An Observational Study on Late Preterm Neonates from a Post-Graduate Teaching Hospital in North East India

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Methods: This prospective observational study included the late preterm neonates (34\textsuperscript{0/7} weeks - 36\textsuperscript{6/7} weeks) born at Nazareth Hospital, Shillong, Meghalaya, India for a period of six months. Short term outcome was assessed in the form of morbidity during the study period and at follow up at 2 weeks and 6 weeks. The enrolled neonates were divided into three groups of 34\textsuperscript{0/7} to 36\textsuperscript{0/7}, 35\textsuperscript{0/7} to 36\textsuperscript{0/7} and 36\textsuperscript{0/7} to 36\textsuperscript{6/7} weeks. Results: During the study period, 1025 neonates were born at a large tertiary care teaching hospital located at Shillong, Meghalaya, India, of which 72 were late preterm. In the present study the data was collected from 66 late preterm neonates (91.6 %) of which, 26 neonates (39.4 %) were born at 34\textsuperscript{0/7} week of gestation (WG), 19 neonates (28.8 %) were born at 35\textsuperscript{0/7} WG and 21 neonates (31.8 %) were born at 36\textsuperscript{0/7} WG. We observed that 22 out of 26 (84.6%) neonates of 34 WG, 17 out of 19 (89.4%) of neonates of 35 WG and only 11 out of 21 (52.3%) required NICU admission because of various associated morbidities. In our study 15.1% late preterm neonates developed hypothermia. We observed that 36.3% neonates developed hypoglycemia. A total of 18 (27.3%) late preterm neonates developed perinatal asphyxia. Respiratory distress syndrome (RDS) was present in 27 out of 66 neonates (40.9%). Feed intolerance developed in 6 out of 66 (9.09%) late preterm neonates. Jaundice developed in 31 out of 66 (46.9%) late preterm neonates. Probable sepsis developed in 17 out of 66 neonates (25.7 %). Sepsis was confirmed in 4 out of 66 (6 %) late preterm neonates. Conclusions: Late preterm infants suffer a large number of inter-current medical problems during the neonatal period, especially increased likelihood of resuscitation in the delivery room, hypothermia, hypoglycemia, jaundice requiring phototherapy, respiratory pathologies, sepsis and feeding intolerance. Keywords: Late preterm infants, Morbidity, Outcome.

INTRODUCTION

According to National institute of child health and human development report in 2005, late preterm infants are infants born at gestational weeks 34 \textsuperscript{0/7} to 36 \textsuperscript{6/7}. Previously they were termed as moderately preterm, mildly preterm, minimally preterm, marginally preterm, and near-term neonates [1, 2]. The data of last 25 years have showed that the birth rate of late preterm infants have risen by 33%, and this is because of its well defined gestational age [3]. The late preterm neonates are physiologically immature and at higher risk of major neonatal morbidities and mortality in comparison to term neonates. The late preterm neonates have increased risk of neonatal mortality and morbidities such as respiratory distress syndrome, apnea, jaundice, hypoglycemia, feeding difficulties, hypothermia and temperature instability, neonatal sepsis, seizures, anemia, intra-ventricular hemorrhage and necrotizing enteroocolitis [1, 2]. The aim of our study was to evaluate the incidence of neonatal morbidities in three different gestational ages, which is 34\textsuperscript{0/7}, 35\textsuperscript{0/7} and 36\textsuperscript{6/7} weeks of gestation. Also to evaluate the prevalence and outcome of these late preterm neonates admitted in a tertiary care hospital in Meghalaya.

This hospital based prospective observational study with short term follow up was carried out in the neonatal intensive care unit and post natal wards of a large tertiary care post graduate teaching private missionary hospital located at Shillong, Meghalaya, India. The period of study was 6 months from 1\textsuperscript{st} January 2017 to 30\textsuperscript{th} June 2017. Inclusion criteria for enrolment in the study were all intramural born live newborns with gestational age between 34\textsuperscript{0/7} to 36\textsuperscript{6/7} weeks. Estimation of gestational age was carried out from recollection of mother’s last menstrual period or dated first trimester antenatal ultrasonography followed by application of modified Ballard score. Neonates
having major congenital malformations, infants of diabetic mothers and neonates in whom an accurate measurement of gestational age could not be done were excluded from the study. The study protocol received ethical clearance from the Institutional Ethics Committee. The neonates were enrolled in the study after obtaining informed consent. Daily clinical examination was carried out, morbidities were recorded, investigations and management of morbidities were done as per standard protocols till discharge. Following discharge, the neonates were followed up in our high risk clinic at 2 weeks and 6 weeks of life.

**RESULTS**

A total of 1025 babies were born (from 1st January 2017 to 30th June 2017) out of which 72 of them were late preterm neonates. Prevalence of late prematurity in the present study was 7.02%.

Table-1: Gestational age wise distribution of late preterm neonates

| Gestational age | Number ( % ) |
|-----------------|--------------|
| 34 weeks        | 26 (39.4 %)  |
| 35 weeks        | 19 (28.8 %)  |
| 36 weeks        | 21 (31.8 %)  |

In our study, the data was collected for 66 late preterm neonates of which, 26 neonates (39.4 %) were born at 34th week of gestation (WG), 19 neonates (28.8 %) were born at 35th WG and 21 neonates (31.8%) were born at 36th WG. We found 28 (42.4%) male neonates against 38 (57.6%) female neonates.

Table-2: Distribution of mode of delivery

| Mode of delivery | Number (%) |
|------------------|------------|
| Caesarean section| 38 (57.6%) |
| Normal vaginal delivery | 26 (39.4%) |
| Instrumental delivery | 2 (3.0%) |

In our study, caesarean section accounted for 38 (57.6%) births while 26 (39.4%) babies were delivered by normal vaginal delivery and only 2 (3.0%) were delivered by assisted vaginal delivery. Of the 66 enrolled neonates, 36 (54.5%) neonates were born appropriate for gestational age (AGA), 28 (42.4%) were born small for gestational age (SGA) and 2 (3%) were born large for gestational age (LGA).

NICU admission: It was found that 33.3 % (22/66) required NICU admission in 34th WG group as against 25.76% (17/66) in 35th WG group and 16.67 % (11/66) in 36th WG group in our study.

Table-3: Rate of NICU admission

| Gestational age | Late preterm neonates admitted in NICU |
|-----------------|---------------------------------------|
| 34 weeks        | 22/66 (33.3%)                          |
| 35 weeks        | 17/66 (25.76%)                         |
| 36 weeks        | 11/66 (16.67%)                         |

Table-4: Comparison of the common morbidities as per gestation in late preterm neonates in our study

| Neonatal morbidity | Gestational age | p value |
|--------------------|-----------------|---------|
| Hypothermia n = 10 | 34 0/7 to 34 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Hypoglycaemia n = 24 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Perinatal Asphyxia n = 18 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Respiratory Distress Syndrome n = 27 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Feed intolerance n = 6 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Neonatal Jaundice n = 31 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Probable Sepsis n = 17 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |
| Confirmed Sepsis n = 4 | 34 0/7 to 35 6/7 | 6 (60.0%) | 4 (40.0%) | 0 | p = 0.04 |
|                   | 35 0/7 to 35 6/7 | 12 (50.0%) | 10 (41.7%) | 2 (8.3%) | p = 0.007 |
|                   | 36 0/7 to 36 6/7 | 12 (66.7%) | 5 (27.8%) | 1 (5.6%) | p = 0.007 |

Table-4 shows the different morbidities frequently associated with the late preterm neonates in our study.

Table-5: Gestational age against weight at discharge, at 2 weeks and 6 weeks

| Time             | Mean weight (SD) as per gestational age | p < 0.007 |
|------------------|----------------------------------------|-----------|
|                  | 34 weeks | 35 weeks | 36 weeks |          |
| At Discharge     | 2243.1 (412.9) | 2532.6 (435.8) | 2747.9 (452.2) |          |
| At 2 Weeks       | 2548.2 (486.4) | 2764.0 (448.3) | 3162.5 (471.3) |          |
| At 6 Weeks       | 2859.7 (453.2) | 3142.6 (417.7) | 3395.7 (494.9) |          |
Table-5 shows a statistically significant association between gestational age and mean weight (p<0.007) at discharge, at 2 weeks and at 6 weeks. Weight is seen to be highest in 36 weeks gestational age (GA) followed by 35 weeks GA then 34 weeks GA.

Table-6: Apgar scores of the late preterm neonates enrolled in the present study

| Gestational age (in weeks) | Apgar score | p (1min) | p (5min) |
|---------------------------|-------------|----------|----------|
| At 1 min Mean (SD)        | At 5 min Mean (SD) |
| 34\textsuperscript{th} to 34\textsuperscript{th} | 8.0 (1.29) | 8.2 (0.82) | 0.149 | 0.009 |
| 35\textsuperscript{th} to 35\textsuperscript{th} | 8.0 (1.33) | 8.6 (0.92) | 0.149 | 0.009 |
| 36\textsuperscript{th} to 36\textsuperscript{th} | 8.3 (1.02) | 9.0 (0.79) | 0.149 | 0.009 |

Table-6 describes the evaluation by Apgar score at 1 minute didn’t show any differences between groups, but at 5 minutes significantly lowest points were in the group of 34\textsuperscript{th} weeks GA.

Table-7(A): The pattern of feeding among late preterm neonates of the study at birth

| FEEDING AT BIRTH | 34 WG | 35 WG | 36 WG |
|------------------|-------|-------|-------|
| DBF              | 23    | 17    | 20    |
| (88.5%)          | (89.4%) | (95.3%) |       |
| DBF +CF or PF    | 1     | 1     | 1     |
| (3.8%)           | (5.2%) | (4.7%) |       |
| Only CF or PF    | 1     | 1     | 0     |
| (3.8%)           | (5.2%) |       |       |
| TPN or GF        | 1     | 0     | 0     |
| (3.8%)           |       |       |       |

(DBF: Direct breastfeeding. CF: Cup and spoon feeding. PF: Paladai feeding. TPN: Total parental nutrition. GF: Gavage feeding.)

Table-7(A) shows that 60 (90.9%) of late preterm infants were directly breastfed, 3 (4.5%) were fed by both cup & spoon or paladai feeding and direct breast feeding, 2 (3.0%) late preterm infants were fed by only cup & spoon or paladai feeding and only 1 (1.5%) late preterm infant was given total parenteral nutrition. Breastfeeding rate at birth was significantly higher in the group of 36\textsuperscript{th} weeks group. In the study, 9% (6/66) late preterm neonates showed feeding problem at birth.

Table-7(B): Comparison of pattern of feeding among late preterm neonates of the study

| FEEDING PATTERNS ACCORDING TO GESTATIONAL AGE | 34 WG | 35 WG | 36 WG |
|----------------------------------------------|-------|-------|-------|
| At discharge                                 | At 2 weeks | At 6 weeks | At discharge | At 2 weeks | At 6 weeks | At discharge | At 2 weeks | At 6 weeks |
| DBF                                          | 25 (96.5%) | 24 (92.3%) | 26 (100%) | 18 (94.7%) | 18 (94.7%) | 19 (100%) | 21 (100%) | 21 (100%) |
| DBF +CF or PF                                | 1 (3.8%) | 1 (3.8%) | 0       | 1 (5.2%) | 1 (5.2%) | 0       | 0       | 0       |
| Only CF or PF                                | 0     | 1 (3.8%) | 0       | 0       | 0       | 0       | 0       | 0       |
| TPN or GF                                    | 0     | 0       | 0       | 0       | 0       | 0       | 0       | 0       |

(DBF: Direct breastfeeding. CF: Cup and spoon feeding. PF: Paladai feeding. TPN: Total parental nutrition. GF: Gavage feeding.)

Table 7(B) shows that 64 (96.9%) of late preterm infants were directly breastfed. None were discharged on gavage feed. Breastfeeding rate at discharge was significantly higher in the group of 36 weeks group.

At 2 weeks, 63 neonates were on direct breastfeeding; only one late preterm infant was fed by only cup and spoon or paladai feeding and no late preterm were given gavage feed.

At 6 weeks, 66 (100%) late preterm neonates were on direct breastfeeding irrespective of their gestational age at birth.

Table-8: Late preterm neonates requiring readmission

| Re-admission | Number of neonates | Percentage |
|--------------|--------------------|------------|
| Required     | 2                  | 3.0 %      |
| Not Required | 64                 | 97.0 %     |
Table-8 Shows that only 2 out of 66 (3%) of the late preterm neonates required readmission after discharge within 6 weeks of life

**DISCUSSION**

During the period of six months from 1st January 2017 to 30th June 2017, total 1025 newborns were born at a post graduate teaching hospital located in Shillong, the capital city of the north eastern Indian state of Meghalaya, of which 72 were late preterm neonates.

Prevalence of late preterm neonates in our study was 7.02 % in the year 2017, which was comparable to the study conducted by Tsai ML, et al., in Taiwan [3]. Another study reported a rate of 8.9% conducted by Wagh SA et al., in Kerala [4]. Our rate of late preterm births was less as compared to 10.6 % seen in another study published by Haroon A. et al in Pakistan [5].

In our study we found that among the 66 late preterm neonates, 54.5 % were AGA, 42.4 % babies were SGA and 3 % were LGA. Wagh SA et al., reported 81% AGA, 11% SGA and 8 % LGA neonates in their study [4].

There was a statistically significant association between the gestational ages and the birth weight in late preterm newborns. Late preterm newborns born 34th week GA weighed less than late preterm newborns born 35th and 36th (p=<0.001). Gestational age is important for the newborn to develop and explains about their size and weight. As long as the infant stays inside the womb, it will grow and get bigger. Late preterm born as early will have less weight compare to the other late preterm gestational ages [6-8].

In the present study, we compared morbidities among gestational ages 34th, 35th, and 36th weeks of gestation and it showed that neonatal jaundice and respiratory morbidity occurred more often in late preterm infants born in 34th week GA comparing to newborns born at 35th and 36th week GA. Late-preterm infants have increased chances of developing neonatal jaundice because of feeding difficulties that predispose them to an increase in entero-hepatic circulation, decreased stool frequency, and dehydration [9, 10].

We observed that 22 out of 26 (84.6%) neonates of 34 WG, 17 out of 19 (89.4%) of neonates of 35 WG and only 11 out of 21 (52.3%) required NICU admission because of various co morbidities. Ten (15.1%, p = 0.04) late preterm neonates developed hypothermia in our study. Out of the 10 neonates, 6 (60%) belonged to 34 WG, 4 (40%) belonged to 35 WG and none to the 36 WG. We observed that 36.3% late preterm neonates developed hypoglycaemia in our study. Among the neonates with hypoglycemia, 50% belonged to 34 WG, 41.7% belonged to 35 WG and 8.3% belonged to 36 WG. Wang et al., reported 15.6 % hypoglycemia in late preterm neonates; Wagh SA et al., found 29.8 % hypoglycaemia in their study [4, 10]. The incidence of hypoglycaemia was high in our study.

In our study, we found that 27.3 % (18/66) late preterm neonates developed perinatal asphyxia who were given some resuscitation. Wagh SA et al., reported that 14 % of late preterm neonates were given some resuscitation in their study [4]. The need of resuscitation was higher in our study.

Respiratory distress syndrome (RDS) was present in 27 out of 66 neonates (40.9%, p = 0.009). Our study also found that more late preterm neonates- 48.1 % at 34 week of gestation had more respiratory distress in comparison to 11.1% at 36 weeks of gestation.

Feed intolerance developed in 9% (6/66) late preterm neonates. Among our neonates, 88.5% of 34 WG, 89.4% of 35 WG and 95.3% of 36 WG could be initiated on direct breast feeding at birth. Wang et al described feeding difficulties to be more in late preterm neonates (32.2 %) [10].

In our study, we found that 46.9% (31/66) late preterm neonates developed neonatal jaundice requiring phototherapy. Our study also revealed that more neonates- 48.4% at 34 week of gestation required treatment for neonatal jaundice as compared to 32.3% and 19.4 % at 35 and 36 weeks respectively. This was comparable to the studies reported by Wagh SA et al., (50.8 %) and Wang et al., (54.4 %) [4, 10].

In our study we evaluated 31.8 % (21/66) late preterm neonates for neonatal sepsis and given empirical antibiotics. Neonatal sepsis was confirmed by growth in blood culture in 6 % of the total late preterm neonates. Wang et al., evaluated 36 % of late preterm neonates for sepsis in their study [10].

**CONCLUSION**

It has been observed that the rate of preterm births has been increasing globally. These neonates are physiologically and metabolically not mature enough. They have higher risks for acute medical complications, mortality and future complications as compared to their term counter parts. There is an ongoing need for research in the etiology, clinical presentations and rational management protocols for prevention of late preterm births [5, 10, 11, 12].

**DECLARATION**

Principal investigator: Dr. Rajarshi Das, Co-investigators: Dr. Palash R Gogoi, Dr. Santanu Deb, Dr. Prasenjit Paul, Dr. Sabrina Yesmin, Dr. Premod Paharia.
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