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ORIGINAL ARTICLE

Spectrum of respiratory distress and outcome in neonates admitted in National Institute of Child Health, Karachi, Pakistan.

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ABSTRACT… Objective: To find out the spectrum of respiratory distress and outcome in neonates admitted to Neonatal Intensive care unit (NICU) of National Institute of Child Health (NICH), Karachi, Pakistan. **Study Design:** Cross-sectional study. **Setting:** NICU of NICH, Karachi, Pakistan. **Period:** June 2022 to May 2023. **Methods:** We analyzed 148 neonates of either gender presenting with respiratory distress. At the time of enrollment, demographic and clinical information was noted in all neonates along with detailed maternal history. Relevant laboratory and radiological studies were performed. Final outcomes were recorded in terms of discharged, expired or referred. **Results:** In a total of 148 neonates, 96 (64.9%) were boys. The mean age was 4.04±5.65 days. Tachypnea, nasal flaring, intercostal recession, subcostal recession, grunting, and cyanosis 148 (100%), 146 (98.6%), 138 (93.2%), 133 (89.9%), 97 (65.5%), and 83 (56.1%) were the most frequent clinical presentations among neonates with respiratory distress. The most frequent causes behind respiratory distress were noted to be respiratory distress syndrome, sepsis, and meconium staining of labour in 31 (20.9%), 25 (16.9%), and 24 (16.2%) neonates. Mortality was observed in 21 (14.2%) neonates. Significant association of neonates presenting with congenital pneumonia ($p=0.048$), or congenital anomalies ($p<0.001$) were found to with poor outcomes. Mechanical ventilation was found to have significant relationship with poor outcomes ($p<0.001$). **Conclusion:** Tachypnea, Nasal flaring, intercostal and subcostal recessions, grunting, and cyanosis were the primary clinical presentations among the neonates with respiratory distress. Congenital pneumonia, and congenital anomalies emerged as key predictors of poor outcomes.

Key words: Grunting, Mechanical Ventilation, Nasal Flaring, Respiratory Distress, Tachypnea.

INTRODUCTION

The neonatal period is the most vulnerable time for a child's survival.[1] During the neonatal period, the reported global deaths rate is 17 per 1,000 live births while annually, around 2.4 million children lose their lives in the first month of life.[2,3] Globally, nearly half of all under five years of age deaths occur in the neonatal period.[3]

Respiratory distress in the newborn is one of the important clinical manifestations of variety of disorders of the cardiopulmonary or non-cardiopulmonary origin.[4,5] The majority of causes of respiratory distress are treatable, so, timely appropriate diagnostic and therapeutic interventions are required for the better outcomes.[6] Around 15% term infants and 29% late preterm infants are admitted to the neonatal intensive care units (NICUs) with significant morbidity having respiratory morbidity.[7,8] The reported prevalence of respiratory distress is 4.6 to 8% in Pakistan, 6.6% Nepal, and 8.1% in Ethiopia and Pakistan 8% in 2020.[7,9-11]

Global statistics show that Pakistan is among those countries who have the highest burden of neonatal mortality.[12] National Institute of Child Health (NICH), Karachi, Pakistan is a main referral center located in the most populous city of Pakistan. The objectives of this study were to find out the spectrum of respiratory distress and outcome in neonates admitted in NICU of NICH, Karachi, Pakistan. The findings of this study were thought to be helpful in guiding the timely identification and management of the neonates with respiratory distress which in turn will be

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beneficial in reducing the existing burden of neonatal morbidity and mortality.

METHODS

This cross-sectional study was conducted in NICU of National Institute of Child Health, Karachi, Pakistan from June 2022 to May 2023. Approval from Institutional Ethical Committee was acquired (IERB-43/2021(16.11.2021). Informed and written consents were obtained from the parents or guardians of all the enrolled neonates. A sample size of 148 children was calculated taking 95% confidence level, with 5% margin of error based on a local study's findings[11] that reported birth asphyxia to be the cause of respiratory distress in 10.75% neonates. Non-probability convenient sampling technique was adopted. Inclusion criteria were neonates present with two or more of following: Tachypnea (respiratory rate>60 breaths/min); Nasal flaring; Intercostal recession; Subcostal recession; Grunting; Cyanosis. Exclusion criteria were neonate with ambiguous genitalia or syndromic diseases. Neonates who expired within 24 hour following admission or those who left against medical advice (LAMA) were also excluded.

At the time of enrollment, neonatal information including age, gestational age, gender, weight, singleton or multiple, and etiology of respiratory distress. M**aternal information like a**ge, parity, chronic illnesses, booked or unbooked, hemorrhage, fever before labor, place of delivery, mode of delivery, and complications were also noted. Neonates were examined thoroughly and overall treatment plan was carried out as per NICU protocols that could involve oxygen therapy, continues positive airway pressure (cPAP), and mechanical ventilation. Baseline investigations like complete blood picture, urine complete examination, liver function tests, blood culture and sensitivity analysis were done. Chest X-ray were performed and echocardiography were asked among neonates who had suspicion for congenital heart diseases. Respiratory distress syndrome RDS) was labeled as PaO2 <50 mmHg, central cyanosis at room temperature, and radiographs showing ground glass appearance and air bronchogram within 24 hours. Hypoxic ischemic encephalopathy (HIE) was termed if umbilical pH < 7, APGAR Score 0-3 for >5 minutes, neurological abnormalities (e.g. seizures, hypotonic) and multi organs involvement (e.g. kidney, liver, heart). Neonatal sepsis was described as systemic illness accompanied by bacteremia occurring in the first 4 weeks of life and supported with WBCs count, platelets count, CRP, and culture and sensitivity analysis. Transient tachypnea of the newborn (TTN) was labeled as a clinical syndrome of self-limited respiratory distress as a result of delayed in clearance of fetal lung fluid depected by chest radiographs showing fluid in intralobar fissures. Meconium aspiration syndrome (MAS) was defined as sudden onset of respiratory distress in neonates immediately at birth or within in few hours, having history of meconium stained amniotic fluid. Typical chest radiograph characterized by patchy infiltrates, coarse streaking of both lung fields, increased antero-posterior diameter, and flattening of the diaphragm.

Final outcomes were recorded in terms of discharged, expired or referred. A special proforma was made to record all study data.

Data analysis was performed using "IBM-SPSS Statistics", version 26.0. Quantitative data were highlighted as mean and standard deviation. Categorical variables were shown as frequency and percentages. Data was stratified with regards to etiology and outcomes with respect to effect modifiers. Post-stratifiction, chi-squre or analysis of variance were applied taking $p<0.05$ as significant.

RESULTS

In a total of 148 neonates, 96 (64.9%) were boys and 52 (35.1%) girls, representing a boys to girls ratio of 1.8:1. The mean age, and weight were 4.04±5.65 days (ranging between 1 to 28 days), and 2.46±0.58 kg (1 to 4kg), respectively. The mean maternal and gestational age were 31.13±5.67 years (ranging between 20 to 48 days), and 36.00±1.81 weeks (ranging between 30 to 40 weeks), respectively. Tachypnea, nasal flaring, intercostal recession, subcostal recession, grunting, and cyanosis 148 (100%), 146

(98.6%), 138 (93.2%), 133 (89.9%), 97 (65.5%), and 83 (56.1%) were the most frequent clinical presentations among neonates with respiratory distress. The most frequent causes behind respiratory distress were noted to be respiratory distress syndrome, sepsis, and meconium staining of labour in 31 (20.9%), 25 (16.9%), and 24 (16.2%) neonates.

Analysis of maternal characteristics revealed that 82 (83.1%) were primigravida. Chronic illness, and premature rupture of membrane were noted in 26 (17.6%) and 22 (14.9%) mothers, respectively. There were 123 (83.1%) neonates who were discharged successfully wheres 4 (2.7%) were referred. Mortality was observed in 21 (14.2%) neonates. Table-I is showing comparison of neonatal and maternal characteristics with respect to outcomes and it was found that maternal age was associated with outcomes ($p=0.041$). All other characteristics were not found to influence the outcomes ($p>0.05$) as shown in Table-I. Comparison of outcomes with baseline laboratory parameters are is shown in Table-II.

Maternal history revealed no association with outcomes ($p>0.05$). Significant association of neonates presenting with congenital pneumonia ($p=0.048$), or congenital anomalies ($p<0.001$) were found to with poor outcomes, and the details are shown in Table-III. Mechanical ventilation was found to have significant relationship with poor outcomes ($p<0.001$). In 25 culture positive sepsis cases, the distribution frequency of isolates involved is shown in Figure-1.

Study Variables			Outcomes			P-Value
			Discharged	Expired	Referred	
Neonatal characteristics	Gender	Boys	79 (64.2%)	14 (66.7%)	3 (75.0%)	0.890
		Girls	44 (35.8%)	7 (33.3%)	1 (25.0%)	
	Age in days		3.83±5.40	5.14±7.14	4.75±5.0	0.599
	Weight in kg		2.44±0.58	2.54±0.56	2.83±0.24	0.331
	Gestational age in weeks		34.97±1.85	36.00±1.75	37.00±0	0.537
Maternal characteristics	Maternal age in years		30.53±5.48	33.65±6.20	34.25±4.35	0.041
	Parity	Primigravida	71 (57.7%)	9 (42.9%)	2 (50.0%)	0.438
		Multigravida	52 (42.3%)	12 (57.1%)	2 (50.0%)	
	Booking status	Booked	114 (92.7%)	19 (90.5%)	4 (100%)	0.796
		Unbooked	9 (7.3%)	2 (9.5%)	-	
	Mode of delivery	Vaginal	60 (48.8%)	13 (61.9%)	3 (75.0%)	0.340
		Cesarean	63 (51.2%)	8 (38.1%)	1 (25.0%)	
	Delivery place	Hospital	104 (84.6%)	18 (85.7%)	3 (75.0%)	0.861
		Home	19 (15.4%)	3 (14.3%)	1 (25.0%)	

Table-I. Comparison of neonatal and maternal characteristics with respect to outcomes (n=148)

Laboratory Parameters	Outcomes			P-Value
	Discharged	Expired	Referred	
Hemoglobin (g/dl)	14.44±3.09	13.52±3.25	16.75±2.22	0.144
Total Leukocytes Count (10^9/L)	14.29±5.31	11.47±5.09	15.75±2.88	0.068
Platelets (10^9/L)	251±108	237±86	279±69	0.730
Urea (mg/dl)	25.84±16.27	24.08±13.43	18.33±1.53	0.684
Creatinine (mg/dl)	0.21±0.16	0.19±0.16	0.13±0.06	0.649
Na (mEq/L)	136.59±5.59	136.73±4.37	149.00±27.65	0.004
K (mEq/L)	4.08±0.71	3.74±0.71	3.53±0.05	0.104
Cl (mEq/L)	100.49±3.15	99.82±2.32	100.00±0.00	0.780

Table-II. Association of baseline neonatal laboratory parameters with outcomes

Clinical Findings		Outcomes			P-Value
		Discharged	Expired	Referred	
Maternal findings	Chronic illness	21 (17.1%)	3 (14.3%)	2 (50.0%)	0.214
	Fever	8 (6.5%)	3 (14.3%)	-	0.385
	Premature rupture of membrane	18 (14.6%)	4 (19.0%)	-	0.608
	Prolonged labour	2 (1.6%)	1 (4.8%)	-	0.615
Clinical Presentation of neonates	Nasal flaring	122 (99.2%)	20 (95.2%)	4 (100%)	0.341
	Intercostal recession	114 (92.7%)	20 (95.2%)	4 (100%)	0.785
	Subcostal recession	110 (89.4%)	19 (90.5%)	4 (100%)	0.785
	Grunting	82 (66.7%)	12 (57.1%)	3 (75.0%)	0.643
	Cyanosis	69 (56.1%)	10 947.6%)	4 (100%)	0.154
Causes of neonatal respiratory distress	Sepsis	22 (17.9%)	3 (14.3%)	-	0.606
	Respiratory distress syndrome	27 (22.0%)	4 (19.0%)	-	0.554
	Meconium staining of labour	22 (17.9%)	2 99.5%)	-	0.426
	Transient tachypnea	22 (17.9%)	-	-	0.072
	Hypoxic ischemic encephalopathy	10 (8.1%)	4 (19.0%)	-	0.232
	Meconium aspiration syndrome	23 (18.7%)	2 (9.5%)	-	0.385
	Congenital pneumonia	-	1 (4.8%)	-	0.048
	Congenital anomalies	3 (2.4%)	6 (28.6%)	1 (25.0%)	<0.001
Treatment	Antibiotics use	82 (66.7%)	11 (52.4%)	1 (25.0%)	0.122
	Oxygen	33 (26.8%)	5 (23.8%)	1 (25.0%)	0.957
	Continuous positive airway pressure	75 961.0%)	9 (42.9%)	2 950.0%)	0.282
	Mechanical ventilation	15 (12.2%)	10 (47.6%)	-	<0.001
	Surgery	1 (0.8%)	-	-	0.903

Table-III. Association of maternal and neonatal findings with outcomes (n=148)

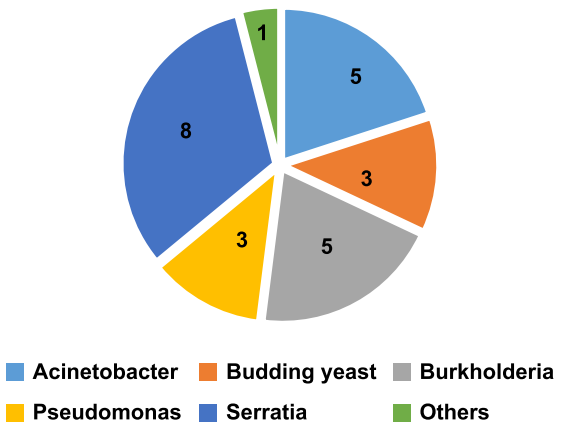

Figure-1. Distribution frequency of microorganisms in neonatal sepsis (n=25)

DISCUSSION

Respiratory distress in neonates remains a critical concern globally, especially in a developing country like Pakistan where healthcare resources might be constrained. Understanding the spectrum, contributing factors and associated outcomes of respiratory distress are crucial for improving neonatal care. The present study revealed that there was a predominance of male gender (64.9%) among cases of respiratory distress. These findings are consistent with the existing literature where a clear predominance of male gender is observed among newborns with respiratory distress.[13,14] In this study examining neonatal respiratory distress, the mean age was found to be 4.04±5.65 days (median 2.00 days). Compared to our findings, the contemporary data shows that age of neonates with respiratory distress at the time of admission is relatively young as shown by Bulimba et al (median age 1.3 hours).[16]

We noted that tachypnea (100%), nasal flaring (98.6%), intercostal recession (93.2%), subcostal recession (89.9%), grunting (65.5%), and cyanosis (56.1%) 147 (99.3%), 146 (98.6%), 138 (93.2%), 133 (89.9%), 97 (65.5%), and 83 (56.1%) were the most common clinical presentations among neonates with respiratory distress. Our findings were very consistent with the previously published local data describing tachypnea 100%), nasal flaring (100%), subcostal retractions (60.9%)

and cyanosis (39.5%) as the most frequent signs and symptoms in neonatal respiratory distress.[11] The literature describes respiratory distress in neonates manifesting through various signs and symptoms, serving as critical indicators of potential underlying conditions. Apnea, along with cyanosis, inspiratory stridor, snorting, nasal flaring, grunting, feeding difficulties, and tachypnea are crucial clinical signs indicative of respiratory distress in neonates.[17,18] Intercostal and subcostal retractions are also very frequent clinical presentations that further signify respiratory distress in neonates.[19] Primary conditions like respiratory distress syndrome, transient tachypnea of the neonate (TTN), and meconium aspiration syndrome (MAS) are among the most prevalent causes of respiratory distress and these conditions further result in compromised lung function, leading to breathing difficulties and respiratory distress in neonates.[20] Prompt recognition and management of these conditions are pivotal to ensure timely interventions and improve outcomes in neonates presenting with respiratory distress.

Respiratory pathology stands out as the most prevalent finding during autopsies conducted on early neonatal deaths, accounting for a significant proportion, estimated between 32% to 54%.[21] This high prevalence underscores the criticality of respiratory conditions as contributors to mortality in the early stages of neonatal life. Mortality was noted in 14.2% neonates with respiratory distress in this study. Sauparna et al from India reveled 31.0% mortality among neonates with respiratory distress which is much higher that what we found.[22] A study by Kommawar A et al analyzing neonatal respiratory distress observed mortality among 21.5% neonates.[23] Local data shows mortality in neonatal respiratory distress to be 31.7% which seems much higher that what we noted in this study.

We noted congenital pneumonia ($p=0.048$), or congenital anomalies ($p<0.001$) to have significant association with mortality. A study from Egypt revealed residence, causes of RD, birth weight and place of delivery to have significant association with mortality.[24] Some researchers have depicted sepsis to be the most common cause of death in neonates with respiratory distress but we did not witness that.[25,26]

This study had some limitations as well. Single center study setting and a relatively modest sample size reduce the generalisability of our findings. Data were restricted to neonates admitted to NICU and hence did not cover deaths of those who did not reach any specialized care.

CONCLUSION

Tachypnea, nasal flaring, intercostal and subcostal recessions, grunting, and cyanosis were the primary clinical presentations among the neonates with respiratory distress. Congenital pneumonia, and congenital anomalies emerged as key predictors of poor outcomes. Mechanical ventilation indicated a critical association with unfavorable neonatal prognosis. These insights emphasize the need for early identification, targeted interventions, and vigilant management strategies to improve outcomes in neonates presenting with respiratory distress in NICU settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Lachhman Singh Rajput	Data collection, Data analysis, Drafting.	
2	Mashal Khan	Conception and Design, Critical revisions, Proof reading.