

Original Research Article

Clinico-epidemiological study of respiratory distress in newborn and associated risk factors

Rishi Sodawat^{1*}, Pukhraj Garg¹, Chaturbhuj Singh¹, Priyanka Sharma²

¹Department of Pediatrics, J.L.N. Medical College, Ajmer, Rajasthan, India

²Department of Pediatrics, RUHS, Jaipur, Rajasthan, India

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*Correspondence:

Dr. Rishi Sodawat,

E-mail: rishisodawat2015@gmail.com

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ABSTRACT

Background: Respiratory distress (RD) is one of the most common causes of admission in neonatal intensive care unit (NICU) for a variety of pulmonary and non-pulmonary disorders. This study has been undertaken to evaluate prevalence of the known causes and risk factors associated with development of respiratory distress in neonates and finally to assess the clinical correlation with blood investigations, X-RAY, ECG, ABG and 2D ECHO.

Methods: The present study was conducted in the department of Pediatrics at JLNMC Ajmer between February 2017 – February 2018, over a period of 12 months. It is a prospective case study.

Results: Out of 600 newborns admitted with respiratory distress, Transient Tachypnea of Newborn (TTN) was found to be the most common cause (n = 196, 32.6%) followed by HMD (n = 145, 24.1%).

Conclusions: Transient tachypnea of newborn is the most common cause among new-borns with respiratory distress. Majority of newborns develop severe distress within 6 hours after birth. In preterm and term babies the major cause of RD is Hyaline membrane disease (HMD) and HIE/CHD (hypoxic encephalopathy/congenital heart disease) respectively. While in post term babies MAS is major cause of RD. Newborns with low and very low birth weight are more prone for development of severe distress.

Keywords: Respiratory distress syndrome, Hyaline membrane disease, Meconium aspiration syndrome, Transient tachypnea of newborn

INTRODUCTION

Respiratory distress (RD) is a challenging problem and is one of the most common causes of admission in neonatal intensive care unit. India contributes to one-fifth of global live births and more than a quarter of neonatal deaths. Nearly, 0.75 million neonates died in India in 2013.¹

The current NMR (neonatal mortality rate) is 25 per 1000 live births in our country and 30 per 1000 live births in state of Rajasthan (SRS Statistical Report 2015).² There has been tremendous advances in the management of respiratory distress such as newer High frequency

ventilators, early surfactant replacement therapy, Extra Corporeal Membrane Oxygenation (ECMO) and advanced monitoring devices. In spite, of these recent advances the average annual rate of reduction (AARR) of NMR was only modest. There have been very less clinical studies on the neonatal respiratory distress in our country. Therefore, there is a need to study the clinico-epidemiological profile and outcome of the babies with respiratory distress.

The aim of present study was to find out the known causes of respiratory distress in neonatal period, their associated risk factors, correlation with investigation

findings and to know the outcome of these neonates at the time of discharge.

METHODS

The present cross sectional study was conducted in the department of Pediatrics JLNMC Ajmer (during 12 months period of February 2017- February 2018). This study was approved by institutional ethics committee.

Inclusion criteria

Both inborn and outborn neonates within 28 days of life admitted to NICU with respiratory distress.

Exclusion criteria

- Whose parents refused to be included in the study.
- Wt <1000g.
- Neonate less than 28 weeks of gestation.

Neonates admitted in NICU, who were fulfilling the inclusion criteria were enrolled for the study after gaining informed consent. Respiratory distress was diagnosed by presence of at least 2 of the following on two consecutive examinations at least 1 hour apart:

- Respiratory rate of >60/min or more
- Chest retraction (subcostal, xiphoid, suprasternal retraction)
- Flaring of alae nasi
- Expiratory grunt
- Cyanosis at room temperature

A detailed history, including antenatal, natal and postnatal history and detailed examination of each newborn was recorded on a predesigned semi structural proforma on the day of admission. Severity of respiratory distress was assessed by DOWNE'S Score and maturity of newborn was assessed by NEWBallard scoring system.

Clinical diagnosis of respiratory distress was made and was confirmed by Sepsis screen, Blood culture and Drug Sensitivity, chest Xray, ECG, Echocardiography, ABG and USG of cranium. The association of variable risk factors both maternal and neonatal were studied for the development of severe respiratory distress.

Statistical analysis

Data was collected and analyzed using SPSS version 16. Fisher's exact test was used for categorical variables. P value of <0.05 was considered significant.

RESULTS

Overall Transient Tachypnea of Newborn (TTN) was found to be the most common cause of respiratory distress in neonates (n = 196, 32.6%) followed by HMD (n = 145, 24.1%), out of total 600 newborn of respiratory distress, 300 newborn each were delivered outside and in our hospital. 33.67% cases of TTN, 55.86% cases of HMD, 68.96% cases of sepsis including pneumonia, 53.57% cases of MAS, 53.33% cases of HIE and 45.83% cases of CHD were delivered outside and referred to us for management (Table 1). Occurrence of causes of respiratory distress in newborns according to place of delivery was statistically significant (p<0.001).

Table 1: Comparison between various causes of respiratory distress according to the place of delivery.

Place of delivery	TTN n=196 (%)	HMD n=145 (%)	Sepsis/ Pneumonia n=116 (%)	MAS n=56 (%)	HIE n=45 (%)	CHD n=24 (%)	Others n=18 (%)
Inpatients (n=300)	130 (66.32)	64 (44.13)	36 (31.03)	26 (46.42)	21 (46.66)	13 (54.16)	10 (55.55)
Outpatients (n=300)	66 (33.67)	81 (55.86)	80 (68.96)	30 (53.57)	24 (53.33)	11 (45.83)	8 (44.44)

Chi-square = 40.455 with 6 degrees of freedom; P< 0.001

The male female ratio for neonates developing respiratory distress was 1.21:1 and was statistically insignificant.

Newborn with TTN were almost equally distributed among those of 37-42 weeks of gestation (99, 50.5%) and less than 37 weeks of gestation (95,48.4%). Majority of babies with Hyaline membrane disease (HMD) were pre term (147,97.9%). Term babies formed the majority in HIE (25,55.5%) and CHD (13,54.1%). Majority of babies of MAS were post term (35,62.5%). Occurrence of

causes of respiratory distress in newborns according to gestational age was statistically significant (p<0.001).

Maximum cases [n=243(40.5%)] of respiratory distress were of 1500-2499 gm birth weight and n= 221(36.8%) cases were ≥2500 gm and n= 136(22.6%) cases were between 1000-1499 gm. When birth weight is analyzed for the development of respiratory distress, it is found that more than 47.9% newborn with TTN were of ≥2500gm and rest around 52% newborn were of low or very-low birth-weight. Maximum cases (n=84, 57.9%) of HMD were between 1000-1499 grams. 41.3% (n=48) cases of Sepsis including Pneumonia were of 1500-

2499gm. In MAS (n=34, 60.7%) and HIE (n=30, 66.6%) maximum cases fall in ≥ 2500 gm group. Overall occurrence of causes of respiratory distress in newborns according to birth weight was statistically significant ($p < 0.001$). Among inborn patients all cases of HMD, TTN, MAS and majority of HIE (14, 66.66%) cases had onset of respiratory distress within 6 hours of life. Respiratory distress RR > 60 /mm, flaring of alae nasi

and chest retractions had maximum incidence in all the six groups. While cyanosis was most common in CHD and cough was most common in Sepsis including pneumonia. Adventitious sound on chest auscultation were found in maximum number in cases of sepsis including pneumonia (n=41, 35.34%) and in CHD (n=9, 37.5%). Severity of Downe score was maximum in HMD followed by CHD (Table 2).

Table 2: Assessment of Downe Score in various causes of respiratory distress.

Downe Score	TTN n=196 (%)	HMD n=145 (%)	Sepsis/ pneumonia n=116 (%)	MAS n=56 (%)	HIE n=45 (%)	CHD n=24 (%)	Others n=18 (%)	P value
≤ 3	164 (83.67)	18 (12.41)	70 (60.34)	26 (46.42)	20 (44.44)	8 (33.33)	6 (33.33)	< 0.001
4-6	32 (16.32)	90 (62.06)	28 (24.13)	20 (35.71)	21 (46.66)	11 (45.83)	8 (44.44)	< 0.001
7-10	0	37 (25.51)	18 (15.51)	10 (17.85)	4 (8.88)	5 (20.83)	4 (22.22)	< 0.001

Antenatal risk factors highlight prolonged rupture of membranes, maternal fever, leaking per vaginum and

single unclean/ > 3 sterile PV examinations as statistically significant ($p < 0.01$) factor contributing to sepsis including pneumonia in neonates (Table 3).

Table 3: Comparative table of antenatal risk factors and their percentage wise occurrence in various causes of respiratory distress.

Antenatal risk factors	TTN n=196	HMD n=145	Sepsis/ pneumonia n=116	MAS n=56	HIE n=45	CHD n=24	Others n=18	P value
Antepartum maternal fever	-	10	25	3	5	1	2	< 0.001
Prolonged rupture of membranes > 24 hours	-	16	30	4	6	-	1	< 0.001
Leaking Per vaginum	-	18	35	2	8	-	2	< 0.001
H/O diabetes in mother	5	6	1	-	-	1	-	< 0.01
H/O maternal/renal/lung disease	-	4	1	3	2	-	2	< 0.001
H/O HTN in mother	-	10	1	6	33	-	1	< 0.01
H/O maternal anemia	20	18	6	4	3	1	2	0.446
PV examination single unclean or > 3 sterile	3	15	45	10	4	1	3	< 0.001
H/O Foetal distress	-	2	10	32	20	8	4	< 0.001
Past H/O neonatal mortality or morbidity	6	15	2	-	4	1	2	0.005

A history of fetal distress leading to emergency LSCS was found in 32 cases of meconium aspiration syndrome. HTN in mother was commonly found in HIE and few cases of HMD and MAS.

significant ($p < 0.01$) in all risk factors except maternal anaemia.

Occurrence of causes of respiratory distress in newborns according to antenatal risk factors was statistically

None of the factors like maternal fever, prolonged rupture of membranes, leaking per vaginum or foul smelling liquor were found to have any association at all with transient tachypnea of newborn TTNB Mothers of

neonates with Hyaline membrane disease (HMD) had association with PROM (prolonged rupture of membrane) and LPV (leaking per vaginum). Precipitate labour had high significant association for development of respiratory distress in neonates with TTNB. There was no association of transient tachypnea of new born (TTNB) with prolonged / traumatic labour or a history of poor cry. H/O Prolonged Labour was found to be associated with Sepsis, MAS and HIE. Occurrence of causes of respiratory distress in newborns according to H/O Prolonged Labour (1 + 2 stage ≥ 24 hrs), Foul smelling liquor, H/O Poor Cry / Resuscitation were statistically significant ($p < 0.001$).

89.65% of cases of Sepsis including pneumonia were supported by positive sepsis screen followed by Positive blood culture results in 56.89% cases. While only 35.34% cases were supported by suggestive feature on CXRay. TTN was supported by CXR features in 49.48% cases only, making it a diagnosis of exclusion in most of the cases. CXray features suggestive of diagnosis were found in 100% cases of HMD and 91.07% cases of MAS.

The bacterial isolates in our study suggests an increasing trend of klebsiella (30.3%, Figure 1). In the present study, (Figure 1) CONS was positive in 24% cases, *E. coli* 15%, *S. aureus* 21.6%, Enterobacter 5%, Pseudomonas in 4% of total blood culture positive cases.

Most cases of TTN (92.34%) were discharged in <3 days, majority of HMD (42.10%), CHD (50%) and Sepsis

(58.20%) cases were admitted for >10 days. 41.66% cases of MAS remained in NICU for 3-7 days, while 41.37% cases of HIE were admitted for a duration of 7-10 days. Occurrence of causes of respiratory distress in newborns according to duration of admission was statistically significant ($p < 0.001$).

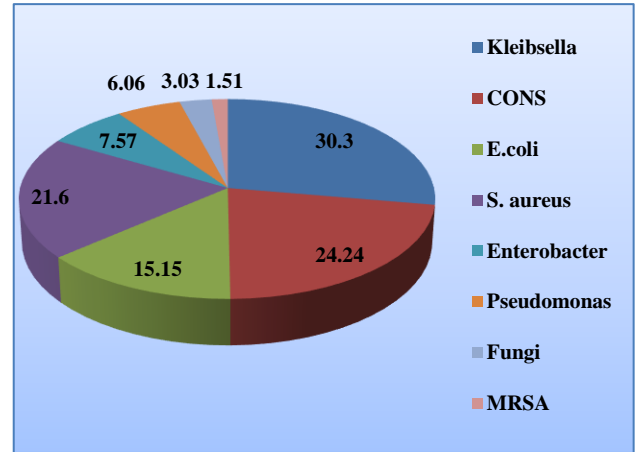


Figure 1: Percentage of pathogen among all blood culture positives of respiratory distress.

The mortality figure was highest in HMD (Hyaline membrane disease 47.58%) followed by sepsis (42.24% of cases). Overall mortality among cases of respiratory distress was 28% (Table 4). There was no mortality in newborns of TTNB.

Table 4: Final outcome among various causes of respiratory distress.

Disease	TTN n=196 (%)	HMD n=145 (%)	Sepsis/ Pneumonia n=116 (%)	MAS n=56 (%)	HIE n=45 (%)	CHD n=24 (%)	Others n=18 (%)	Total n=600 (%)
Expired cases	0	69 (47.58)	49 (42.24)	20 (35.71)	16 (35.55)	8 (33.33)	6 (33.33)	168 (28)
Discharged / referred	196 (100)	76 (52.41)	67 (57.75)	36 (64.28)	29 (64.44)	16 (66.66)	12 (66.66)	432 (72)

Chi-square = 119.00; $p < 0.001$

Table 5: Association of fatality with other risk factors in newborn with respiratory distress.

Parameters	Fatality N=168	Survival N=432	
Need for resuscitation	36	54	Chi-square= 128.36; $p < 0.001$
Outborn	112	188	
Fio 2>40%	110	62	
Ph<7.2	59	81	
Base excess >-10	21	38	
Evidence of sepsis	41	77	
Mechanical ventilation	130	24	
Downe score, Mean (SD)	7.2 (2.6)	3.49 (2.65)	t= 15.48; $p < 0.001$

Mortality was more with low birth weight and <37 weeks gestational age and it was statistically significant ($p < 0.001$ and $p = 0.007$ respectively). Mortality was not associated with sex (statistically insignificant p value < 0.91).

Need for resuscitation, outborn deliveries, $FiO_2 > 40\%$, $Ph < 7.2$, Base excess > -10 , evidence of sepsis, Mechanical ventilation, Downe score were the most significant risk factors (p value < 0.001) associated with fatality in newborns with respiratory distress (Table 5).

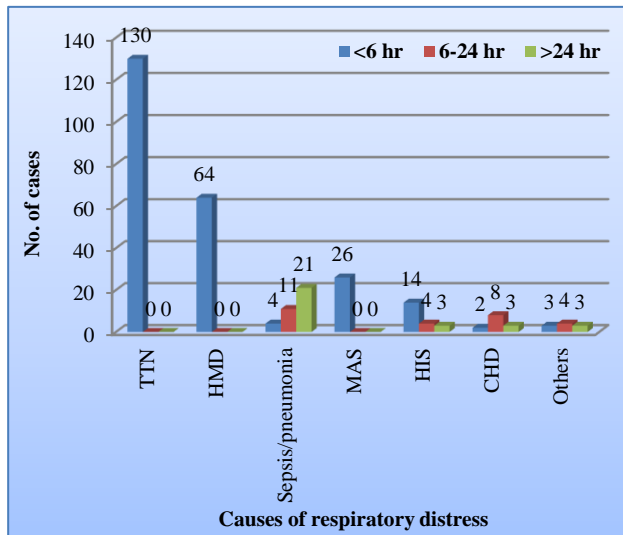


Figure 2: Comparison of distribution of causes of respiratory distress according to timing of onset.

DISCUSSION

Studies in the past by Schaffer et al, had found RDS as the leading cause in premature newborns and massive aspiration is followed by pneumonia as second cause in full term newborns.³ Cunningham and Smith attributed the respiratory distress as belonging to RDS in 75% cases and massive aspiration in 23%. Khatua SP, reported highest incidence of aspiration syndrome (57.1%) followed by pneumonia 9.35% and RDS 8.8%.^{4,5} While, Santosh S et al and Haque A et al reported TTN as the most common cause of RD in newborns.^{6,7}

This wide variation in proportion of causes of respiratory distress among various studies may be due to antenatal care in that community, availability of obstetricians including trained birth attendants, use of preventive measures during antenatal period, proportion of term and preterm deliveries, non uniform inclusion criteria, various other factors such as status of community and type of facilities in institution.

In our study among inborn neonates TTN (43.3%) followed by HMD (21.33%) were the leading causes of respiratory distress while among outborn neonates HMD

(27%) and sepsis (26.66%) were the leading causes of respiratory distress.

HMD is leading cause among both outborns and inborns may be due to poor antenatal care and socioeconomic status of population leading to higher proportion of preterm deliveries. Sepsis is more prevalent among outborns because of poor intrapartum and postnatal asepsis maintenance among outborn as compared to inborn deliveries. These results are comparable to those found by Dutta et al among inborn patients in their study with Transient tachypnea of the newborn (TTNB) was the commonest (32.23%) cause of respiratory distress followed by pneumonia (24.35%).⁸ Among outborn neonates similar results were found in study done by Rohit et al with Sepsis (29.49%) and RDS (21.64%) being the leading causes of respiratory distress.⁹

When birth weight is analyzed for the development of respiratory distress, it was found that maximum cases (63.1%) of respiratory distress were of < 2500 gm (with 40.5% of them were 1500-2499 gm). This is similar to study done by Khatua and Prodhom who found that more than $> 50\%$ cases of respiratory distress were below 2500 gm.^{5,10} In previous studies done by Shaffer, Prodhom, Thomas and Khatua maximum occurrence of respiratory distress was in newborns weighing < 1500 gm followed by those with weight > 2500 gm with least evidence in newborn weighing 1500-2500 gm.^{3,5,10,11} Statistically no significant relationship between weight and development of respiratory distress can be established due to the fact that we have excluded babies of < 1000 gm from present study.

When respiratory distress was compared with gestational age we found that 348 (58%) newborn was preterm and 55 (9.1%) newborn was post term, of which 35 post terms were of MAS. In present study 91.3% cases of Sepsis, 97.9% cases of HMD and 48.4% cases of TTN were preterm. Thomas S et al reported 51% cases of sepsis/pneumonia and 100% cases of HMD were preterm.¹¹ Thus in present study preterm deliveries are mainly complicated by TTNB, HMD and sepsis.

We found tachypnea ($RR > 60$ / minute), flaring of alae nasi and chest retractions in all the groups, while cyanosis was specific for CHD (54.16%), HMD (38.62%). Cough was present in 24% of babies of Sepsis including pneumonia and adventitious auscultatory chest signs were found in 37.5% and 35.34% cases of CHD and Sepsis/pneumonia respectively.

When severity of respiratory distress was compared in various causes of respiratory distress, we found that Severe Respiratory Distress (Downe score 7-10) was seen in HMD (25.51%), CHD (20.83%), MAS (17.85%), Sepsis (15.51%). Mild Respiratory Distress (Downe score ≤ 3) was seen in majority (83.67%) of babies with TTN (Table 2). There are only a few previous studies which

compared severity of respiratory distress with various diseases associated with respiratory distress in newborn.

In present study, Sepsis with pneumonia, cases having antenatal history of prolonged rupture of membrane > 24 hrs (25.8%), maternal fever (21.5%), leaking per vaginum (30.17%) and PV examination unclean/>3 sterile (38.8%). Similar observations are reported by Mathur et al, Khatua SP and Thomas S et al.^{5,11,12} There was no association of TTNB with factors like maternal fever, prolonged rupture of membranes, leaking per vaginum or foul smelling liquor. However, TTNB was associated with maternal anemia (10.2% cases). 11% babies of HMD had antenatal history of prolonged rupture of membranes, 12.4% babies had ante-natal history of leaking per vaginum and maternal anemia. Both risk factors might have resulted in preterm labour and thus are responsible for development of HMD.

In present study among inborn patients all cases of TTN, HMD and MAS had onset of respiratory distress within 6 hours of birth. 66.6% cases of HIE had onset of distress within 6 hours of birth (Figure 1). 84.5% cases of CHD presented with respiratory distress after 6 hours of life. 88.8% cases of sepsis/pneumonia presented with respiratory distress after 24 hours of birth. Overall 84% of total inborn patients had onset of respiratory distress within 6 hours of life, 92% had onset within 24 hours. This observation is supported by the fact that TTN, HMD and MAS were the major contributors of respiratory distress in inborn patients, which mostly present in initial hours of birth. Barkiya SM et al in their study observed that most of the cases developed RD at time of birth (80%) followed by 1st day (14%), 2nd day (5%), and 3rd day (1%).¹³

In present study 42.33% of all neonates with respiratory distress were delivered vaginally while 57.66% were delivered by LSCS. In a study done by Rajavarapu Chandrasekhar et al 49.3% of new-borns (37 out of 75) born by caesarean section developed severe respiratory distress compared to 44% of the new-borns (11 out of 25) born by normal vaginal route.¹⁴ Thomas S et al (found that there was no significant correlation between the mode of delivery and the development of pneumonia.¹¹ He also found that most of babies with MAS were born by LSCS, for which the indication was fetal distress due to meconium staining of amniotic fluid MSAF.

No earlier study has mentioned detailed diagnostic criteria for sepsis/pneumonia in neonates utilizing blood culture and sepsis screen positively. In present study, babies with sepsis/pneumonia had positive sepsis screen in 89.65% and blood culture was positive in 56.89% of total cases, which is slightly higher than that reported by earlier authors. This could be due to sending the blood samples for respective investigations before administration of antibiotics. 41 cases of sepsis/pneumonia, shown CXR findings suggestive of

pneumonia (35.34%). In the cases studied by Mathur (2002), only 4.8% neonates had sepsis screen positive.¹²

In our study we get CXRay (CPA) suggestive features supportive of respective illness in all cases of HMD and 91.07% cases of MAS, 87.5% cases of CHD, 49.48% cases of TTN, 35.34% cases of Sepsis/pneumonia 84% cases of MAS.

91.66% cases of CHD had ECG findings and 75% had ABG and 2D ECHO findings suggestive of diagnosis. Blood culture was positive in 56.89% of total cases of sepsis/pneumonia. Klebsiella was most notorious contributing 20(30.3% of total blood culture positive) of total cases. CONS was found in 16 cases (24.24%) of pneumonia. *E. coli* and *Staphylococcus aureus* in 10 and 8 cases respectively.

Other studies in the past which have mentioned on increasing incidence of Klebsiella are Thomas et al, on Bhakoo (20.5%), Mishra JN et al, Mishra S et al (11.3%), Mathur¹² et al 92002) (57.9%).^{11,12,15-17} Bhakoo et al and Jeffery et al had shown higher incidence of Gram negative septicemia in neonates with higher onset sepsis.^{15,18} This is again proved by our study, which shows a higher incidence of Klebsiella, which is a gram negative bacteria.

In our study various risk factors like low birth weight, prematurity, need for resuscitation, high downe score, evidence of sepsis, provision of ventilatory support, $ph\ FiO_2 > 40\%$, $Ph < 7.2$ were related to mortality with statistically significant relationship. In a study conducted by Rajavarapu Chandrasekhar et al risk factors which found to be statistically significant ($p < 0.05$) were age of mothers, socio economic status, parity, liquor, mode of delivery, gestation of baby, 1min APGAR score, birth weight and sex of the newborn.¹⁴

In present study Overall mortality among cases of respiratory distress was 28%. When fatality was compared in neonates among various study groups. Mortality figures were 47.58% for HMD, 42.24% for sepsis, 35.71% for MAS, 35.55% for HIE and 33.33% for cases of CHD. In a recent study done by Sahoo MR et al death occurred in 11.1% cases of RD.¹⁹ Mortality was seen in 24.13% newborns of HMD, 11.11% of newborns with MAS, 9.09% of newborns with congenital pneumonia.

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

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