Respiratory Morbidity in Late-Preterm Births: A Prospective Observational Study at a Tertiary Care Hospital

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Received: 26 February 2016 / Accepted: 12 April 2016 / Published online: 4 May 2016
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Abstract

Objectives To study the neonatal respiratory morbidity in late-preterm neonates.

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Materials and methods This study was done over a period of 6 months (November 2014–April 2015) including 120 late-preterm births at a tertiary referral center.

Results Among the 120 late-preterm babies, 42 (35 %) developed respiratory morbidity. Respiratory distress syndrome (RDS) developed in 43 % of the babies who had not received steroid prophylaxis against 25.8 % receiving the same ($p < 0.05$). Among the indicated late-preterm deliveries, 45 % of babies developed respiratory morbidity in comparison with 22 % of the babies born following spontaneous onset of labor ($p < 0.05$). In the neonates with respiratory morbidity, male babies had a higher incidence than their female counterparts (48 vs. 24 % $p < 0.05$). Severity of RDS declined from 57 % for babies born at 34 weeks of gestation to 26.3 % for those born at 36 weeks ($p 0.14$). With each advancing week of gestation a significant reduction in the need for ventilator support (78 % at 34 weeks to 15 % at 36 weeks of gestation $p < 0.05$) was

observed. Presence of antenatal risk factors did not significantly contribute to the respiratory morbidity.

Conclusion The severity of respiratory morbidity and need for ventilator support declines with advancing gestational age; hence, every attempt must be made to prolong pregnancy till 36 weeks of gestation.

Keywords Late preterm ·

Respiratory distress syndrome (RDS) ·

Transient tachypnea of the newborn (TTNB) ·

Respiratory morbidity

Introduction

The availability of advanced neonatal care has encouraged early interventions in high-risk pregnancies resulting in a shift to left of mean gestational age at birth. The perception that late-preterm infants are at minimal risk of developing morbidity when compared to preterm births, might have also led to a trend toward these early interventions [1].

As the number of late-preterm births is increasing, it is essential to understand the unique problems that this growing population of infants may experience. There is limited data available on the short-term complications faced by these neonates in the Indian setup. This study was undertaken to observe the respiratory morbidities faced by late-preterm neonates in the immediate neonatal period.

Methodology

This prospective observational study was conducted at a tertiary care hospital. This study was approved by the hospital ethical committee. All live born late-preterm ($34^{0/7}$ – $36^{6/7}$ weeks) babies born between November 2014 and April 2015 were included in this study. The American College of Obstetricians and Gynecologists (ACOG) defines late-preterm, early-term and full-term birth as delivery of a neonate between $34^{0/7}$ – $36^{6/7}$, $37^{0/7}$ – $38^{6/7}$ and $39^{0/7}$ to $40^{6/7}$ weeks, respectively [2]. Babies with congenital anomalies and inborn errors of metabolism were excluded.

Maternal baseline demography details such as age and parity index were noted. The last menstrual period or the first trimester dating scan was used to estimate the gestational age. Maternal medical conditions such as hypertensive disorders of pregnancy, gestational as well as overt diabetes, cardiac, renal diseases in the mother were included as they may contribute to early delivery of the baby. In those mothers who received corticosteroids, the number of doses and period of gestation at administration were noted.

Patients delivering following spontaneous onset of labor and indicated deliveries were studied. The influence of mode of delivery on RDS was noted.

All neonates who were included in the study were followed till discharge from the hospital. The standard definitions for respiratory disorders were determined by IAP standards in our Neonatal Intensive Care Unit (NICU). Mild RDS consisted of grunting, flaring, tachypnea, chest retractions and transient tachypnea of the newborn (TTNB). Severe RDS included pneumonia, atelectasis, persistent pulmonary artery hypertension, acute lung injury. The diagnosis was verified by chest X-ray findings for air bronchogram and reticulogranular patterns.

Management depended on the severity of RDS, and this included observation, oxygen delivery by nasal cannula or hood oxygen, use of ventilator support like biphasic positive airway pressure and continuous positive airway pressure depending on the severity of distress.

Statistical analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS version 16). The association between risk variables and outcome was done using Chi-square test (Fisher's exact probability test).

Results

Figure 1 depicts the study population and the distribution of neonates according to gestational age and development of RDS.

The study group comprised of 14 % of the total deliveries. Respiratory distress syndrome (RDS) developed in 42 (35 %) of late-preterm babies, while it was seen 21 (10.4 %) and 24 (5.6 %) of early-term and full-term infants, respectively, which was statistically significant ($p < 0.05$).

The maternal and neonatal demography details are specified in Table 1.

The factors contributing to RDS are studied in Table 2.

Among the babies who developed RDS, we had noted that 27 (43.5 %) of the late-preterm babies had not received steroids antenatally in comparison with 15 (25.8 %) of the babies who had received the same ($p < 0.05$).

The development of RDS was independent of antenatal complications, though these risk factors contributed to indicated deliveries and mode of delivery. However, when we analyzed common risk factors like hypertensive disorders of pregnancy and, diabetes, these were more often associated with RDS. Eighteen out of 36 (50 %) of the late-preterm babies born to mothers with hypertensive disorders of pregnancy developed RDS. Among the seven babies

Fig. 1 Study population and distribution of neonates according to gestational age and development of RDS

Table 1 Maternal and neonatal demography

Characteristics	Study population 34 ^{0/7} –36 ^{6/7} wks n = 120 (%)
Mean maternal age (years)	28 ± 3.14
Parity	
Primi	49 (41)
Multi	71 (59)
Gender	
Male	54 (45)
Female	66 (55)
Mean birth weight (gms)	2118.48 ± 234.4
AGA*	86 (71.6)
SGA [#]	34 (28.3)
Spontaneous	54 (45)
Indicated	66 (55)

AGA appropriate for gestational age, SGA small for gestational age

born to diabetic mothers, four (57 %) developed RDS out of whom severe RDS was seen in 3 who were born to overt diabetic mothers.

Spontaneous onset of labor was noticed in 54 (45 %) of late-preterm deliveries, whereas 66 (55 %) of the late-preterm deliveries were indicated deliveries for maternal or fetal indications. It is of interest to note that, of the 54 spontaneous deliveries, only 12 (22.2 %) of the babies

developed respiratory morbidity, when compared to indicated deliveries of whom 30 (45.5 %) developed RDS. Among the indicated deliveries, 30 (45 %) were induced by misoprostol and 27 (41 %) were induced by dinoprostone. RDS developed in 18 (60 %) out of the 30 induced by misoprostol, while 12 (44 %) out of 27 developed RDS in the dinoprostone group. Among the misoprostol-induced group 9 (30 %) of the 30 babies developed mild RDS in comparison with 4 (15 %) out of 27 babies in the dinoprostone-induced group. There was no difference in TTNB between misoprostol and dinoprostone group (22 vs 23 %).

The route of delivery and its association with development of neonatal RDS was also analyzed. We found that 30 (40 %) out of 74 babies born by cesarean section developed respiratory morbidity when compared to 12 (25 %) out of 46 babies who were delivered by vaginal route, although this was not statistically significant.

We found that 48 % of the respiratory morbidity developed in male babies, when compared to 24 % of the female babies, matched for gestational age ($p < 0.05$).

The severity and management of respiratory morbidity according to gestational age at birth is described in Table 3.

Severe respiratory distress was observed to be higher in babies born at 34–35 weeks (57 %) than at 36 weeks (26.3 %). As compared to 78 % of the babies born between 34 and 35 weeks, only 15 % of babies born at 36 weeks of gestation required mechanical ventilation ($p < 0.05$).

Table 2 Comparison of contributing factors in the late-preterm babies

<i>n</i> = 120 (%)	With RDS <i>n</i> = 42 (%)	Without RDS <i>n</i> = 78 (%)	<i>p</i> value
Received steroids <i>n</i> = 58 (48.3)	15 (25.8)	43 (74.1)	0.05
Not received steroids <i>n</i> = 62 (51.7)	27 (43.5)	35 (56.4)	
Antenatal risk factors present <i>n</i> = 93 (77.5)	35 (37.6)	58 (62.3)	0.36
Antenatal risk factors absent <i>n</i> = 27(22.5)	7 (25.9)	20 (74)	
Spontaneous onset of labor <i>n</i> = 54 (45)	12 (22.2)	42 (77.7)	<0.05
Indicated deliveries <i>n</i> = 66 (55)	30 (45.4)	36 (54.5)	
Male <i>n</i> = 54 (45)	26 (48)	28 (51.8)	<0.05
Female <i>n</i> = 66 (55)	16 (24)	50 (75.7)	

Fisher's *t* test, *p* value <0.05 statistically significant

Table 3 Severity and management of respiratory morbidity according to gestational age

Total no. of neonates with RDS <i>n</i> = 42 (%)	34 weeks <i>n</i> = 14 (%)	35 weeks <i>n</i> = 9 (%)	36 weeks <i>n</i> = 19 (%)	<i>p</i> value*
Mild RDS (chest retractions, TTNB) <i>n</i> = 24 (57.2)	6 (42.8)	4 (44.4)	14 (73.6)	0.14
Severe RDS (with X-ray changes) <i>n</i> = 18 (42.8)	8 (57.1)	5 (55.5)	5 (26.3)	
Management				
Non-ventilatory support <i>n</i> = 19 (45.7)	3 (21.4)	2 (22)	14 (73)	<0.05
Ventilatory support <i>n</i> = 23 (54.7)	11 (78.5)	9 (77.7)	3 (15.7)	

* Chi-square test, *p* value <0.05 significant

We had no neonatal mortalities due to respiratory morbidity during the study period.

Discussion

This study was carried out to determine the probable factors which may influence respiratory morbidity in late-preterm babies.

In our study, 69 % of the late preterms had developed at least one neonatal complication like neonatal jaundice, respiratory morbidity, hypoglycemia sepsis, seizures and intra-ventricular hemorrhage (IVH) warranting NICU admission. Respiratory morbidity (35 %) and hyperbilirubinemia (34.7 %) were the most predominant complications.

Our study showed decrease in severity of respiratory morbidity with each advancing week of gestation in the late preterms from 34 to 36 weeks. This is in accordance with other studies, namely Wang et al. and Jaiswal et al. [3, 4]. Incidence of respiratory morbidity in our study in the late preterms was 35 %. In studies conducted by Judith et al.,

Jaiswal et al. and Wagh et al. [4–6], the incidence of respiratory morbidity in the late-preterm group was found to be 9, 10.5 and 29.8 %, respectively. Our study appears to show a higher incidence as we have included babies who had mild RDS lasting for few hours immediately after birth requiring no active intervention. Being a tertiary referral center, the number of cases requiring early delivery was more. In our study, the late preterms were noted to have a sevenfold higher incidence of respiratory morbidity when compared to neonates born at term, which was consistent with the results of Shapiro et al. [7].

A significant decline was observed in the incidence of severity of RDS from 57 % at 34 weeks of gestation to 26 % at 36 weeks. Although the incidence of RDS at 36 weeks (42 %) was higher than those born at 34–35 weeks (32 %), it is essential to note that neonates at 36 weeks had higher incidence of mild RDS, requiring oxygen support at the most. In contrast, babies born at 34–35 weeks with RDS needed more aggressive management with ventilator support, thus prolonging the hospital stay. This implies that by prolonging the pregnancy by just 2 weeks, we may significantly decrease the severity, NICU

admission rates as well as the need for invasive ventilatory support.

In our study, the major maternal and fetal contributors for late-preterm deliveries were hypertensive disorders of pregnancy (36 %) and IUGR (19 %). Fetal factors like multiple gestation (12 %), severe oligoamnios (14 %) and IUGR contributed to the majority of late-preterm births. However, none of these factors were statistically significant to contribute to neonatal respiratory morbidity. Though on the whole antenatal risk factors did not significantly contribute to RDS, nevertheless, mothers with risk factors like hypertensive disorders of pregnancy and diabetes contributed to development of respiratory morbidity. This was consistent with results of Shapiro et al. [7] who also found that late-preterm births and maternal medical conditions were independent risk factors for neonatal morbidity.

Among the 15 (25.8 %) babies who had RDS in spite of receiving steroids, four of the babies were born to diabetic mothers at 35 weeks, 5 had received only single dose of steroid and remaining 6 had received steroids before 32 weeks of gestation. Majority of the 35 (56 %) babies who had not received steroid prophylaxis and had not developed any form of respiratory morbidity, belonged to 35–36 weeks of gestation.

The respiratory morbidity was not only severe in the babies who had not received steroids but also required higher ventilatory support, exogenous surfactant and also had prolonged NICU stay. Neonates born at 34 weeks who had received at least a single dose of steroid prior to delivery were found to have decreased severity of RDS. Shanks et al. and Cindy et al. [8, 9] found that a single course of corticosteroid in pregnancies with documented fetal lung immaturity even after 34 weeks, significantly increased surfactant/albumin ratio thereby reducing the risk of RDS. We suggest rescue dose antenatal corticosteroid administration between 34 and 36 weeks of gestation when early delivery is anticipated.

Indicated deliveries, when coupled with cesarean section, had a higher incidence of RDS in comparison with spontaneous vaginal deliveries. TTNB and chest retractions with grunting were noticed to be high among the babies born by cesarean section. The plausible explanation could be retention of lung secretions which are generally expelled during the process of vaginal delivery. Also, the rapid transition in the fetal milieu in a cesarean may contribute to RDS by hindering neonatal adaptation to the new environment as compared to the gradual physiological changes that take place during a vaginal delivery [10]. We found no statistical significance in the development of RDS between the misoprostol and dinoprostone groups.

When matched for gestational age, we found an increased incidence of RDS in male babies compared to their female counterparts. Similarly, Anadkat et al. [11] observed the male neonates to have a higher incidence of RDS. They also noted that although the severity decreased

with advancing gestational age in both genders, the difference in risk of developing RDS between males and females persisted until 38 weeks of gestation. Seaborn et al. [12] found that male babies are more likely to develop RDS than females, with a ratio of 1.7:1. They also found the lungs of male babies to be immature by approximately one week when compared to females [12]. They have hypothesized that fetal androgens specifically dihydrotestosterone have a role in inhibition of synthesis of surfactant and cause late appearance of phosphatidylglycerol.

The limitations in our study were that we have studied only respiratory morbidity and not correlated it with other morbidities that late preterms may develop. Readmission and long-term follow-up of these babies who developed respiratory morbidity were not studied. The duration of the study was short; 6 months only.

Various studies have shown that late-preterm infants have considerable short- and long-term morbidity and mortality; hence, every attempt must be made to prolong the pregnancy till 36 completed weeks [3, 5, 13]. Maternal and fetal indications for early delivery should be critically evaluated and risk benefit ratio should be judiciously analyzed, keeping in mind the risks of neonatal morbidity.

Conclusion

The decision to induce delivery in the late preterm is imperative in determining neonatal outcome. The benefits and risks must be weighed, as a prudent choice goes a long way in benefitting the newborn. Hence, prolonging pregnancy to at least 36 weeks will play a major role in reducing the severity of respiratory morbidity.

Acknowledgments The authors express their sincere thanks to Dr. Leslie Lewis, Professor and Head of Neonatal Intensive Care Unit, for making this study possible and for managing these late-preterm babies.

Funding None.

Compliance with Ethical Standards

Conflict of interest The authors report no conflicts of interest in this work.

Ethical Statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical clearance obtained from the hospital ethical committee (IEC 26/2015).

Informed consent Informed consent was obtained from all individual participants included in the study.

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