ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 05 | May - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ETIOLOGICAL PROFILE AND OUTCOME OF RESPIRATORY DISTRESS IN NEWBORNS: A PROSPECTIVE TERTIARY CARE HOSPITAL STUDY

Paediatrics

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ABSTRACT

Background: Respiratory distress is the most common cause for NICU admissions in a tertiary care referral centre which also contributes to significant mortality of patients admitted with RD. It is important to conduct regular studies to follow the trends of etiological and demographical characteristics of newborns developing respiratory distress at different healthcare levels in a country.

Methods: This study was conducted for a period of 3 months (from mid-November 2020 to mid-February 2021) in the neonatal intensive care unit of Sawai Man Singh medical college and hospital Jaipur, a major outborn tertiary care referral centre in the North-west part of India to find out the etiologies and their association with other demographic factors behind respiratory distress in newborns. All the newborn with clinically diagnosed RD and age less than 28 days were enrolled in the study and followed until their outcome.

Results: In this observational study, we found that the majority of NICU admissions were due to respiratory distress (184, 27.38%) and among them, RDS was the most common aetiology followed by perinatal asphyxia, MAS, congenital pneumonia, sepsis, CHD and others. More than half of the newborns were born preterm, had low birth weight and were born to mothers in the age group 20-25 years. Baseline antibiotics and oxygen therapy were given to almost all newborns admitted with RD and mechanical ventilation was provided to moderate and severe cases. In the study period, 53 out of 184 RD patients succumbed to death despite maximum treatment with MAS having a case fatality of 52%.

Conclusion: RDS being more common and MAS being more fatal, should be diagnosed early and treated appropriately via newer medical advancements such as CPAP and Mechanical Ventilation. Preterm birth, low birth weight and cesarian delivery were associated with poor outcome of RD patients and must be taken into account when managing RD patients.

KEYWORDS

Respiratory distress, newborn, RDS (respiratory distress syndrome), MAS (meconium aspiration syndrome), CPAP (continuous positive airway pressure)

INTRODUCTION

Respiratory distress is considered the most common cause of NICU admissions in a tertiary care centre. Nearly half of the NICU deaths occur because of respiratory distress and its related complications. Thus, it becomes prudent to assess and treat respiratory distress in newborns in order to decrease neonatal morbidity and mortality.

Respiratory distress is a symptom complex arising from disease processes that cause failure to maintain adequate gaseous exchange in the lungs [1]. Disorders such as meconium aspiration syndrome, hyaline membrane disease, congenital pneumonia, transient tachypnoea of newborn, perinatal asphyxia are known to cause respiratory distress in neonates. Non-respiratory causes such as congenital heart diseases, septicemia, congenital malformations and metabolic disorders can also cause respiratory distress.

The management of RD lies in prompt evaluation, assessment, and treatment of the causative factors. Recent advancements in the healthcare system allow newborns with respiratory distress to be treated with mechanical ventilation, CPAP (continuous positive airway pressure), surfactant replacement therapy and phototherapy that can make a significant difference in the prognosis if used according to standard protocols.

The purpose of this study is to gain insight into the demographics (including maternal and neonatal factors), aetiology, clinical features, treatment and outcome of RD patients in a tertiary care referral centre in the northwest part of India. There have been very few similar studies in our country, especially in this part of India, that receive patients from nearby towns and cities in Punjab, Gujrat, Haryana and Madhya Pradesh.

METHOD

Study design – This is a hospital-based observational study

Duration of study – This study was conducted between 15th November 2020 and 15th February 2021

Study setting – The study is conducted in the neonatology unit of the Department of Pediatrics, Sawai Man Singh medical college and hospital Jaipur; a major outborn tertiary care referral centre in Rajasthan

Study aims and objectives –To estimate the proportion of newborns admitted with RD among all NICU admissions, to find out the most common aetiologies responsible for RD in newborns and to study the management and the outcome of these newborns.

Study inclusion and exclusion –

INCLUSION CRITERIA –

All outborn newborns with RD (assessed by either Downe's or Silverman Anderson scoring system) admitted to neonatal intensive care unit of SMS medical college and hospital Jaipur

EXCLUSION CRITERIA –All outborn newborns admitted in the NICU during the study period not fulfilling the criteria of RD with either Downe's or Silverman-Anderson scoring system

Method of data collection – All newborns admitted to NICU of SMS medical college and hospital Jaipur with respiratory distress symptoms were included in the study for 3 months i.e. from November 15th, 2020 to February 15th, 2021. All outborn (private hospital and community hospital), as well as home, delivered babies who developed respiratory distress within 28 days of birth were assessed based on either Downe's scoring system or Silverman-Anderson scoring system or both.

The basic clinical diagnosis of respiratory distress is made when at least 2 of the following criteria, namely respiratory rate >60/minute, retractions (sub-coastal, xiphoid and suprasternal recession), expiratory grunt, flaring of the nasal alae and cyanosis at room air and temperature on two consecutive occasions at least an hour apart, were met.

The demographics of newborns were noted on a pre-structured proforma which included characteristics such as name, sex, age at admission, gestational age, birth weight, mode of delivery, place of birth, post-natal history, etiological diagnosis, treatment given in NICU, length of NICU stay and outcome of RD.Gestational age was calculated using ultrasonography reports (if available) or Bellard's scoring system, clinical symptoms were assessed bedside and other variables were noted from the documents brought by the patient from the place of birth.

All the neonates were kept under constant supervision according to the treatment and management protocols of the hospital until their outcome death, discharge, leave against medical advice (LAMA) or referral to a higher centre.

STATISTICAL ANALYSIS –
All the data were collected, and tabulated in Microsoft Excel and analysed via the SPSS program (version 23). Comparison of data was done appropriately using respective tests.

Consent – Informed consent was taken from every parent whose baby was enrolled in the study.

Investigations – For the confirmation of the aetiology of RD, appropriate investigations were performed. X-rays were performed bedside and reporting was done by a radiologist, Blood samples were taken using necessary precautions and were sent to labs for immediate results. Blood glucose was measured regularly using *Abbott Glucose Strips*, oxygen saturation was monitored continuously via a pulse oximeter, ABG analysis and a sepsis workup were done whenever clinically indicated.

RESULTS

In this 3 months observational study, a total of 672 newborns were admitted to the neonatology unit of SMS medical college and hospital Jaipur, out of which 184 (27.38%) newborns had clinically diagnosed respiratory distress on admission.

Respiratory distress syndrome (62,33.7%) was the most common cause of respiratory distress in this study, followed by perinatal asphyxia (41, 22.3%), meconium aspiration syndrome (29, 15.8%), congenital pneumonia (24, 13%) and transient tachypnoea of newborn (3, 1.6%). Non-respiratory causes such as sepsis (12, 6.5%), congenital heart disease (9, 4.9%) and others (congenital malformations, metabolic disorders, persistent pulmonary hypertension of the newborn [4, 2%]) also contributed significantly to the aetiology of RD (Table 1).

In this study, the male to female ratio was 2.35, exhibiting male dominance with 129 (70%) patients whereas female patients were only 55 (30%). Etiologically, a similar trend was noted in RDS, PA and CHD where the male population was significantly more than the female and in other etiologies, the gap was narrow but still showing a male preponderance (Table 1).

In this study, more than half of the patients enrolled (97, 52.7%) were born preterm, 85 (46.2%) were born at term and only 2 were born at post-term. In preterm babies, RDS, sepsis, TTNB and congenital pneumonia were the more common causes of respiratory distress compared to term babies where perinatal asphyxia and congenital heart disease were more frequent.

In our study, 119 mothers belonged to the 20-25 years age group and 65 to more than 25 years group. 40 (64.5%) cases of RDS were found in babies born to 20-25 years age group mothers.

Normal vaginal delivery was the most common mode of delivery in the study with 143 (77.71%) patients undergoing vaginal delivery. 24 (13.04%) neonates were born from the emergency cesarian section and 17 (9.23%) from the elective cesarian section. MAS was comparatively more common in babies born with emergency cesarian section. In this study, among 184 respiratory distress patients, 62 (33.7%) had respiratory distress syndrome. All of the RDS patients were administered antibiotics and required oxygen support via CPAP. 30 RDS patients that had a severe form of the disease were shifted to mechanical ventilation, out of those, 15 succumbed to death and 15 shifted back to CPAP and ultimately discharged.

Among 29 MAS patients, 18 required mechanical ventilation and out of those, 15 died due to the severity of the disease. The case fatality of MAS was the highest of 52% (15 deaths out of 29 admissions with MAS). 42 cases of RD were due to perinatal asphyxia, 24 were because of congenital pneumonia and 3 cases were of TTNB origin.

Among non-respiratory causes of RD, the most common was sepsis (12, 6.5%), followed by CHD (9. 4.9%), PPHN (2, 1%), congenital malformations (1) and metabolic disorders (1). All of the sepsis patients were administered with baseline antibiotics that were upgraded or downgraded based on clinical response and CRP values. 6 of the sepsis patients required mechanical ventilation, in which 3 died and 3 were shifted back to CPAP. During the 3 months, 9 cases of respiratory distress were because of CHD, among which 5 were operated inside this referral centre and 1 was referred to a higher centre.

The basic treatment strategy for respiratory distress patients referred to our hospital was the administration of baseline antibiotics (182 newborns) and oxygen therapy (183 newborns). Since it is an outborn tertiary care referral centre, there was an injudicious use of antibiotics owing to the uncertain place of birth of the newborn. However, antibiotics were soon downgraded or completely stopped if the neonate shows no signs of sepsis based on clinical symptomatology and CRP values.

Oxygen therapy was given in the form of either nasal prongs (9 patients) or continuous positive airway pressure (174 patients). Mechanical ventilation was used when the neonate has moderate to severe RD or is not stable on CPAP. A total of 85 patients required mechanical ventilation and out of those, 39 were shifted back to CPAP while 46 died owing to the severity of respiratory distress.

Surfactant therapy was provided to 40 patients, most of them were RDS patients (15, 37.5%) and MAS patients (9, 22.5%). A total of 3 patients developed intra-pulmonary bleeding as an adverse reaction to surfactant therapy, among them 2 were RDS patients, 1 had meconium aspiration syndrome. 2 of these 3 patients died because of intra-pulmonary bleed, both of them had RDS.

Intensive phototherapy was given to 29 patients who had clinically and laboratory diagnosed jaundice as per the standard protocols. Ionotropic support was provided to 29 patients, the majority of them had perinatal asphyxia with some form of hypoxic-ischaemic encephalopathy (Table 2).

The average length of stay in NICU was a minimum of 8 days for newborns having TTNB on admission, a maximum of 26 days for newborns having congenital malformations requiring surgical correction. Neonates having RDS, PA, MAS, CHD and sepsis spent around 12 to 15 days on average in NICU whereas congenital pneumonia patients spent 18 days in NICU on average (Table 3).

In this 3 months study, out of 184 respiratory distress patients, 53 died due to its complications. RDS and MAS contributed to the majority of deaths, 17 and 15 respectively with MAS having the highest case fatality of 52%. 10 newborns with perinatal asphyxia, 4 with congenital pneumonia, 3 with sepsis, 3 with CHD and 1 with PPHN died in the study period (Table 3).

DISCUSSION

In this study, out of 184 respiratory distress patients, 97 (52.7%) were born preterm, 85 (46.2%) were born at term and only 2 (1%) were born at term. Among 85 patients who were born at term, the most common causes of respiratory distress were perinatal asphyxia (23, 56%), followed by MAS (15, 51%) and CHD (6, 67%). Out of 97 preterm babies, more than a third had RDS (37, 44%) as the cause of their RD. A 2007 study by Hermansen et al [2] concluded that respiratory distress syndrome occurs in premature infants as a result of surfactant deficiency and underdeveloped lung anatomy.

Male babies were more than twice the number of females in having RDS, perinatal asphyxia, sepsis and CHD whereas they were only marginally higher in MAS, congenital pneumonia and other etiologies causing respiratory distress. This is the most common trend seen in similar kind of studies such as a large prospective study by Hjalmarson O et al [3] in 1981, depicting the total incidence of Respiratory distress in males (3.5%) was higher than females (2.2%). However, in India, a disproportion of sex ratio in NICU admissions due to respiratory distress could be partly due to social and economic factors which lead people to believe that males are more important than females, thus fewer females present in Indian hospitals. A multicenter South-American conducted by Elisa Fehlmann et al [4] in 2010 shows that

RDS had a high incidence in very low birth weight infants despite the frequent use of antenatal steroids. In our study, we found out that 41 RDS patients had a low birth weight of fewer than 2500 grams in which 18 belonged to the below 1500 grams birth weight group. Whereas on the other hand, approximately half of the patients having perinatal asphyxia, MAS and CHD had normal birth weight.

In our study, we found that the most common cause of RD in a tertiary care referral centre is RDS (62, 33.7%), followed by perinatal asphyxia (41, 22.3%), MAS (29, 15.3%), congenital pneumonia (24, 13%) and TTNB (3, 1.6%). Other non-respiratory causes were sepsis (12, 6.5%), congenital heart disease (9, 5%) and others including PPHN, congenital malformations and metabolic disorders. In Nagendra K et al [5] and Kumar A et al [6] studies in 1999 and 1996 respectively, the most common aetiologies of RD in newborns were TTNB, RDS, MAS and congenital pneumonia.

The number of TTNB cases in our study were significantly less (3, 1.6%) when compared to other similar studies because transient tachypnoea of newborn usually develops and get diagnosed within a few hours after birth, mostly at the place of birth and often resolves in a day or two. Since our centre is an outborn tertiary care referral centre, most of the NICU admissions are from cities and villages at remote distances. Moreover, conditions such as TTNB are most effectively managed in primary and secondary care centres and only those conditions which are complicated or unresolved such as RDS, MAS and congenital pneumonia are referred to our tertiary care centre.

In this 3 month study period, 41 perinatal asphyxia patients presented with respiratory distress indicating that significant morbidity of RD in the newborn is associated with low APGAR scores at birth and birth asphyxia. Our results go along with a study conducted by O Linderkamp et al [7] in 1978 which concluded that the highest incidence of RD and the highest mortality rate were found in infants with low APGAR scores or birth asphyxia.

Surfactant therapy was given to 40 babies out of 184 patients admitted with respiratory distress, the majority of which had RDS (15, 37.5%) and MAS (9, 22.5%). As shown in Auten RL et al [8] study in 1991, Surfactant therapy was shown to have a significant impact on the improvement of RDS and perinatal asphyxia patients. However, as concluded in a metanalysis by Raju and Langenberg [9] in 1993 that there appears to be a small increase in the risk for pulmonary haemorrhage (50% higher) with surfactant use, our study encountered 3 patients who developed intrapulmonary haemorrhage as an adverse effect of surfactant therapy. 2 of these 3 patients died despite maximum treatment support with mechanical ventilation and inotropes.

Almost all of the RD patients received Antibiotics (182, 98.9%) according to the standard protocols of the hospital and oxygen therapy (183, 99.5%) via either nasal prongs or CPAP. Mechanical ventilation was provided to moderately to severe RD patients, among them, 33 (38.8%) were discharged, 6 were either referred to a higher centre or left against medical advice and 46 (54.1%) died.

The longest stay in the NICU was recorded for babies admitted with PPHN and congenital malformation as the cause of their respiratory distress, 26 days on average.After that congenital pneumonia patients spent most time of 18 days on average in the neonatal intensive care unit. Babies having RDS, MAS, perinatal asphyxia and sepsis, spent 12-15 days on average, while those who had TTNB and the aetiology of RD spent the least of 8 days on average in the NICU.

During the study period, only 5 (2.7%) patients were referred to a higher centre for further management, such as CHD and congenital malformation patients whose surgeries weren't possible at our hospital. 15 out of 29 meconium aspiration patients died in the study period with a case fatality of 52%, among them 9 patients had meconium-stained amniotic fluid. In 1994, Berkus MD et al [10] also showed that the bad outcome of MAS babies is associated with meconium-stained amniotic fluid.

Table 1

ETIOLOGY / NEONATAL AND MATERNAL CHARACTERISTICS		RDS (*n=62*)	Perinatal asphyxia (*n=41*)	MAS (*n=29*)	Congenital pneumonia (*n=24*)	Sepsis (*n=12*)	CHD (*n=9*)	TTNB and others (n=*7*)
Gestational age	Very preterm [*n=49*]	18 (29%)	11 (27%)	8 (28%)	6 (25%)	2 (17%)	3 (33%)	2 (28%)
	Early preterm [*n=18*]	7 (11%)	1 (2%)	2 (7%)	3 (13%)	3 25%)	0 (0%)	1 (15%)
	Late preterm [*n=30*]	12 (20%)	6 (15%)	4 (14%)	4 (16%)	3 (25%)	0 (0%)	1 (15%)
	Term [*n=85*]	23 (37%)	23 (56%)	15 (51%)	11 (46%)	4 (33%)	6 (67%)	3 (42%)
	Post term [*n=2*]	2 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Birth weight	ELBW [*n=6*]	2 (3%)	1 (2%)	2 (7%)	0 (0%)	0 (0%)	0 (0%)	1 (14%)
	VLBW [n=*34*]	16 (26%)	6 (15%)	3 (10%)	5 (21%)	1 (8%)	3 (33%)	0 (0%)
	LBW [*n=66*]	23 (37%)	12 (29%)	11 (38%)	11 (46%)	5 (42%)	1 (11%)	3 (43%)
	NBW [*n=77*]	21 (34%)	22 (54%)	13 (45%)	8 (33%)	5 (42%)	5 (56%)	3 (43%)
Sex (M/F)	129/55	45/17	32/9	18/11	14/10	8/4	8/1	4/3

Table 1= RDS-respiratory distress syndrome; MAS-meconium aspiration syndrome; CHD-congenital heart disease; TTNB-transient tachypnoea of newborn; ELBW-extremely low birth weight (<1000 grams), VLBW-very low birth weight (1000-1500 grams); LBW- low birth weight (1500-2500 grams); NBW-normal birth weight (2500-4000 grams)

Table 2

Treatment given during NICU stay	Number of patients (*n=184*)
O2 therapy	183 (99.5%)
Antibiotics	182 (98.9%)
CPAP	174 (94.6%)
Mechanical ventilation	85 (46.2%)
Surfactant therapy	40 (21.8%)
Phototherapy	29 (15.8%)
Required ionotropic support	25 (13.6%)
Nasal prongs	9 (4.9%)

Table 2= CPAP-continuous positive airway pressure

Table 3

STATISTICS / ETIOLOGY	Average length of stay in NICU (in days)	OUTCOME (*n=184*)			
		Death (n=53)	Discharge (*n=120*)	Referred (*n=5*)	LAMA (*n=6*)
RDS [*n=62*]	13	17 (27%)	38 (61%)	3 (5%)	4 (6%)
Perinatal asphyxia [*n=41*]	12	10 (24%)	31 (76%)	0 (0%)	0 (0%)
MAS [*n=29*]	13	15 (52%)	13 (45%)	0 (0%)	1 (3%)
Congenital pneumonia [*n=24*]	18	4 (17%)	19 (79%)	1 (4%)	0 (0%)
Sepsis [*n=12*]	15	3 (25%)	8 (67%)	0 (0%)	1 (8%)

CHD [*n=9*]	13	3 (33%)	5 (56%)	1 (11%)	0 (0%)
TTNB [*n=3*]	8	0 (0%)	3 (100%)	0 (0%)	0 (0%)
Others [*n=4*]	26	1 (25%)	3 (75%)	0 (0%)	0 (0%)

Table 3= LAMA-leave against medical advice

CONCLUSION

In our 3 months study, respiratory distress accounts for 27.8% (184) of all NICU admissions and 26.9% (53) of total deaths in the given time frame. RDS was the most common aetiology causing RD followed by perinatal asphyxia, MAS, congenital pneumonia, sepsis, CHD and TTNB. Premature birth, low birth weight and delivery via cesarian section were related to poor prognosis in respiratory distress patients. Male predominance is seen in the study sample and it was also the group having moderate to severe respiratory distress symptoms. Early clinical diagnosis, referral and treatment of RD is thus important to improve neonatal morbidity and mortality in the population. Treatment advancements such as the use of CPAP and Mechanical ventilation has proved to be a promising treatment option for RD patients, however, the benefit of surfactant therapy in RDS patients must be weighed with its adverse effects. Studies like this give an insight into the regional etiological variation of such major diseases and are crucial to establish and maintain national healthcare data to improve the overall healthcare system of the country.

DECLARATIONS

Funding- No funding sources
Conflict of interest- None declared
Ethical Approval- No ethical approval required
Consent- Informed consent was taken from the parents of all the participants

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