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Original Research Article

Risk factors, causes and hospital outcome of respiratory distress among neonates admitted in neonatal intensive care unit of a tertiary hospital

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ABSTRACT

Background: Respiratory distress is the most frequent cause of neonatal intensive care unit (NICU) admission. Despite tremendous advancement in the management, it is still a major cause perinatal deaths particularly in this part of world. Objective were t**o** determine the risk factors, causes and outcome of respiratory distress in neonates admitted in a NICU.
Methods: This cross-sectional study was carried out in NICU of institute of child and mother health, Dhaka from July 2020 to June 2021. Total 78 newborns aged below 28 days admitted with respiratory distress were enrolled. Respiratory distress was categorized as mild, moderate and severe according to Downe's scoring.
Results: Most of the babies (78.2%) belonged to age group ≤24 hours. The leading causes of distress in preterm were respiratory distress syndrome (RDS) and that in term were perinatal asphyxia (PNA) and transient tachypnoea of neonates (TTN), both with statistical significance. Pneumonia, sepsis, congenital heart disease (CHD) and meconium aspiration syndrome (MAS) were among the other important causes. There was no significant difference between mode of respiratory support and length of hospital stay with the outcome of neonates. Severe respiratory distress was significantly associated with poor outcome. Majority 64 (82.1%) of babies were discharged, 12(15.4%) neonates succumbed to death and 2(2.6%) babies were referred.
Conclusions: PNA, TTN, RDS, pneumonia, sepsis, CHD and MAS were the predominant causes of NICU admission with respiratory distress. Severe respiratory distress was single most association with poor outcome.

Keywords: Respiratory distress, Neonate, Risk factors, NICU

INTRODUCTION

Respiratory distress (RD) is most frequent cause of admission in NICU in both term and preterm infants.[1] Despite massive advancement in the management of RD it still is responsible for 40-50% of all perinatal deaths.[2]

In Bangladesh neonatal mortality rate was 30/1000 live birth and common causes were prematurity (29.7%), birth asphyxia and trauma (22.9%) and sepsis (19.9%) including neonatal pneumonia.[3] Neonatal RD is a main cause of neonatal morbidity with mortality in developing countries.[4] RD occurs in approximately 0.96%-12% of live births, and results in about 20% of neonatal

mortality.[5] The well-established common causes of neonatal RD include TTN, RDS, MAS, PNA, Pneumonia, and Neonatal sepsis. Other less common causes include CHD, congenital diaphragmatic hernia, Esophageal atresia.[6]

In this study we aimed to determine the risk factors, causes and hospital outcome of RD among neonates admitted in NICU of a tertiary hospital.

METHODS

This cross-sectional study was conducted at NICU of institute of child and mother health (ICMH), Dhaka from July 2020 to June 2021. Newborn, aged less than 28 days, admitted with RD were enrolled into the study.

Babies with birth weight less than 1000 gm, gestational age less than 28 weeks, multiple congenital malformations, parents not willing to enroll in the study were excluded.

Sample size calculation

The sample size was determined using following formula-

$n=(Z^2\ p\ q)/d^2$

Where,

Z=Standard normal deviate=1.96

p=prevalence (prevalence of RD in NICU of ICMH from July 2019 to June 2020 is 11.11%/0.11)

q=(1-p)=0.89, and

d=Desired accuracy or degree of allowable error (here 5% of p).

$n=Z^2p(1-p)/d^2$

$(1.96)^2$x0.11x(1-0.11)/$(0.05)^2$=150

The study was done during COVID-19 pandemic period and there was less admission in NICU. So, we took 78 newborn as study sample.

RD was diagnosed clinically by presence of at least 2 of the following: Respiratory rate of >60/min or more, chest retraction (subcostal indrawing, xiphoid retraction, suprasternal indrawing) and expiratory grunt/groaning.

Severity of RD was assessed by Downe's scoring.[7] Etiological diagnosis of RD was made on clinical ground, and it was confirmed by related investigations like septic screen, blood culture, chest X ray, other blood biochemical tests (blood sugar, electrolytes, calcium, urea, creatinine) done in laboratory of institute of child and mother health.

Neonates were managed according to standard management protocol of neonates.[8] Neonates were oxygenated by using nasal prong, Hood box, CPAP or ventilator according to need. Daily monitoring of oxygen saturation was measured by using pulse oxymeter. Daily follow up was done to find out the complications, hospital stay and outcome of neonates. No clinical intervention was done by the investigator.

Those babies who were discharged with or without sequelae had 'good outcome' while those who expired during the treatment had 'bad outcome'. Two referred cases are followed up, good wellbeing were confirmed. So, they were included in good outcome.

Statistical analysis was performed with statistical package for social science (SPSS) version 23. The qualitative variables were expressed as frequency and percentage and the quantitative variables were expressed as mean ± standard deviation. Chi-square statistical test was done to determine the association between categorical variables. Unpaired student t test was done to determine the difference between continuous variables. Multivariate logistic regression analysis was done to find out the association of risk factors with poor outcome of RD.

Ethical clearance certificate was obtained from institutional review board (IRB) of ICMH. Informed written consent was secured from each legal guardian of the study subject.

RESULTS

Among the study subjects, most of the neonates (78%) were presented before 24 hours of life, while 12.8% were presented in between 25-48 hours and only 9% were presented after 48 hours. Male predominance (1.36:1) was observed in them.

Detailed maternal perinatal history was obtained. Among the mothers 73.1% were in between 18-35 years of age, while 17.9% were below 18 years and 8.9% were above 35 years of age. About three fourth (76.9%) of them were under regular antenatal care. Ante partum hemorrhage was experienced in 62 (79.5%) mothers. Comorbidities like HTN, DM, bronchial asthma and infection were observed in 21 (27%) mothers.

Prolonged labor, PROM and meconium-stained liquor were documented in 13 (16.7%), 11 (14.1%) and 7 (9%) mothers, respectively. Among them 10 (12.8%) mothers got antenatal steroid therapy. Two (2.6%) mothers underwent unclean vaginal examination while another 10 (12.8%) underwent ≥3 times vaginal examination. Number of LUCS (47) surpassed that of NVD (31). Term deliveries resulted in 52 (69.2%) pregnancies where

hospital or clinic deliveries were carried out in 53 (68%) cases and 25 (32.1%) mothers had home delivery.

A significant number (44.9%) of babies had delayed crying. Neonatal resuscitation was needed in 35 babies (44.9%). RD found immediately after birth in 27 (34.6%) neonates, within 24 hours in 30 (38.5%) neonates and after 24 hours in 21 (26.9%) neonates, respectively.

The leading cause of RD diagnosed in our study was PNA in 46 (59.0%) followed by 21 (26.9%) cases of RDS, 20 (25.6%) cases of pneumonia, 15 (19.2%) cases of TTN, 12 (15.4%) cases of sepsis, 8 (10.3%) cases of CHD, 7 (9.0%) cases of MAS, single case of COVID-19 and single case of CDH (Table 1).

PNA and TTN were significantly higher in term gestational age. However, RDS, pneumonia and sepsis were significantly higher in preterm gestational age. Low birth weight was significantly associated with RDS, male gender was significantly associated with PNA and normal vaginal delivery was significantly associated with PNA, Pneumonia and sepsis.

Majority 64 (82.1%) babies were discharged followed by 12 (15.4%) neonatal death and 2 (2.6%) babies were referred (Figure 1). There was no significant difference found between length of hospital stay and outcome (p=0.916).

According to Downe's scoring, 11 neonates had severe RD, among them good outcome found in 3 (27.3%) and poor outcome (death) occurred in 8 (72.7%) cases. The difference was statistically significant (p<0.001) between types of RD and outcome.

Oxygen was introduced by nasal canula in 52 cases, by CPAP in 17 cases and ventilation was needed in 9 cases. There was no significant difference found between mode of oxygen support for RD and outcome (p=0.186). There was no significant association was observed between causes of RD and outcome (p>0.05) (Table 2).

Irregular antenatal visit, delayed crying, need of resuscitation and onset of RD had statistically significant difference (p<0.05) when compared to patients outcome. However, ante partum hemorrhage, prolonged rupture membrane, antenatal steroid therapy, meconium-stained liquor, gestational age, mode of delivery, gender and weight of infant in gm were not statistically significant (p>0.05) when compared to outcome (Table 3).

From multivariate logistic regression analysis, it was observed that severe RD (OR=35.09 with 95% CI 2.82 to 97.7%) was significant statistically for poor outcome. However irregular antenatal visit, delayed crying, need of resuscitation and onset RD were not significantly associated with outcome (Table 4).

Table 1: Causes of RD in studied neonate, (n=78).

Causes of respiratory distress	N	Percentage (%)
PNA	46	59.0
RDS	21	26.9
Pneumonia	20	25.6
Sepsis	12	15.4
Transient tachypnoea of neonate	15	19.2
CHD	8	10.3
MAS	7	9.0
COVID-19	1	1.3
Congenital diaphragmatic hernia	1	1.3

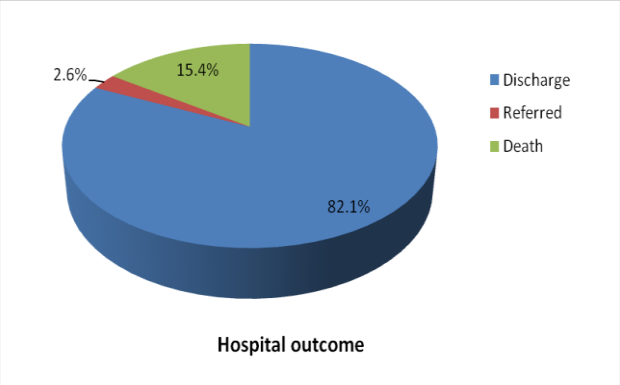

Figure 1: Hospital outcome of study patients, (n=78).

Table 2: Association of causes of RD and outcome of neonates with RD, (n=78).

Causes of RD	Total	Good outcome, (n=66)		Poor outcome, (n=12)		P value
		N	%	N	%	
PNA	46	39	84.8	7	15.2	0.960^{ns}
RDS	21	19	90.5	2	9.5	0.383^{ns}
Pneumonia	20	17	85.0	3	15.0	0.955^{ns}
Sepsis	12	9	75.0	3	25.0	0.315^{ns}
Transient tachypnoea neonate	15	14	93.3	1	6.7	0.297^{ns}
CHD	8	8	100.0	0	0.0	0.203^{ns}
MAS	7	7	100.0	0	0.0	0.267^{ns}
COVID-19	1	1	100.0	0	0.0	0.667^{ns}
Congenital diaphramatic hernia	1	1	100.0	0	0.0	0.667^{ns}

*Multiple response, p value reached from Chi square test.

Table 3: Analysis of risk factors and outcome of neonates with RD, (n=78).

Parameters	Total	Good outcome, (n=66)		Poor outcome, (n=12)		P value
Antenatal visit						
Irregular	18	11	61.1	7	38.9	0.001
Regular	60	55	91.7	5	8.3	
Antepartum hemorrhage						
Yes	16	13	81.3	3	18.8	0.703
No	62	53	85.5	9	14.5	
Prolonged rupture membrane						
Yes	11	11	100	0	0.0	0.127
No	67	55	82.1	12	17.9	
Antenatal steroid therapy						
Yes	10	9	90.0	1	10.0	0.613
No	68	57	80.9	11	16.2	
Meconium-stained liquor						
Yes	07	07	100	0	0.0	0.127
No	71	59	83.3	12	17.9	
Gestational age						
Term	52	44	84.6	8	15.4	
Preterm	24	20	83.3	4	16.7	0.856
Post term	2	2	100.0	0	0.0	
Mode of delivery						
NVD	31	28	90.3	3	9.7	0.257
LUCS	47	38	80.9	9	19.1	
Delayed crying						
No	43	33	76.7	10	23.3	0.033
Yes	35	33	94.3	2	5.7	
Need of resuscitation						
Yes	35	35	100.0	0	0.0	0.001
No	43	31	72.1	12	27.9	
Onset of respiratory distress						
Immediate after birth	27	18	66.7	9	33.3	
Within 24 hours	30	28	93.3	2	6.7	0.005
After 24 hours	21	20	95.2	1	4.8	
Gender						
Male	45	37	82.2	8	17.8	0.494
Female	33	29	87.9	4	12.1	

P value reached from Chi square test

Table 4: Association of statistically significant risk factors of RD with poor outcome in studied neonates by multivariate logistic regression model.

Prognostic factors	Adjusted OR	P value	95% CI	
			Lower	Upper
Irregular antenatal visit	0.069	0.069	0.85	70.09
Delayed crying	3.18	0.339	0.29	34.16
Need of resuscitation	0.00	0.998	-	-
Onset of RD	0.044	0.055	0.002	1.06
Severe RD	35.09	0.006	2.82	97.7

DISCUSSION

This cross-sectional study was carried out with an aimed to determine the risk factors, causes and hospital outcome of RD in neonates. Most of the babies were male (57.7%) and 78.2% were admitted within 24 hours of age. Previous studies also found males are more affected than female.[5,6,9,10]

PNA (59%) was the commonest cause RD followed by RDS (27%), pneumonia (26%), transient tachypnoea of newborn (19%), sepsis (15%), CHD (10%) and MAS (7%) to be documented in our study. Haque et al found transient tachypnoea of newborn (42.7%) was most common cause of RD in newborn followed by RDS (27.6%), PNA (25%), septicaemia (16.1%), congenital pneumonia (11.9%) and CHD (10.4%).[6] Surgical causes

and MAS were found as causes of RD in 2% and 1.5% respectively. Gouyon et al found the commonest cause for RD in newborns was TTN followed by MAS and RDS.[11] Kommawar et al found that the most common cause of neonatal RD was TTN (40%).[5] They also found RDS present in 27% cases and birth asphyxia in 12% cases. Rakholia et al found that RDS is the top cause of RD followed by birth asphyxia (17%) in inborn neonates and had sepsis in out born neonates.[12] Baseer et al found major cause of RD was RDS (50%), followed by transient tachypnea of newborn (22%), pneumonia (17%), MAS (6%), congenital diaphragmatic hernia (2%) and tracheosophegeal fistula (1%).[9] In current study, major cause of RD was PNA which was not consistent with previous studies. It may be due to small sample size and geographical background.

In this study, PNA and transient tachypnoea of neonate were significantly higher in term gestational age and RDS significantly higher in preterm and low birth weight. Quian et al also found RDS mostly related to preterm and low birth weight neonates.[13] Similar findings also found in Haque et al and Raha et al.[6,14]

Current study showed that 41% neonates required oxygen inhalation by nasal canula, 25% by Hood box, 21% by CPAP and mechanical ventilation required in 11% cases. A study by Chandrasekhar et al reported 15 babies were put on Bubble CPAP; surgical intervention was done in one case of congenital diaphragmatic hernia that also required ventilator care.[15] In that study majority (62%) required O_2 less than 24 hours. Previous study also showed similar findings where majority of neonates need oxygen therapy by nasal canula followed by CPAP and ventilator support respectively.[2,10,14]

Our study showed that in half (50%) of the babies, hospital stay were 6-10 days. Baseer et al also reported that mean duration of hospital stay was 9.37±1.59 days.[9] Majority of babies in our study were discharged (82%), 2.6% were referred and death occurs in 15.4%. This finding correlates with Sathenahalli et al where mortality-40% and with Kommawar et al where mortality-27%.[16,5]

When we categorize the type of RD by Downe's score 31% had mild RD, 55% had moderate and 14% develop severe RD. Babies with severe RD had more mortality and p value was significant (p=0.001) in our study. Sathenahalli et al also showed higher Downe's score associated with increased mortality.[16]

In current study, mortality was high in those who were in ventilator support (33.3%) followed by 23.5% in CPAP and 11.5% with oxygen inhalation by nasal canula and Hood box though p was not significant (p=0.186). Haque et al observed mortality was high (56.2%) in those who required mechanical ventilation that like current study.[6]

In present study, the mortality rate was high in sepsis (25%) followed by pneumonia and PNA (15%) and in RDS (9.5%). Sathenahalli et al observed that mortality rate was high in RDS (65%) and sepsis (52%).[16] As our hospital is in semi urban area and about 39% of study population were delivered at home, chances of infection related mortality was more. Haque et al also reported mortality was highest in neonate with RDS (71.8%) followed by septicaemia (40.6%) and PNA (37.3%).[6] Current study showed that there was no significant difference between causes of RD and outcome (p>0.05).

To find out association of risk factors with outcome of study patient showed irregular antenatal check-up, delayed crying, resuscitation needed at birth, onset of RD immediately after birth statistically significant (p<0.05). However, antepartum hemorrhage, maternal co-morbidity, prolonged rupture membrane, steroid therapy, meconium-stained liquor, gestational age, mode of delivery, gender and weight of the infant in gram were not statistically significant (p>0.05) when compared with outcome. Similar study was done by Sathenahalli et al that revealed mean respiratory rate, mean Downe's score, mean FiO_2 requirement, mean gestational age, mode of delivery significantly associated with poor outcome.[16]

Regarding multivariate logistic regression analysis of risk factors, it was observed that only severe RD (OR=35.09 with 95% CI 2.82 to 97.7%) was significantly associated with poor outcome. Though initially significant but irregular ANC, delayed crying, need of resuscitation and onset of RD (after 24 hours) not significantly associated with poor outcome in multivariate logistic regression.

Limitations

Due to time constraint and COVID-19 pandemic situation, the researcher cold not achieve the calculated sample size. Long time prospective cohort study is recommended to see the sequelae of outcome.

CONCLUSION

PNA and transient tachypnoea of neonate were significantly higher in term gestational age and RDS significantly higher in preterm and low birth weight. Severity of RD was significantly associated with poor outcome. Common causes of RD in hospitalized neonates were PNA, RDS, pneumonia, sepsis, transient tachypnoea of newborn, CHD and MAS. More than three fourth neonates were discharged with good outcome.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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