sachdev CP, all of whom reported TTN as the leading cause of neonatal RD [29]. Studies by Bajad M et al., [22] and Nagendra K et al., similarly, identified RDS as a major cause of RD among preterm infants [6]. Birth asphyxia (18.3%) and meconium aspiration syndrome (11.7%) were other significant contributors, comparable to observations by Yadav S et al., Ramana Sastry CPV and Padmavathi M, who reported birth asphyxia and MAS as important causes in term neonates [5,30].

Regarding severity, 26.7% of neonates presented with severe RD, which is comparable to the findings of Ahuja S et al., who reported higher severity scores among neonates with prolonged RD and underlying sepsis or RDS [31].

In the present study, 36.7% of neonates required only supplemental oxygen, while 38.3% required CPAP, and 25% required mechanical ventilation. These findings are in agreement with studies by Yadav S et al., who reported CPAP as the most commonly used non-invasive respiratory support modality [5]. The requirement of mechanical ventilation in one-fourth of cases underscores the severity of illness in a significant subset of neonates. Fernandes N and Chawla S similarly reported higher mortality among mechanically ventilated neonates, highlighting the need for early intervention and optimal respiratory management [32]. Surfactant therapy was administered to 25%

of neonates, predominantly those diagnosed with RDS, with most receiving a single dose. Comparable surfactant utilisation patterns were observed in studies by Dargaville PA et al., where early rescue surfactant therapy was associated with improved outcomes [33].

The overall survival rate in this study was 76.7%, with a mortality rate of 13.3%, which is comparable to mortality rates reported earlier. Variations in mortality across studies may reflect differences in case mix, availability of advanced neonatal care, and referral patterns. Prematurity, severe RD, requirement of mechanical ventilation, and neonatal sepsis were significantly associated with adverse outcomes in the present study. These findings are consistent with those reported by Berhanu B et al., who identified similar predictors of mortality in neonates with RD [34]. The strong association between sepsis and adverse outcome emphasises the critical importance of early diagnosis and aggressive management of neonatal infections, particularly in rural and resource-limited settings.

The present study provides valuable insight into the clinical profile and outcomes of neonatal RD in a rural tertiary care settings. The strength of the current study includes prospective data collection, inclusion of a broad spectrum of aetiologies, and the use of standardised clinical severity assessment. The study also evaluated multiple maternal and neonatal risk factors and respiratory support modalities, in a rural tertiary care setting, where published data are limited.

Limitation(s)

The present study was limited by its single-centre design and relatively small sample size, which may restrict generalisability. The absence of long-term follow-up precluded assessment of neurodevelopmental outcomes. In addition, advanced investigations and newer respiratory support strategies were not uniformly available, potentially influencing management practices and outcomes.

CONCLUSION(S)

Neonatal RD is a primary driver of morbidity and mortality in rural tertiary settings, mostly affecting preterm and low-birth-weight neonates, while TTN being the most prevalent aetiology, while RDS and birth asphyxia were the leading contributors to clinical severity and adverse outcomes. Key predictors of mortality identified include prematurity, sepsis, severe RD, and the requirement for mechanical ventilation. Improving antenatal survival in rural tertiary centres necessitates a tripartite approach enhanced steroid coverage, early identification of high-risk pregnancies, and the timely initiation of non-invasive respiratory support.

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Authors' contributions: NJ conceived and designed the study and collected data. KN contributed to study design, data interpretation, and manuscript preparation. AC critically reviewed the manuscript and contributed to data analysis. SJ contributed to radiological evaluation and manuscript revision. All authors read and approved the final manuscript.

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