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Evaluation of Etiology, Risk Factors and Outcome of Neonates with Respiratory Distress Admitted in Neonatal Intensive Care Unit at a Tertiary Care Hospital

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Abstract
Respiratory distress is a leading cause of hospital admissions in newborns contributing to significant morbidity and mortality. It could be due to respiratory and non-respiratory causes. Various etiological factors like RDS, meconium aspiration, birth asphyxia ,congenital pneumonia, congenital heart diseases, TEF etc cause respiratory distress in neonates. This was a prospective observational study done in NICU, Government General hospital, Kakinada, for a period of 18 months from January 2018 to June 2019 where 402 newborns with respiratory distress were enrolled to study the etiology, risk factors and outcomes of newborns with respiratory distress. The study showed that respiratory causes like meconium aspiration syndrome (34.3%), RDS (26.8%)was the major contributing factor to respiratory distress in newborns (69.2%). RDS is common in preterm babies who can be managed appropriately with timely surfactant administration. Mortality was high in newborns admitted with birth asphyxia (30%) and meconium aspiration syndrome(20%). 100% mortality was seen in cases due to congenital anomalies like TEF and CDH. Respiratory distress in newborns is a challenging problem in developing countries. Early recognition of fetal distress, institutional deliveries, timely referral to specialized centres for management, antenatal administration of steroids and frequent training of medical staff can go a long way in preventing morbidity and mortality due to respiratory distress in these neonates.
Keywords: *Respiratory distress, neonates, RDS, surfactant, meconium aspiration*

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I. Introduction

Respiratory distress is common, occurring in up to 7% of newborns[1]. It is the most common cause for admission into Neonatal Intensive Care Unit (NICU). The clinical presentation of respiratory distress in newborns includes nasal flaring, intercostal retractions, tachypnea, grunting and cyanosis. The incidence of neonatal respiratory distress ranges from 2.2% to 7.6% in developed countries and from 0.7% to 8.3% in India.[1] It has been estimated that 40-50% of all the perinatal deaths occur following respiratory distress[2]. So, its prevention and adequate management will decrease the neonatal mortality significantly.

Respiratory rate (RR) should be counted for full one minute with a timer and when the baby is quiet and preferably when baby is not hungry or immediately after feeds[4]. Common causes of RD are Respiratory distress syndrome, pneumonia, meconium aspiration syndrome, transient tachypnoea of the newborn, pneumothorax, primary or secondary pulmonary arterial hypertension, aspiration of milk or blood, pulmonary hemorrhage, and non-respiratory causes like cardiac failure (due to congenital heart disease), and hypoxic-ischemic encephalopathy.

Outcome of respiratory distress in newborn depends on early diagnosis of etiological factors Appropriate and timely interventions is essential for better outcomes. Transient tachypnea of newborns (TTNB) is the most common cause of neonatal RD (>40%) in term infants, followed by meconium aspiration syndrome (MAS) whereas RDS is responsible for majority of cases of respiratory distress in preterm babies. This study mainly aims at identifying the etiological factors responsible for neonatal respiratory distress, the clinical presentation and management of RD due to various causes and to determine the risk factors and immediate outcome of RD in newborns admitted in this hospital.

II. Material And Methods

This was a prospective observational study done in NICU, GGH, Kakinada during the period January 2018 to June 2019. Data of all newborns with respiratory distress who were enrolled in the study was collected. In babies with respiratory distress, birth details and time of onset of respiratory distress was noted and severity of respiratory distress was assessed using DOWNE'S scoring in term babies and Silverman Anderson score in preterm babies. Chest X-ray was taken in all neonates and radiograph findings were documented after taking radiologist opinion. Based on the probable cause of respiratory distress, other investigations were carried out as per need [Septic screen, Blood c/s, X ray abdomen, Neurosonogram, Electrocardiogram, 2D ECHO, etc]. All neonates enrolled in the study were managed as per unit protocol. Treatment details like respiratory support given [oxygen therapy, CPAP, mechanical ventilation], surfactant administration and surgical interventions performed were recorded. Response of these neonates to the given treatment and outcome were documented. Chi-square test and SPSS software version 23 was used for statistical analysis.

III. Observations And Results

In the present study, 402 cases were enrolled with respiratory distress. Table 1 shows the common causes of respiratory distress in these newborns. 69.2% cases were respiratory in origin, 24.4% were of CNS origin, 4.5% were of cardiac causes, and 1.9% were due to rare causes such as CDH,TEF and inborn errors of metabolism.

Table 1: *Distribution of respiratory and non-respiratory causes of respiratory distress.*

Etiology	**Frequency (no. Of cases)**	**Percentage**
Respiratory causes	278	69.2%
Cns causes	98	24.4%
Cardiac causes	18	4.5%
Others	8	1.9%
Total cases	**402**	**100%**

Table 2: *Final diagnosis of respiratory distress.*

Etiology	**No of cases (%)**
Meconium Aspiration Syndrome	138 (34.3%)
Respiratory Distress Syndrome	108 (26.8%)
Birth Asphyxia	98 (24.3%)
Ttnb	22 (5.5%)
Congenital Heart Disease	18 (4.4%)
Congenital Pneumonia	10 (2.5%)
Others (Cdh-2, Tef-4, Iem-2)	8 (1.9%)
Total Cases	**402**

Table 2 shows that meconium aspiration syndrome was the leading cause of respiratory distress in the 402 newborns included in the study (34.5%). Respiratory distress syndrome was the cause in 26.8% cases followed by birth asphyxia seen in 24.3% cases.

Table 3: *Birth weight vs frequency of RD.*

Birth weight	**Frequency**	**Percentage**
<1.5 kg	97	24.2%
1.5 – 2.5 kg	147	36.5%
>2.5 kg	158	39.3%
Total cases	**402**	**100%**

In the present study, out of the total 402 newborns with respiratory distress, the mean birth weight of the babies was 2.3 kgs, 24.2% weighed <1.5kg, 36.5% weighed between 1.5 to 2.5 kg, and 39.3% weighed >2.5 kg.

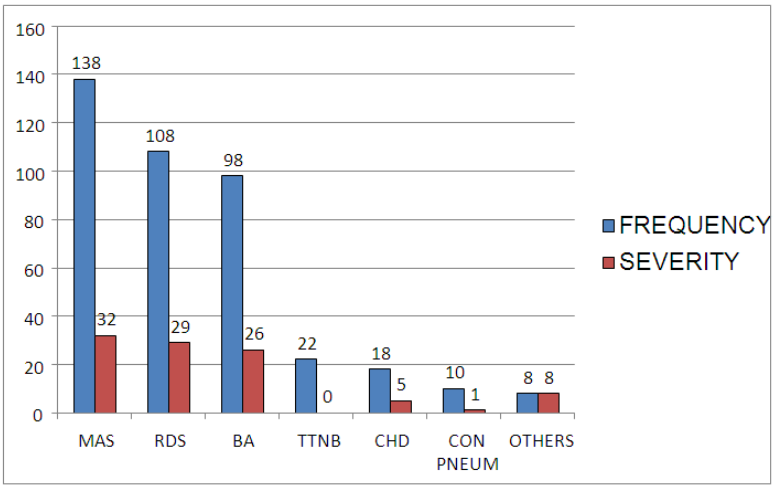

Figure 1: *Etiology vs severity of RD.*

Out of 138 cases with RD due to MAS, 32 cases (23.1%) had severe RD. 29 out of 108 (26.8%) cases of RDS had severe RD and 26 out of 98 (26.5%) cases of BA had severe RD. All cases of TTNB had mild or moderate RD. 5 out of 18 (27.7%%) cases of CHD had severe RD. 1 out of 10 (10%) cases of congenital pneumonia had severe RD. All 8 (100%) cases of TEF, CDH and IEM had severe RD.

Table 4: *Gestational age versus severity of RD.*

Gestational age	**Mild to moderate RD (downes < 7/10)**	**Severe RD (downes > 7/10)**	
<34 weeks (83)	41	42(50.6%)	Chi square= 38.72, Df= 2, P= 0.00001
34-36 weeks (25)	17	8 (32%)	
>37 weeks (294)	243	51 (17.3%)	
Total (402)	**301**	**101**	

50.6% (42 out of 83) of newborns born with gestational age <34 weeks developed severe respiratory distress compared to 32% (8 out of 25) of newborns born with a gestational age 34-36 weeks and 17.3% (51 out of 294) of newborns born with a gestational age >= 37 weeks. These findings suggest that severe RD is more common in preterm newborns (especially <34 weeks) than term newborns which was statistically significant with a p value 0.00001.

Table 5: *Role of surfactant in RD due to RDS.*

Surfactant (ST)	Number of cases	Duration of hospital stay			Mortality (%)	
		<3 days	4-7days	>7days		
ST given	51	4	36	11	4 (7.8%)	Chi square= 3.9204, p= 0.047705
ST not given	57	0	42	15	14(24.5%)	
Total cases	**108**	**4**	**78**	**26**	**18**	

Out of 108 preterms with RDS, 51 cases were given surfactant. Out of these 51 cases, 4 cases (7.8%) required oxygen for < 3 days, 36 cases (70.5%) required oxygen for 4-7days, and 11 cases (21.5%) required oxygen for >7 days. 4 out of 51 (7.8%) cases expired. Out of the 57 cases who were not given surfactant, 42 cases (73.6%) required oxygen for 4-7days, and 15 cases (26.3%) required oxygen for >7 days. 14 out of 57 (24.5%) cases expired. Only 7.8% of cases expired among babies for whom ST was given, while 24.5% of cases expired among babies who were not given ST. This was statistically significant with a p-value < 0.05.

Table 6: *Morbidity and mortality of cases with RD on CPAP and Mechanical ventilator.*

	No of cases	Duration of oxygen administration			Mortality (%)
		<3 days	4-7days	>7days	
CPAP	89	24	34	31	16 (17.9%)
CPAP+ MV	62	4	26	32	24 (38.7%)
Total cases	**151**	**28**	**60**	**63**	**40**

Out of 89 cases requiring CPAP, 24 cases required oxygen for < 3 days, 34 cases required oxygen for 4-7days, and 31 cases required oxygen for >7 days. 16 out of 89 (17.9%) cases expired. Out of the 62 cases requiring MV, 4 cases required oxygen for <3 days, 26 cases required oxygen for 4-7days, and 32 cases required oxygen for >7 days. 24 out of 62 (38.7%) cases expired.

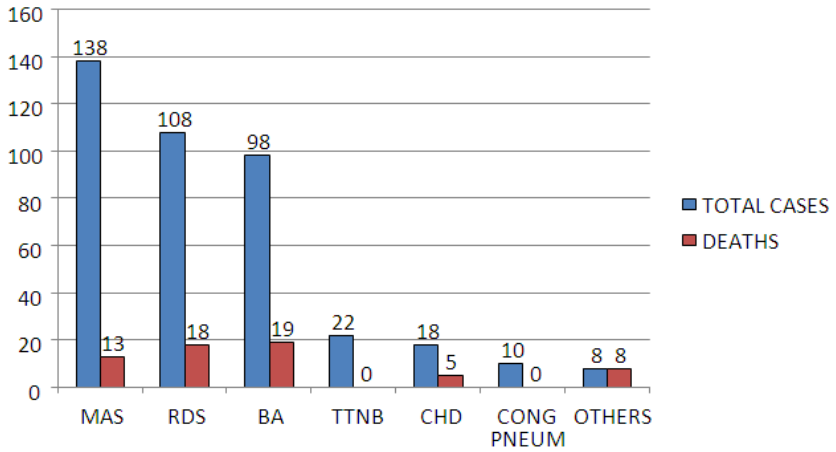

Figure 2: *Mortality versus etiology of RD.*

Out of a total of 402 cases with RD, 63 babies expired with a mortality of 15.7%. Out of the 63 babies expired, the majority (30%) of the deaths were due to birth asphyxia, followed by 28% deaths due to RDS. Other causes of mortality were MAS (20%) and CHD (8%). All the 8 cases enrolled with CDH, TEF, and IEM expired. Best outcomes were seen with TTNB and congenital pneumonia, with all cases being discharged.

Table 7: *Severity of RD versus mortality.*

Etiology	**Total number of cases**	**Severe RD**	**Mortality**
MAS	138	32(23.1%)	13 (40.6%)
RDS	108	29(26.8%)	18 (62%)
BA	98	26(26.5%)	19 (73%)
TTNB	22	-	-
CHD	18	5(27.7%)	5 (100%)
Congenital pneumonia	10	1 (10%)	-
Others (CDH, TEF, IEM)	8	8(100%)	8(100%)
Total	**402**	**101**	**63**

Out of 402 newborns, 101 cases (25.1%) developed severe RD. 73% (19 out of 26) of cases of BA with severe RD expired. 62% (18 out of 29) of cases of RDS with severe RD expired. 40.6% (13 out of 32) of cases of MAS with severe RD expired. All cases of TTNB and congenital pneumonia were discharged. 100% (13 out of 13) cases with severe RD among CHD, TEF, CDH and IEM expired.

IV. Discussion

The etiology of RD differs with gestational age. The most common etiological factor of RD was identified as TTNB in term newborns and RDS in preterm newborns in various studies. In the present study, out of 402 cases identified with respiratory distress, 70% were respiratory in origin, 24% were of CNS origin,4% were of CVS causes, and 2% were due to other rare causes such as CDH, TEF and inborn errors of metabolism. In the present study, Meconium aspiration syndrome (34.5%) was the most common etiological factor, followed by Respiratory distress syndrome (27%), Birth asphyxia (24.5%), Transient tachypnea of newborn (5.5%), Congenital heart disease (4.4%), Congenital pneumonia (2.5%), Congenital diaphragmatic hernia (0.4%), Tracheoesophageal fistula (0.8%) & Inborn errors of metabolism (0.4%).

According to study done by Alok Kumar and Bhat [5,] Transient tachypnea of newborn (TTN) was found to be the most frequent (42.7%) cause of RD followed by infection (17.0%), meconium aspiration syndrome (10.7%), hyaline membrane disease (9.3%) and birth asphyxia (3.3%). According to Santosh S et al [2], it was observed that 35 (46%) babies had TTNB, 24 (31.5%) babies had RDS, 19 (25%) had BA, 19(25%) babies had pneumonia and sepsis, 6 (7.8%) babies had MAS, 2 (2.6%) babies had CHD, and one (1.3%)

neonate each had pneumothorax and laryngomalacia as a cause for RD. In the present study, MAS was the most common cause of RD. This variability was due to the increased number of term babies in the present study and also most of the referral cases with RD from outside were due to meconium aspiration syndrome from remote areas.

46% of preterm newborns (50 out of 108) developed severe respiratory distress compared to 17.3% (51 out of 294) in term newborns. These findings suggest that severe RD is more common in preterm newborns (especially <34 weeks) than term newborns which is statistically significant with a p value of 0.00001. In the present study, the severity of respiratory distress increased with decreasing gestational age. As the gestational age decreases, there is an increased risk of developing severe respiratory distress due to RDS. The study done by C. Dani et al[6] confirmed the role of gestational age and birth weight as risk factors for RDS. Santosh et al [2] and M Lureti et al [8] reported similar findings regarding gestational age and incidence of RDS.

In the present study, the mean birth weight of newborns with RD was 2.3 kg. Severe RD was seen in 30.6% of babies with birth weight <1.5 kg, 19% of babies with birth weight 1.5 to 2.5kg, and 26.5% of babies with birth weight > 2.5kg. Birth weight<2.5kg is associated with severe RD. This can be explained by the fact that the incidence and severity of RDS or HMD increases with decreasing gestational age and birth weight.

In the present study, most of the cases - 238(59%) had 4-7 days duration of respiratory distress. Duration of respiratory distress of 4-7 days was seen in 62.3% cases of MAS, 72.2% of RDS, 53% of birth asphyxia, 66.6% of CHD, and 100% of cases with congenital pneumonia. These findings suggest that most of the cases of MAS, RDS, and BA had a mean duration of RD of 4-7 days, which is statistically significant with a p value of 0.00001. All cases with TTNB (100%) had less than three days of duration of respiratory distress, which shows the self-limiting nature of the disease.

150 babies of the 402 cases in this study were delivered by LSCS, and 252 cases were delivered by NVD. 33 out of 150 (22%) cases delivered by LSCS developed severe respiratory distress, while 67 out of 252 cases (26.6%) delivered by NVD developed severe RD. This indicates that severe respiratory distress is more common with NVD when compared to LSCS which can be explained by the fact that NVD is associated with prolonged labor and hence, the risk of birth asphyxia and MAS leading to severe respiratory distress. TTNB is the most common cause of RD in term babies and one of the important risk factors for TTNB is delivery by cesarean section with or without labor and precipitous labor. This is attributed to delayed or abnormal fetal lung fluid clearance due to the absence of the hormonal changes(adrenergic stimulation) that accompany spontaneous labor. In the present study, all the babies with TTNB were delivered by cesarean section

In our study,51 cases out of 108 preterm babies with RDS were given surfactant. Out of these 51 cases, 4 cases(7.8%) required oxygen for < 3 days, 36 cases(70.5%) required oxygen for 4-7days, and 11 cases(21.5%) required oxygen for >7 days. 4 out of 51 (7.8%) cases expired. Out of the 57 cases who were not given surfactant, 42 cases (73.6%) required oxygen for 47days, and 15 (24.5%) cases required oxygen for >7 days. 14 out of 57(24.5%) cases expired. Mortality was significantly low (7.8%) among surfactant administered babies when compared to those who were not given surfactant (24.5%), and this result was statistically significant with a p value of 0.04 ($p<0.05$). Hence timely intervention among preterm babies with early surfactant administration has a significant role in reducing the morbidity and mortality of RDS. In this study, Surfactant could not be given to 57 babies due to logistic reasons like shortage of surfactant in government hospital and non affordability of parents. If we give surfactant to all the required babies, mortality due to RDS will reduce significantly among preterm neonates. In a study done by Sabzehei MK et al [3] 3 cases expired out of 12 babies who were administered surfactant, and 15 cases expired out of 81 cases (18.5%) who were not given surfactant.

In the present study, 63 babies expired with a mortality. Majority (30%) of the deaths were due to birth asphyxia followed by RDS(28%). In the present study, RDS was the most common cause of mortality in preterm babies as they are at risk with other comorbidities like sepsis, PDA, NEC which further adversely affect the prognosis and outcome. A study done by Sabzehei MK et al [3] showed a mortality of 19.4%, with 18 deaths out of 93 cases and RDS, pneumonia, and CHD were the most common causes of mortality. Tochie et al[7] found sepsis and RDS as the most common causes of hospitalization for respiratory distress, and 24.5% of cases died due to neonatal infection, prematurity, and RDS. On the contrary, Rao et al [9] reported mortality of 2.5% due to RDS.

In the present study, rare causes of RD like Inborn errors of metabolism and surgical causes of RD like congenital diaphragmatic hernia and tracheoesophageal fistula had high mortality of 100%.These conditions should always be considered while evaluating any newborn with respiratory distress because early identification, prompt referral to advanced centers with super specialty services would improve survival chances with good outcome in these neonates .

Unlike other studies, Birth Asphyxia is the most common cause of mortality in the present study. Severe asphyxia is usually associated with severe respiratory distress due to several pulmonary complications

like increased pulmonary vascular resistance leading to PPHN, pulmonary hemorrhage and pulmonary edema due to cardiac dysfunction in addition to multi organ dysfunction.

V. Conclusion

1. Respiratory distress in neonates is due to a variety of disorders of the respiratory system and non-respiratory causes.
2. It is the most common cause of admissions into the NICU, contributing to 40-50 % of all the perinatal deaths. Technological advances, increased neonatal specialization, early recognition, and appropriate management of RD in newborn babies led to an impressive fall in neonatal mortality due to respiratory distress in tertiary care centers all over the world. However, this is still not attained in developing countries due to various causes.
3. In developing countries early recognition of fetal distress, assessment of maternal risk factors for neonatal sepsis, usage of corticosteroids in anticipated preterm deliveries, encouraging mothers for institutional deliveries and frequent training to health workers who conduct deliveries particularly in peripheral and remote areas play a significant role in decreasing the incidence of respiratory distress due to birth asphyxia, MAS and RDS.

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