Respiratory Distress among Preterm Infants in a Backward District of Kerala: A Retrospective Cohort Study

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Abstract
Background: Premature infants are at a relatively higher risk of morbidity and mortality when compared to term babies especially if gestational age at birth is below 34 weeks. It is essential to establish the factors leading to preterm delivery and the clinical profile of preterm infants.

Objectives: 1) To study the relationship between respiratory distress and gestational age in preterm infants in a backward district of Kerala, 2) To study the various risk factors for the development of respiratory distress among preterm infants and 3) To evaluate the outcome of intervention in respiratory distress in a level 3 NICU of a backward district of Kerala.

Methodology: This is a retrospective analysis of hospital records of preterm infants admitted in a level-3 neonatal ICU of a tertiary teaching hospital for one year from 1st January 2017 till 31st December 2017. Detailed analysis of all the risk factors for preterm delivery, causes of respiratory distress among preterm infants and various interventions adopted to treat respiratory distress are done. All infants are treated in a level 3 NICU and the type of treatment and outcome are studied.

Results: A total of 1036 babies were admitted in the NICU of the institution during the study period. 947 were in born and 89 were born in other institution and referred in. Out of 1036, 124 (11.96%) were born below 34 weeks of gestation. The overall incidence of Respiratory distress was 34%. 64% of the infants less than 28 weeks developed respiratory distress, 44% of the infants among 29 - 31 weeks and 27% of the infants among 32 - 34 weeks developed respiratory distress. 55% of the infants with birth weight less than 1000 gm, 45% of the infants with birth weight 1101 - 1500 gm, 24% of the infants with birth weight 1501 - 2500 gm had developed Respiratory distress. 6 babies out of 124 died constituting a mortality of 4.83% for those below 34 weeks of gestational age. Only 6 out of the remaining 912 (above 34 weeks of gestation) died during the study period constituting a mortality of 0.65%.

Conclusion: This study explores the possibility of respiratory distress among preterm infants and the resuscitative and supportive care to these infants. This study also looks at major risk factors for respiratory distress and the outcome such as morbidity among survivors and mortality. Among this cohort mortality is only 4.83% and only one baby among the 13 extremely low birth weight category was lost. This study highlights that survival can be considerably improved if immediate NICU care is provided to all newborns with level-3 NICU facility.

Keywords: Preterm Infants; Respiratory Distress; Level-3 NICU

Introduction
Preterm infants by definition are babies born before completion of 37 weeks of gestational age. These infants are at a relatively higher risk of morbidity and mortality when compared to term babies especially if gestational age at birth is below 34 weeks. Infants born before 28 weeks of gestation (28 weeks of gestational age and a minimum birth weight of 500 gms are the legal cut off points for viability in our

country as it stands now) if having multiple congenital anomalies also are more prone for neonatal asphyxia, respiratory distress, sepsis, hypoglycemia and prolonged neonatal hyper-bilirubinemia. With advances in perinatal and neonatal care, more infants are surviving at lower gestational age [1-3]. However, the rates of mortality and severe neonatal morbidity increases with decreasing gestational age [4-6]. Death and major morbidity can be avoided if prompt care is given to these infants in a level 3 neonatal ICU. It is essential to establish the factors leading to preterm delivery and the clinical profile of preterm infants. This is particularly important in a backward district where 18% of population are tribal with poor access to health care. Wayanad is an officially declared backward district of Kerala. It has the largest contingent (35%) of tribal population in the state. About 17 - 18% of the district's population (11 lakhs) are tribes. DMWIMS Medical College Hospital wherein this study is conducted provides Level-3 neonatal care and is the only institution with a level-3 NICU in this hill district catering to a total population of about 20 lakhs taking in to account the adjacent districts of Tamilnadu and Karnataka for whom this is nearest such institution.

Objectives of the Study

- To study the relationship between respiratory distress and gestational age in preterm infants in a backward district of Kerala.
- To study the various risk factors for the development of respiratory distress among preterm infants.
- To evaluate the outcome of intervention in respiratory distress in a level 3 NICU of a backward district of Kerala.

Study Methodology

This is a retrospective analysis of hospital records of preterm infants admitted in a level-3 neonatal ICU of a tertiary teaching hospital for one year from 1st January 2017 till 31st December 2017. Both inborn and out born infants born below 34 weeks of gestational age are included. Maternal factors like parity, anaemia, gestational Diabetes Mellitus (GDM), Ante partum Hemorrhage (APH), pregnancy Induced Hypertension (PIH) and birth by Caesarean Section (CS) are recorded. Factors in the babies like birth weight of the baby, length of hospital stay, presence of respiratory distress, sepsis, congenital anomalies etc. are noted. Detailed analysis of all the risk factors for preterm delivery, causes of respiratory distress among preterm infants and various interventions adopted to treat respiratory distress are done. All infants are treated in a level 3 NICU and the type of treatment and outcome are studied. Outcome is assessed as alive without disability, alive with disability and death. This study was approved by the institutional ethics committee.

The data is charted out in Microsoft Excel and statistical analysis was done using statistics package for social sciences and Output software (SPSS). The statistical significance is calculated using Chi-square test for factor variables with Respiratory distress and mortality as the target variables.

Results

A total of 1036 babies were admitted in the NICU of the institution from 01-01-2017 to 31-12-2017. 947 were in born and 89 were born in other institution and referred in. Out of 1036, 124 (11.96%) were born below 34 weeks of gestation. These 124 babies where included in this retrospective cohort study. Mean birth weight increased with each increasing gestational age, from 354 g at 24 weeks to 2450 g at 34 weeks. 71 infants in the cohort were male (57.25%) and 53 (42.74%) were females (Table 1).

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>71</td>
<td>57.25%</td>
</tr>
<tr>
<td>Female</td>
<td>53</td>
<td>42.74%</td>
</tr>
<tr>
<td>Total</td>
<td>124</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 1: Sex distribution of study cohort.

107 infants (86.29%) were born in this hospital and 17 (13.71%) were born in peripheral hospitals and referred for neonatal care. Among these 13 (10.6%) were between 24 - 28 weeks of gestation, 19 (14.9%) were between 29-31 weeks of gestation and 92 (74.5%) were between 32 - 34 weeks of gestation (Figure 1).
The overall incidence of respiratory distress was 34%. 64% of the infants less than 28 weeks developed respiratory distress, 44% of the infants among 29 - 31 weeks and 27% of the infants among 32 - 34 weeks developed respiratory distress (Figure 2).

Figure 1: Distribution of gestational age among the cohort.

Figure 2: Respiratory distress among study cohort and its relation with gestational age.

55% of the infants with birth weight less than 1000 gm, 45% of the infants with birth weight 1101 - 1500 gm, 24% of the infants with birth weight 1501 - 2500 gm had developed respiratory distress (Figure 3).

Among the maternal risk factors anaemia was identified to be the major risk factor accounting to 64%, followed by PIH (24%), sepsis (21%) and Cesarean section accounting to 19% (Figure 4).
Minimum stay in the hospital was 1 day and maximum was 79 days with a mean of 21 days. Out of 6 deaths 5 occurred in the first week and one in the third week. Major congenital anomalies detected were down syndrome with congenital heart disease, ASD, PDA, Hydrocephalus, Lung immaturity, Retinopathy of prematurity (ROP), Limb and chest wall abnormalities, jejunal atresia, undescended testes, trachea esophageal fistula and hydro-ureteronephrosis. Multiple major abnormalities were detected more in infants born below 31 weeks of gestation. Major associated comorbidities noted were perinatal asphyxia, hyaline membrane disease, respiratory distress, neonatal sepsis, hypoglycemia, neonatal hyper-bilirubinaemia, pneumothorax, metabolic acidosis and multi organ dysfunction Syndrome. Respiratory distress syndrome was present in 42 (34%), ASD in 4 (3.22%) and Retinopathy of prematurity (ROP) in 6 (4.83%) infants. All the preterm deliveries were attended by pediatrician. All preterm deliveries were informed in advance to NICU prior to delivery and most of the cases referred from outside are informed before being shifted from those institutions, so that NICU is prepared for receiving the baby. All babies < 34 weeks were shifted to NICU for preterm care. 22 (17.74%) infants needed resuscitation at birth. All the premature infants were nursed in thermo-neutral environment (around 36.5°C). Oil is applied to skin to reduce convective heat loss and evaporative water loss. Stable babies were given kangaroo mother care to provide warmth. All preterm infants developed jaundice within the first week. If baby is found to be jaundiced serum bilirubin is estimated and phototherapy started based on bilirubin level. Jaundice was not controlled by phototherapy in one infant and was subjected to exchange transfusion.

6 babies out of 124 died constituting a mortality of 4.83% for those below 34 weeks of gestational age. Only 6 out of the remaining 912 (above 34 weeks of gestation) died during the study period constituting a mortality of 0.65%. Statistical analysis showed the following results for various risk factors with RDS as target variable (Table 2).

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inborn/out born</td>
<td>0.026</td>
</tr>
<tr>
<td>Term</td>
<td>0.014</td>
</tr>
<tr>
<td>Birth weight</td>
<td>0.0218</td>
</tr>
<tr>
<td>Sex</td>
<td>0.6548</td>
</tr>
<tr>
<td>Parity</td>
<td>0.0267</td>
</tr>
<tr>
<td>Anaemia</td>
<td>0.0368</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0.0046</td>
</tr>
<tr>
<td>Caesarian Section</td>
<td>0.0475</td>
</tr>
<tr>
<td>PIH</td>
<td>0.0866</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>0.4969</td>
</tr>
<tr>
<td>Antepartum Hemorrhage</td>
<td>0.9155</td>
</tr>
</tbody>
</table>

*Table 2: Statistical significance of various risk factors in the development of RDS.*

Statistical analysis of the various treatment modalities used showed the following results with mortality being the target variable (Table 3).

<table>
<thead>
<tr>
<th>Variables</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambu bag resuscitation</td>
<td>0.0065</td>
</tr>
<tr>
<td>Chest Compression</td>
<td>0.04</td>
</tr>
<tr>
<td>Oxygen supplement</td>
<td>0.5333</td>
</tr>
<tr>
<td>CPAP</td>
<td>1</td>
</tr>
<tr>
<td>Intubation</td>
<td>0.034</td>
</tr>
<tr>
<td>Surfactant</td>
<td>0.041</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>0.4105</td>
</tr>
<tr>
<td>Inotropes</td>
<td>0.047</td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>0.0397</td>
</tr>
<tr>
<td>Length of Hospital Stay</td>
<td>0.0144</td>
</tr>
</tbody>
</table>

*Table 3: Statistical significance of various treatment modalities influencing the outcome.*

Discussion

In a hospital-based cohort of infants born between 24 and 34 weeks of gestation and taken care of in a level-3 NICU, survival during the hospital stay was substantially good across all gestational age and birth weight. Although 84% of infants had one or other morbidity, all of them responded well to resuscitation and supportive care in the NICU. Even though sepsis, respiratory distress and ROP have been reported among this cohort it is less when compared to other studies [7-11]. Few other studies have shown higher rates of cerebral palsy, cognitive impairment, and behavioral problems among those born at very early gestations age [12-15] and causing major neonatal morbidities and high risk for significant impairment in later life. These possible morbidities can be assessed only on subsequent follow up for a sufficiently long period after discharge from NICU. The rates of attempted resuscitation for infants in our study were similar to several other studies [16]. These infants received interventions such as surfactant therapy, tracheal intubation, ventilator support, parenteral nutrition, or chest compressions. It is possible that the differences in resuscitation practices may influence survival and mortality. Previous studies have proposed individual decision-making in resuscitation of extremely preterm infants [17,18], whereas other studies have examined more major differences in resuscitation practice and subsequent outcomes at the hospital level [19-21]. Population-based studies and analyses are needed to gain a better understanding of the determinants of, and extent to, which regional practice variations influence mortality and quality of survival rates.

Differences in perinatal factors and maternal demographic characteristics have not influenced mortality. But increased birth weight and female sex, demonstrate favorable predictors for survival, as described by Tyson., et al [22]. Majority of extremely preterm births in this cohort occurred in hospitals and this may be the reason for low mortality. Better survival was seen in infants born at a hospital with a regional-level NICU, which has been reported in other studies [23,24].

Future population-based studies are needed to examine neurodevelopmental and other outcomes in these infants after discharge from the hospital. Large, population-based studies of neurodevelopmental outcomes in survivors of extreme prematurity have been conducted in the United Kingdom [13,25], Sweden [26], Australia [27] and France [12].

Conclusion

This study provides information on mortality of preterm infants treated in a tertiary level-3 NICU in a backward district of Kerala state in India. It also explores the resuscitative and supportive care to the preterm infants and look at major morbidity among survivors. Mortality among this cohort is only 4.83% and only one baby among the 13 extremely low birth weight category was lost. This study highlights that survival can be considerably improved if delivery is conducted in an institution with level-3 NICU facility and immediate NICU care is provided to all newborns that need it. Even though there are multiple anomalies and comorbid conditions in these babies survival is comparable to other advanced NICUs.

Bibliography

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