

## Clinical profile of late-preterm infants admitted to a tertiary care hospital

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### ABSTRACT

**Background:** Late-preterm babies account for nearly 10% of the total births. Understanding clinical profile of late-preterm infants is important for helping newborn care providers to anticipate and manage potential morbidity during the birth hospitalization and early follow-up. **Objective:** The objective of this study is to study the clinical profile of late-preterm newborns (34<sup>0/7</sup> to 36<sup>6/7</sup> weeks of gestation). **Methods:** This was a prospective observational study conducted in the neonatal unit of a tertiary care public hospital. All late-preterm babies delivered in the hospital from July 2016 to December 2016, who met the inclusion criteria, were enrolled after taking consent from parents. Detailed antenatal and natal history were noted along with neonatal morbidities and mortality, and the interventions and treatment required by the infants were noted in a structured pro forma. These late-preterm infants were followed up till death/discharge and readmission to hospital and reasons for readmission were evaluated. **Results:** We enrolled 110 late-preterm babies delivered in our center. The most common morbidity was jaundice requiring phototherapy (63.63%) followed by respiratory distress (24.54%). 25.45% of infants required respiratory support in the form of continuous positive airway pressure or mechanical ventilation. Hypocalcemia and sepsis were observed in 10% of the babies. Feed intolerance was also observed in 16.36% of the babies. The mortality in this group of late preterms was 4.54%. **Conclusions:** Late-preterm infants show a considerably high rate of medical complications, including need for respiratory support and prolonged hospital stay. Awareness about the neonatal morbidities in late-preterm newborns will facilitate better management of these neonates.

**Key words:** *Hyperbilirubinemia, Late preterm, Maternal comorbidities, Neonatal morbidities, Neonatal mortality*

Late-preterm babies (34<sup>0/7</sup> and 36<sup>6/7</sup> weeks of gestation) account for nearly 10% of the total births [1]. While serious morbidities are rare, the late-preterm group has 2–3 fold increased rates for mild-to-moderate morbidities such as hypothermia, hypoglycemia, delayed lung fluid clearance and respiratory distress (RD), poor feeding, jaundice, infection, and readmission after the initial hospital discharge [2]. Understanding clinical profile of late-preterm infants is not only important for helping newborn care providers to anticipate and manage potential morbidity during the birth hospitalization and early follow-up but also may possibly assist in guiding non-emergency obstetric intervention decisions. The present study is an attempt to obtain actual data on incidence and pattern of early neonatal morbidities and maternal comorbidities of the late-preterm infants admitted to a tertiary level urban neonatal intensive care unit (NICU).

### MATERIALS AND METHODS

This was a prospective observational cohort study done in a tertiary care public hospital in Western India. All consecutively delivered late-preterm infants (34<sup>0/7</sup> weeks to 36<sup>6/7</sup> weeks) born during the study period from July 2016 to December 2016 were

eligible for enrolment in the study. The study was approved by the hospital ethics committee, and infants were enrolled in the study after an informed parental consent. Infants with life-threatening congenital anomalies were excluded. Maternal demographic characteristics and clinical variables such as maternal age, type of delivery, presence of risk factors like anemia, pregnancy-induced hypertension (PIH), eclampsia, gestational diabetes, preterm prelabor rupture of membranes, antepartum hemorrhage, multiple gestation, and antenatal steroid coverage were recorded and are presented in Table 1. Gestational age was assessed by maternal last menstrual period/first trimester USG. If neither were available, New Ballard score was used to estimate the gestational age. All enrolled infants received standard treatment and nursing care. They were roomed in with the mother in the postnatal care wards. All infants underwent clinical examination twice daily and evaluated for vital signs, activity, feeding difficulties, and general danger signs. They were admitted to the neonatal unit if birth weight was <2 kg or if they had any morbidity requiring NICU admission such as RD, perinatal asphyxia, sepsis, and feed intolerance. We recorded baby details such as gestational age, sex, birth weight, need for resuscitation and perinatal asphyxia, and APGAR scores. We used standard definitions for the various infant morbidities as mentioned below.

## Neonatal Jaundice

All neonates were screened for jaundice clinically as well as with a transcutaneous bilirubinometry (JM105). If the TcB levels were in phototherapy range as per NICE guidelines, single surface LED phototherapy was started and serum bilirubin levels were obtained. Serum bilirubin levels were monitored 12 hourly thereafter. Need for exchange transfusion was also determined using NICE guidelines. The highest bilirubin value and mode of treatment were recorded.

## RD

RD was defined as tachypnea with respiratory rate of more than 60 breaths per minute with/without retractions. The need for continuous positive airway pressure (CPAP) support or mechanical ventilation was noted along with the need for surfactant replacement therapy. Hypoglycemia was defined as blood glucose <40 mg/dl. Blood sugar was monitored with the point of care glucometer strips (glucose oxidase method) preferred at 12 hourly intervals for initial 72 h after birth. Hypocalcemia was defined as serum calcium level <7 mg/dl. All infants had their total serum calcium level checked once within the first 72 h of life as per unit protocol. Perinatal asphyxia was defined as a failure to start regular respiration within a minute of birth. The severity of encephalopathy was staged as per Sarnat and Sarnat classification. Hypothermia was defined as axillary temperature (measured for 3 min) <36.5°C. Feeding difficulties in the form of refusal of feeds, poor sucking, and regurgitation of feeds were noted. Feed intolerance was defined as gastric residuals of more than 50% of previous feed for 2 consecutive feeds or bloody aspirates or bilious aspirates from the nasogastric tube. Necrotizing enterocolitis was diagnosed and staged as per modified Bell's staging criteria. Polycythemia was defined as central venous hematocrit over 65% or a hemoglobin value above 22 g/dL. Sepsis was diagnosed on the basis of the positive sepsis screen (C-reactive protein >1 mg/dL, total leukocyte count <5000/cumm, I/T ratio >0.2, absolute neutrophil count <1800/cumm, and abnormal micro erythrocyte sedimentation rate) or presence of a positive blood/cerebrospinal fluid culture.

The various infant variables and morbidities are recorded in Tables 2-3. Infants with any morbidity precluding enteral feeding at birth were started on maintenance IV fluids and subsequently on gradually increasing feeds of expressed breast milk (EBM)/donor human milk (DHM) once they were hemodynamically stable. The others who were hemodynamically stable at birth were started on full enteral feeds of EBM/DHM either by gavage or cup and spoon. Direct breastfeeding was tried if they showed good feeding skills. They were evaluated for oromotor function by a trained occupational therapist within 24 h of birth and provided oromotor stimulation with premature infant oromotor intervention if needed. Oromotor stimulation was continued thrice daily till infant achieved full oral feeding ability. We noted time to transition from gavage to oral feeding by watispoon and direct breastfeeding. Anthropometry of all babies was noted on admission and weekly thereafter till discharge. These infants were followed up daily till discharge/death from the neonatal unit, whichever was earlier.

At discharge, we noted the weight, length, and occipitofrontal circumference along with the duration of hospital stay in days. We also recorded data about any readmissions following discharge till day 28 of life, which was proposed as the endpoint of the study. Continuous variables were analyzed by calculating the mean and standard deviation. For categorical variables, frequency and percentages were determined.

## RESULTS

Of 114 cases admitted during the study period, parents of 3 infants refused consent. One infant had life-threatening congenital anomaly (anencephaly) and was therefore excluded from the study. A total of 110 late-preterm infants were enrolled in our observational study. The average age of the mothers was of the late-preterm infants in our study was 25.5 ( $\pm$ 1.3) years. 40 (36.36%) mothers were primigravidas. 51 (46.36%) mothers delivered vaginally. Maternal risk factors were present in mothers of 104 (94.5%) late-preterm infants. No maternal risk factors were identifiable in 6 (5.4%) mothers. Table 1 elaborates the various maternal risk factors identified in our study group which shows that PIH and maternal anemia were the most common risk factors observed in 24 (21.81%) and 19 (17.27%) mothers. Mothers of 12 (10.9%) infants received a full course of antenatal steroids, 30 (27%) received an incomplete course, while mothers of 68 (61.81%) infants received no antenatal steroids.

45 (40.90%) infants were male, with a male:female ratio of 0.69:1. The gestational age and birth weight-wise distribution are presented in Table 2. 22 (20%) neonates were appropriate in weight for gestational age, while 88 (80%) were small for gestational age (SGA). Average weight on admission was 1642 ( $\pm$ 78) g. Among the 110 late preterms, 87 (79%) required admission to the neonatal unit either because they had a birth weight of <2 kg or they had at least one of the morbidities requiring some intervention. 23 (21%) babies were roomed in with their mothers in postnatal ward. Neonatal jaundice (63.63%) and RD (24.54%) constituted the most common neonatal morbidities (Table 3). 24 (21.8%) neonates had RD syndrome, while 3 (0.03%) babies had transient tachypnea of newborn. One infant (0.9%) developed NEC Stage 3 and succumbed to the same. Twelve (10.9%) infants suffered from neonatal sepsis, of which 9 infants (8%) had early-onset sepsis and 3 (2.7%) infants had late-onset sepsis. Among 3 babies who had late-onset sepsis, 2 babies had culture-positive sepsis (*Acinetobacter* and MRCONS in blood culture). Three babies had congenital heart disease: 2 had a ventricular septal defect and one had a tiny patent ductus arteriosus which closed with conservative management. 7 babies suffered perinatal asphyxia, 3 of these had Stage 3 HIE and succumbed to the same, and the other 4 had HIE Stage 1.

Five infants in our cohort died, causes being Stage 3 NEC (one infant), HIE Stage 3 (3 infants), and late-onset sepsis with septic shock (one infant). 70 late preterms (63.6%) required phototherapy for neonatal hyperbilirubinemia, average bilirubin being 12.01 ( $\pm$ 4.6) mg/dl, and maximum bilirubin being 17.4 mg/dl. None of the infants required an exchange transfusion

**Table 1: Maternal comorbidities**

Maternal morbidity	Number=10 (%)
Preterm premature rupture of membranes	12 (11.53)
Anemia	19 (20.19)
Pregnancy-induced hypertension	24 (25.00)
Multiple births	13 (12.5)
Antepartum hemorrhage	7 (6.7)
Gestational diabetes	1 (0.96)
Bad obstetric history	0 (0.00)
Oligohydramnios	5 (4.80)
Meconium-stained amniotic fluid	6 (5.76)
Eclampsia	3 (2.88)
Antenatal steroids (complete/incomplete dose)	42 (38.18)

**Table 2: Gestational age and weight-wise distribution of late preterms (n=110)**

Parameters	Number (%)
Gestational age weeks (days)	
34–34 (6/7)	40 (36.36)
35–35 (6/7)	26 (23.63)
36–36 (6/7)	44 (40.00)
Weight in kg	
<1.5	15 (13.63)
1.5–1.99	72 (65.45)
2–2.5	23 (20.90)

**Table 3: Early neonatal morbidities/mortality**

Morbidities	Number (%)
Respiratory distress	27 (24.54)
Cardiovascular problems	3 (2.72)
Jaundice	70 (63.63)
Sepsis	12 (10.90)
Hypothermia (mild) on admission	15 (13.63)
Hypoglycemia	3 (2.72)
Hypocalcemia	12 (10.90)
Feed intolerance	18 (16.36)
Necrotizing enterocolitis	1 (0.90)
Intraventricular hemorrhage	0 (0.00)
Birth asphyxia	7 (6.36)
APGAR at 1 min*	6.86 (±1.19)
APGAR at 5 min*	7.18 (±1.06)
Polycythemia	1 (0.90)
Death	5 (4.54)

for severe hyperbilirubinemia. 17 (15.45%) babies required CPAP for RD syndrome, of which 6 (35%) babies required surfactant replacement therapy. Three infants required oxygen therapy for transient tachypnea of newborn. 17 infants (15.45%) required CPAP as the primary mode of respiratory support. 11 (10%) babies required mechanical ventilation including 3 infants with HIE 3, 1 infant with NEC, 3 infants with late-onset sepsis, and 4 infants with RDS. 10 (9%) babies required inotrope support for maintaining blood pressure.

27 (24.54%) infants were kept nil per oral on admission because of hemodynamic instability. In these infants, minimal enteral nutrition was started on day 2 of life, and as the clinical condition of baby improved, feeds were gradually advanced by 20–30 ml/kg/day. These 27 infants required 7.2 (±1.4) days to reach full feeds. 55 (50.0%) infants were started on full gavage feeds and 28 (25.45%) infants were started on partial/full watspoon feed and breastfeeding was encouraged. 8 infants could effectively breastfeed from birth; however, they were provided extra EBM/DBM in view of their late-preterm status. 7 (6.36%) infants were diagnosed to have oromotor dysfunction and provided oromotor stimulation by the occupational therapist. 31 (28.18%) infants received Kangaroo mother care during their stay at hospital, and they had all regained birth weight by the time of discharge.

Average weight on discharge of our late preterms was 1760 (±87) g. 46 (41.8%) neonates had <7 days of hospital stay, 53 (48.1%) neonates required 8–14 days, and 11 (10%) neonates required >14 days of hospital stay. Average duration of hospital stay was 9.43 (±5.9 days). Among the 110 neonates, 105 were discharged after successful treatment. Among the 105 discharged babies, only 3 babies (2%) had readmission to the hospital: 2 for neonatal jaundice and 1 for feeding difficulties. All these 3 babies had been discharged before day 7 of life.

## DISCUSSION

Contrary to the belief that late-preterm newborns are nearly mature, the present study proves that they suffer significant morbidity and significant mortality. Late preterm constitutes about 10% of total births [1]. A total of 110 late-preterm babies were enrolled during the study period which constituted approximately 13.27% of the admissions to our unit. 59% of the late preterms in our cohort were females. We observed a male:female ratio of 0.69:1 quite unlike other studies in Indian NICUs where male infants outnumbered female infants [3,4]. 65% of our infants had birth weights between 1.5 and 2 kg, and 80% of the cohort was SGA, similar to the cohort studied by Girinathan *et al.* where 71.4% of infants were growth retarded [5]. The incidence of growth retardation is very high compared to other Indian studies by Jaiswal *et al.* and Sahana *et al.*, who found a very low incidence of growth retardation [3,6]. The greater incidence of SGA in our cohort might be attributable to the greater incidence of maternal morbidities in our population. The presence of at least one maternal risk factor for preterm delivery was noted in 89% of the infants. Other studies on late-preterm Indian infants by Savitha *et al.* and Ezhilvannan *et al.* have also found similar results [7]. Common maternal morbidities implicated are PIH, anemia, multiple births, and PPRM in the decreasing order. The percentage of babies born by lower segment cesarean section was 53.6% which was similar to other studies [3].

The most common neonatal morbidity was neonatal hyperbilirubinemia, incidence being 63.6%. Although there is a high chance of late preterms developing serum bilirubin values greater than 20 mg/dl, the maximum serum bilirubin we observed was 17.4 mg/dl [8]. The incidence of RD was 24.5% which was



similar to other Indian studies [3,4]. Late-preterm neonates are more susceptible to neonatal sepsis, and in our study, 10.95% of infants suffered from neonatal sepsis; these rates are significantly better than the cohort studied by Arunagirinathan where incidence of neonatal sepsis was almost 50%, but our rates were higher than those found by Jaiswal *et al.* [3,5]. Although the rate of feed intolerance was 16.36% in our late preterms, we had only one case of frank NEC who finally succumbed. The low rate of NEC is probably due to exclusive use of mother's own milk or DHM from the milk bank. Other studies have reported rates of higher rates of feed intolerance and NEC [5].

The incidence of various other morbidities such as hypothermia, feeding difficulties, and birth asphyxia was comparable to other studies in literature [3-5]. We did not observe any late preterm developing intraventricular hemorrhage in our cohort. The other metabolic problems such as hypocalcemia and hypoglycemia constituted 10.9% and 2.7%, which was much lesser than that found by Leone *et al.* [9]. Overall, 79% of late preterms had at least one neonatal morbidity requiring medical interventions and NICU care which was slightly higher compared to other studies [3,10]. In the present study, 64 (58.1%) neonates required hospital stay for more than 7 days which was similar to the study done by Ezhilvannan *et al.* [4]. Only 3 neonates were readmitted after discharge in our study probably due to our strict policy to maintain a safe discharge of these late preterms. 5 infants died during the study period which accounts for a mortality rate of 4.5%, which is higher compared to other studies [3-5].

Although difficult to estimate from published studies, many reasons such as the increased rate of labor induction, increased cesarean delivery rate, and increased prevalence of maternal comorbidities that increase the likelihood of adverse pregnancy outcome could contribute to increase in late-preterm births. As the number of late-preterm infants has grown, so has the awareness of their unique set of problems. The late-preterm group has 2–3 fold increased rates for morbidities such as hypothermia, hypoglycemia, delayed lung fluid clearance and RD, poor feeding, jaundice, infection, and readmission after the initial hospital discharge [2].

More importantly, there may be lasting effects with neurodevelopmental delays extending into early school age. As a significant proportion of brain growth occurs during the last 6 weeks of gestation, late-preterm infants are vulnerable to neuronal injury and disruption of normal development [11]. The main limitation of our study was the small sample size, and second, it highlights only the short-term neonatal morbidities. Therefore, further studies are required to know the impact of these morbidities on the long-term neurodevelopmental outcomes.

## CONCLUSION

The present study showed that late-preterm infants had considerably high rate of medical complications, including need for respiratory support and prolonged hospital stay. Understanding clinical profile of late-preterm infants will help newborn care providers to anticipate and manage potential morbidities during the birth hospitalization and emphasize the importance of regular follow-up.

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