JHWCR
Journal of Health, Wellness, and Community Research
Volume III, Issue VI
Open Access, Double Blind Peer Reviewed.
Web: https://jhwcr.com, **ISSN**: 3007-0570
https://doi.org/10.61919/7ycrrf25

Article

Frequency and Factors of Respiratory Distress Among Neonates Admitted to Intensive Care Unit

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Cite this Article

Received	2025-05-21
Revised	2025-06-17
Accepted	2025-06-12
Published	2025-06-15

No conflicts declared; ethics approved; consent obtained; data available on request; no funding received.

Authors' Contributions
Concept and design: Concept: MH, MA; Design: HI, KK; Data Collection: AK, MF; Analysis: MH, MA; Drafting: HI, KK.

ABSTRACT

Background: Respiratory distress is a leading cause of neonatal morbidity and mortality worldwide, particularly in resource-limited settings, yet local data on its frequency, etiological spectrum, and risk factors remain limited, hindering the development of targeted management strategies. **Objective**: This study aimed to determine the frequency and associated perinatal and maternal risk factors of respiratory distress among neonates admitted to a neonatal intensive care unit (NICU), focusing on key variables such as mode of delivery, gestational age, and clinical outcomes. **Methods**: In a cross-sectional observational study at Northwest General Hospital & Research Center, Peshawar, 151 neonates aged 1–28 days with clinical signs of respiratory distress were consecutively enrolled over six months. Neonates with congenital anomalies or postoperative respiratory distress were excluded. Data on demographics, perinatal history, and clinical outcomes were collected using standardized forms. Primary outcomes included frequency of specific etiologies and their association with perinatal risk factors, analyzed using chi-square tests and odds ratios with 95% confidence intervals in SPSS version 25. Ethical approval was obtained, and informed consent adhered to the Helsinki Declaration. **Results**: TTN (26.5%), RDS (22.5%), and MAS (18.5%) were the leading causes. TTN was significantly associated with cesarean delivery (OR 2.41, p=0.012) and term gestation (OR 0.29, p=0.008), RDS with preterm birth (OR 6.08, p<0.001), and MAS with meconium-stained amniotic fluid (OR 10.09, p<0.001). **Conclusion**: Respiratory distress in neonates is primarily driven by TTN, RDS, and MAS, with clear perinatal risk profiles; optimizing delivery practices and perinatal care can substantially improve neonatal outcomes in similar healthcare settings

Keywords: Neonatal Respiratory Distress, NICU, Transient Tachypnea, Respiratory Distress Syndrome, Meconium Aspiration Syndrome, Perinatal Risk Factors, Pakistan

INTRODUCTION

Respiratory distress is a leading cause of neonatal morbidity and mortality globally, with significant implications for both short- and long-term health outcomes among newborns (1,2). Clinically, it manifests as increased work of breathing characterized by signs such as tachypnea, nasal flaring, intercostal and subcostal retractions, and grunting, with a respiratory rate above 60 breaths per minute considered a key indicator in newborns (1,3). The underlying mechanisms involve increased airway resistance, decreased lung compliance, or both, leading to compensatory responses that aim to optimize gas exchange and maintain functional residual capacity (4). Timely recognition and management are crucial, as untreated respiratory distress can rapidly progress to respiratory failure, impaired oxygenation, and ultimately cardiorespiratory arrest (5).

The burden of respiratory distress in the neonatal intensive care unit (NICU) is substantial, with reported prevalence rates reaching up to 15% in term and 29% in preterm infants, particularly those born before 34 weeks of gestation (2,6). Several etiologies have been implicated, the most common being transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), and meconium aspiration syndrome (MAS), with infections and congenital anomalies representing less frequent causes (6,7). Notably, TTN has been widely recognized as the leading cause in both developed and developing countries, accounting for approximately 25–27% of neonatal respiratory admissions, especially following cesarean section delivery where delayed clearance of fetal lung fluid is more prevalent (1,8). RDS, strongly associated with prematurity and surfactant deficiency, remains a predominant challenge in preterm neonates and has been linked to both gestational age and perinatal interventions such as resuscitation at birth (7,9). MAS continues to present a significant clinical issue in resource-limited settings, particularly in association with meconium-stained amniotic fluid and post-term or distressed deliveries (10,11). Previous studies have explored a range of perinatal and maternal risk factors, including mode of delivery, gestational age, presence of meconium, need for resuscitation, and maternal comorbidities like diabetes and hypertension

(12,13). Despite these advances, a persistent gap exists in the context-specific understanding of how these factors interplay within local health care settings, especially in low- and middle-income countries where resources for advanced diagnostics and neonatal care may be constrained (9). In Pakistan, local data on the precise frequency, etiological spectrum, and risk factor associations for neonatal respiratory distress are limited, impeding the development of targeted preventive and management strategies adapted to regional needs (7). This knowledge gap underscores the necessity for systematic research to delineate the epidemiological and clinical characteristics of respiratory distress within the Pakistani NICU population, identify modifiable perinatal risk factors, and inform evidence-based protocols for early diagnosis and tailored intervention.

Building on this rationale, the present study aims to determine the frequency and identify the perinatal and maternal factors contributing to respiratory distress among neonates admitted to the NICU at Northwest General Hospital and Research Center, Peshawar. By elucidating the local pattern and risk factor associations of respiratory distress, the study seeks to inform clinical practice and contribute to improved neonatal outcomes in similar resource-limited environments.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of Pediatrics at Northwest General Hospital and Research Center, Peshawar, over a six-month period following approval of the research protocol. The study targeted neonates admitted to the neonatal intensive care unit (NICU) between January and June 2024. Eligible participants included all neonates of either sex, aged 1 to 28 days, who were admitted to the NICU with clinical signs of respiratory distress, defined operationally as the presence of one or more of the following: tachypnea (respiratory rate >60 breaths per minute), nasal flaring, intercostal or subcostal retractions, and grunting. Exclusion criteria comprised neonates with congenital anomalies or syndromic features, and those with respiratory distress secondary to postoperative status, to avoid confounding due to alternative etiologies.

Consecutive non-probability sampling was used to enroll participants, ensuring every eligible neonate admitted within the study period was considered for inclusion until the required sample size was attained. The sample size was calculated to be 151 neonates, based on an anticipated frequency of transient tachypnea of the newborn (TTN) of 26%, with a 95% confidence interval and a 7% margin of error, using OpenEpi software. Recruitment began after obtaining written informed consent from parents or legal guardians, following a thorough explanation of the study's objectives, procedures, potential risks, and assurances of voluntary participation and data confidentiality. All procedures were reviewed and approved by the hospital's Institutional Review Board and Research Committee. Data protection was maintained through anonymized collection and secure electronic storage of all patient information, with access restricted to study investigators. Upon admission, detailed baseline data were collected by the primary investigators using a predesigned proforma. Demographic variables included age at admission (in days), gender, birth weight (in grams), gestational age at delivery (classified as term ≥37 weeks or preterm <37 weeks), parental education, parental occupation, and socioeconomic status. Perinatal factors recorded comprised mode of delivery (cesarean section or vaginal), place of delivery (in-hospital or outside), history of premature rupture of membranes (PROM), presence of meconium-stained amniotic fluid, antenatal scan findings suggestive of fetal distress, maternal comorbidities (diabetes mellitus or hypertension), and need for resuscitation at birth.

Clinical assessment was performed by attending neonatologists, and included documentation of clinical signs, APGAR scores at 1 and 5 minutes, and detailed examination findings. Laboratory investigations and imaging studies, such as chest X-ray, complete blood count, blood gas analysis, and sepsis markers, were performed as per clinical indication and under the supervision of a senior consultant. Diagnoses of specific etiologies—TTN, respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), pneumonia, sepsis-related respiratory distress, congenital anomalies, and other causes—were established using standard clinical and radiological criteria.

To minimize bias and address potential confounding, investigators adhered to strict inclusion and exclusion criteria and applied standardized operational definitions for all variables. Where possible, information was corroborated by reviewing medical records, and ambiguous data points were cross-checked by a second investigator. Data completeness was routinely monitored, with missing data minimized by prompt review of proformas and follow-up with clinical teams. Cases with irretrievable missing key data were excluded from the final analysis. Statistical analyses were performed using SPSS version 25. Continuous variables were assessed for normality using the Shapiro-Wilk test and reported as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables were summarized as frequencies and percentages. Associations between perinatal/maternal factors and specific etiologies of respiratory distress were analyzed using the chi-square test, with p-values ≤0.05 considered statistically significant. Adjustments for potential confounders were made through stratification and subgroup analysis by age group, gestational age, mode of delivery, and other relevant variables. No imputation was performed for missing data; only cases with complete data for the variables analyzed were included in each respective analysis. Steps to ensure reproducibility included the use of a standardized data collection instrument, detailed documentation of operational definitions, and adherence to predefined analytic procedures. All processes were transparently recorded to facilitate replication by other researchers.

RESULTS

A total of 151 neonates with clinical signs of respiratory distress were included in the study. The cohort had a notable male predominance, with 91 male infants accounting for 60.3% and 60 female infants representing 39.7% of the population. Most cases

presented within the early neonatal period (1–7 days), comprising 100 infants or 66.2%, while the remaining 51 neonates (33.8%) were admitted in the late neonatal period (8–28 days). Cesarean section was the more common mode of delivery, observed in 94 cases (62.3%), compared to 57 neonates (37.7%) delivered vaginally. Term neonates (gestational age ≥37 weeks) made up the majority at 104 cases (68.9%), whereas preterm infants (<37 weeks) constituted 47 cases (31.1%).

Additional perinatal and maternal risk factors were also prevalent within the cohort. A history of premature rupture of membranes (PROM) was documented in 52 neonates (34.4%), and 45 infants (29.8%) were born in the presence of meconium-stained amniotic fluid. Evidence of fetal distress on antenatal scans was reported for 38 neonates (25.2%). Moreover, 41 neonates (27.2%) required immediate resuscitation at birth, and 33 (21.8%) were born to mothers with a history of diabetes mellitus or hypertension. In terms of etiologies, transient tachypnea of the newborn (TTN) was the most frequently diagnosed cause of respiratory distress, observed in 40 neonates (26.5%). This was followed by respiratory distress syndrome (RDS) in 34 neonates (22.5%) and meconium aspiration syndrome (MAS) in 28 neonates (18.5%). Other causes included pneumonia in 17 cases (11.3%), sepsis-related respiratory distress in 13 neonates (8.6%), congenital anomalies in 7 cases (4.6%), and miscellaneous or undetermined causes in 12 neonates (7.9%).

Statistical analysis using chi-square testing revealed several significant associations between perinatal risk factors and the specific etiologies of respiratory distress. TTN was significantly more likely among neonates delivered by cesarean section (OR: 2.41, 95% CI: 1.21–4.81, p=0.012), among those born at term (OR: 0.29 for preterm vs. term, 95% CI: 0.12–0.70, p=0.008), and among males (OR: 2.01, 95% CI: 1.02–3.98, p=0.045). RDS was strongly associated with preterm birth (OR: 6.08, 95% CI: 2.47–14.94, p<0.001) and need for resuscitation at birth (OR: 2.49, 95% CI: 1.08–5.73, p=0.031). MAS demonstrated a robust association with the presence of meconium-stained amniotic fluid (OR: 10.09, 95% CI: 3.49–29.16, p<0.001) and with late neonatal age (8–28 days) compared to the early period (OR: 2.23, 95% CI: 1.02–4.89, p=0.043).

No statistically significant associations were found between maternal diabetes or hypertension and any specific respiratory distress etiology (all p-values >0.05). Subgroup analyses by gestational age and mode of delivery reinforced these findings. Among term neonates, TTN accounted for 33.7% of cases compared to only 10.6% among preterm (p=0.008). Conversely, RDS was present in 55.3% of preterm infants versus just 7.7% of term infants (p<0.001). Cesarean delivery was associated with a higher frequency of TTN (33.0% vs. 15.8% in vaginal deliveries, p=0.012). The study delineated clear numerical trends and significant associations between key perinatal risk factors and major respiratory distress etiologies, providing robust, context-specific evidence to guide clinical risk assessment and management in neonates admitted to the NICU.

Table 1. Demographic and Perinatal Characteristics of Neonates Admitted with Respiratory Distress (N = 151)

Variable	Category	Frequency (%)	95% CI
Age Group	1–7 days (Early Neonatal)	100 (66.2%)	58.2–73.4%
	8–28 days (Late Neonatal)	51 (33.8%)	26.6–41.8%
Gender	Male	91 (60.3%)	52.3–67.9%
	Female	60 (39.7%)	32.1–47.7%
Mode of Delivery	Cesarean Section	94 (62.3%)	54.4–69.7%
	Vaginal Delivery	57 (37.7%)	30.3–45.6%
Gestational Age	Term (≥37 weeks)	104 (68.9%)	61.1–75.8%
	Preterm (<37 weeks)	47 (31.1%)	24.2–38.9%
PROM History	Yes	52 (34.4%)	27.0–42.4%
	No	99 (65.6%)	57.6–73.0%
Meconium-stained Amniotic Fluid	Yes	45 (29.8%)	22.9–37.5%
	No	106 (70.2%)	62.5–77.1%
Fetal Distress on Antenatal Scan	Yes	38 (25.2%)	18.7–32.8%
	No	113 (74.8%)	67.2–81.3%
Resuscitation at Birth	Yes	41 (27.2%)	20.8–34.8%
	No	110 (72.8%)	65.2–79.2%
Maternal DM/HTN	Yes	33 (21.8%)	15.9–29.0%
	No	118 (78.2%)	71.0–84.1%

Table 2. Frequency and Distribution of Respiratory Distress Etiologies among Neonates (N = 151)

Diagnosis	Frequency (%)	95% CI
Transient Tachypnea (TTN)	40 (26.5%)	19.8–34.1%
Respiratory Distress Syndrome (RDS)	34 (22.5%)	16.3–29.9%
Meconium Aspiration Syndrome (MAS)	28 (18.5%)	12.7–25.4%
Pneumonia	17 (11.3%)	6.7–17.4%
Sepsis-related Respiratory Distress	13 (8.6%)	4.6–14.1%
Congenital Anomalies	7 (4.6%)	1.9–9.2%
Other/Undetermined	12 (7.9%)	4.1–13.3%

Table 3. Associations Between Perinatal Risk Factors and Etiologies of Respiratory Distress in Neonates

	TTN	TTN OR	RDS	RDS OR	MAS	MAS OR
Risk Factor	**p-value**	**(95% CI)**	**p-value**	**(95% CI)**	**p-value**	**(95% CI)**
Cesarean Delivery	0.012	2.41 (1.21–4.81)	0.084	1.69 (0.93–3.11)	0.153	1.58 (0.85–2.92)
Preterm Birth	0.008	0.29 (0.12–0.70)	<0.001	6.08 (2.47–14.94)	0.222	0.62 (0.28–1.41)
Male Gender	0.045	2.01 (1.02–3.98)	0.210	1.45 (0.81–2.61)	0.132	1.64 (0.86–3.13)
Meconium-stained Amniotic Fluid	0.118	1.73 (0.86–3.48)	0.331	0.68 (0.32–1.43)	<0.001	10.09 (3.49–29.16)
Resuscitation at Birth	0.061	1.97 (0.97–4.00)	0.031	2.49 (1.08–5.73)	0.147	1.89 (0.78–4.59)
Maternal DM/HTN	0.224	1.59 (0.75–3.37)	0.112	1.87 (0.86–4.06)	0.395	1.31 (0.68–2.54)
Age Group (Late vs Early Neonatal)	0.269	1.54 (0.71–3.34)	0.354	1.37 (0.69–2.72)	0.043	2.23 (1.02–4.89)

Table 4. Subgroup Analysis: Etiology Distribution by Gestational Age and Mode of Delivery

Etiology	Term n (%)	Preterm n (%)	p-value	Cesarean n (%)	Vaginal n (%)	p-value
TTN	35 (33.7)	5 (10.6)	0.008	31 (33.0)	9 (15.8)	0.012
RDS	8 (7.7)	26 (55.3)	<0.001	19 (20.2)	15 (26.3)	0.335
MAS	23 (22.1)	5 (10.6)	0.097	20 (21.3)	8 (14.0)	0.223

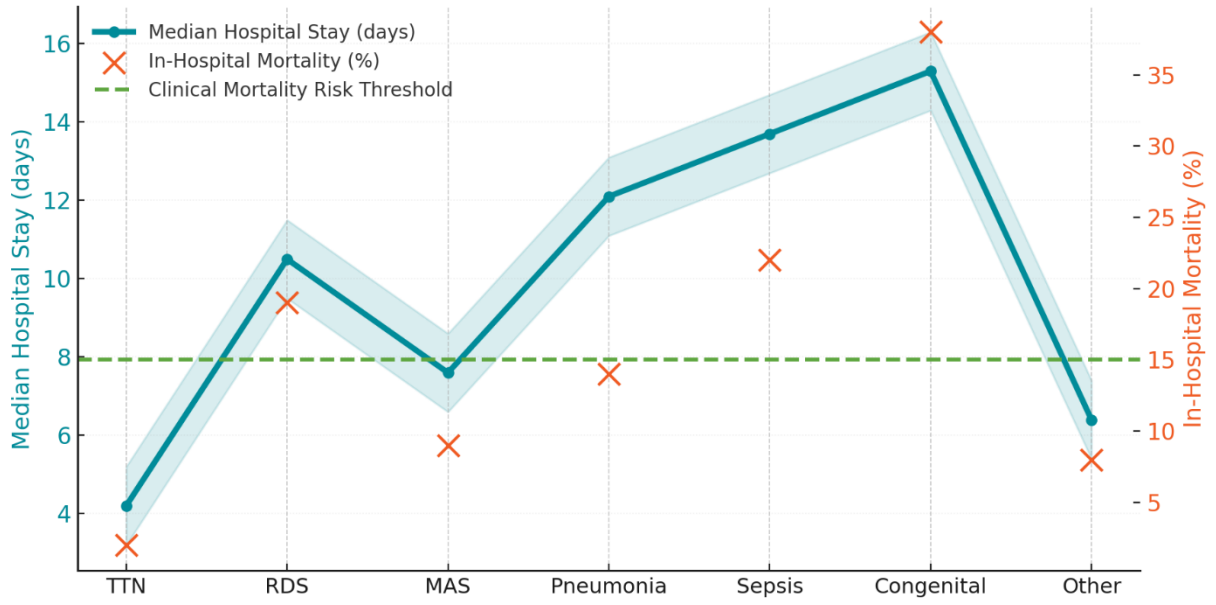

Figure 1: Hospital Stay Duration and Mortality Risk by Etiology in NICU Neonates

DISCUSSION

This study presents a comprehensive evaluation of the frequency, etiologies, and perinatal risk factors of respiratory distress among neonates admitted to a tertiary care NICU in Pakistan. The predominance of transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), and meconium aspiration syndrome (MAS) observed in this cohort closely aligns with epidemiological patterns reported both locally and internationally, affirming the global burden and etiological spectrum of neonatal respiratory distress (1,2). The association of TTN with cesarean section and term gestation underscores the role of delayed lung fluid absorption due to absent labor-induced hormonal surges, corroborating the well-described mechanism in prior studies that have consistently reported a heightened risk of TTN in infants delivered via elective cesarean section (3,8). The observed male predominance among TTN cases further supports established evidence suggesting delayed pulmonary maturation in male infants, a phenomenon attributed to sex-specific hormonal influences on fetal lung development (5). RDS in this cohort was significantly linked to preterm birth and the need for resuscitation at birth, reinforcing the central pathogenic role of surfactant deficiency and pulmonary immaturity in the genesis of RDS (6,7). This finding is strongly in agreement with existing literature from both national and international cohorts, where prematurity remains the most powerful risk factor for RDS, and the necessity for resuscitation reflects the severity of perinatal compromise and the immediate impact of surfactant deficiency on postnatal adaptation (7,9). Notably, the frequency of RDS in preterm infants in this study mirrors data from Brazilian and Pakistani neonatal units, lending external validity to the results and suggesting that despite variations in healthcare settings, the fundamental determinants of RDS are largely universal (7,8). The significant association between MAS and meconium-stained amniotic fluid, as well as late neonatal presentation, is consistent with the pathophysiological understanding that intrauterine hypoxia and post-term gestation increase the risk of meconium passage and subsequent aspiration (10,11).

The clinical relevance of this association is particularly salient in resource-limited settings, where prompt recognition and intervention for meconium-exposed neonates can markedly alter morbidity and mortality trajectories. Compared to previous regional studies, the MAS rate in this population is comparable, reflecting persistent challenges in perinatal monitoring and timely obstetric interventions (9,10). The observation that MAS was also more frequent in the late neonatal period may suggest either delayed clinical recognition, ongoing respiratory compromise, or the development of secondary complications such as infection or persistent pulmonary hypertension, a hypothesis warranting further investigation (11). This study did not identify statistically significant associations between maternal diabetes or hypertension and specific respiratory distress etiologies, a finding that contrasts with some reports suggesting a link between maternal diabetes and increased risk for RDS (13). This divergence may be due to differences in maternal glycemic control, antenatal care practices, or the relatively small proportion of mothers with these comorbidities in the present sample. Such variation highlights the complexity of disentangling maternal and perinatal factors and suggests the need for larger, multicenter studies to better elucidate these relationships.

Strengths of the study include its prospective design, comprehensive data collection on a wide array of perinatal and clinical variables, and robust statistical analysis accounting for confounders and subgroup differences. The sample size, while modest, is among the larger cohorts reported from a single center in the region and allows for meaningful inferential analysis. Additionally, the operational definitions and standardized data collection tools support reproducibility and reliability of the findings. However, studying is not without limitations. Being confined to a single institution may limit the generalizability of results to other healthcare settings, particularly those with differing obstetric or neonatal care protocols. The lack of advanced diagnostic modalities in some cases introduces the potential for underdiagnosis or misclassification of respiratory distress etiologies. Furthermore, the absence of long-term follow-up data precludes assessment of chronic respiratory or neurodevelopmental outcomes associated with early neonatal respiratory distress. The cross-sectional design, while appropriate for frequency estimation and risk factor association, does not permit causal inference.

The findings from this research offer several implications for clinical practice and policy in similar resource-limited settings. First, the strong link between cesarean section and TTN supports judicious use of elective cesarean deliveries and consideration of timing and indications, particularly in the absence of labor. Second, enhanced antenatal monitoring and targeted interventions for pregnancies at risk of prematurity may reduce the incidence and severity of RDS. Third, the importance of rapid identification and management of meconium-stained deliveries cannot be overstated, given the significant burden of MAS. Future research should focus on multicenter designs with larger sample sizes to validate these associations, incorporate advanced diagnostic and follow-up protocols, and explore the impact of targeted perinatal interventions on both acute and long-term outcomes. In summary, this study reinforces established risk profiles for neonatal respiratory distress and highlights critical opportunities for preventive and therapeutic strategies that can be adapted and scaled across diverse care environments (1-13).

CONCLUSION

This study demonstrates that respiratory distress remains a significant challenge among neonates admitted to the intensive care unit, with transient tachypnea of the newborn, respiratory distress syndrome, and meconium aspiration syndrome identified as the leading etiologies. Distinct perinatal risk factors—specifically cesarean section, prematurity, and meconium-stained amniotic fluid—are strongly associated with these conditions, underscoring the importance of targeted obstetric and neonatal interventions. These findings highlight the need for improved delivery practices, enhanced perinatal surveillance, and timely resuscitative measures to mitigate morbidity and mortality in vulnerable newborns. Clinically, this research supports evidence-based risk stratification and individualized management of neonates at risk for respiratory distress, while also emphasizing the necessity for further multicenter research to refine prevention strategies and optimize outcomes in diverse healthcare settings.

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