

Burden of late-preterm infant at a tertiary care neonatal intensive care unit - A prospective observational study

Saikiran Deshabhotla¹, Aafaque Hussain², Baswaraj Tandur³

From ¹Consultant Neonatologist, ²Senior Resident, ³Head, Department of Paediatrics, Princess Durru Shehvar Children's Hospital, Hyderabad, Telangana, India

Correspondence to: Dr. Saikiran Deshabhotla, Department of Paediatrics, Princess Durru Shehvar Children's Hospital, Purani Haveli, Hyderabad – 500 002, Telangana, India. E-mail: drsai17@gmail.com

Received – 04 March 2018

Initial Review – 31 March 2018

Accepted – 30 June 2018

ABSTRACT

Background: Infants born at 34⁰⁷ through 36⁶⁷ weeks' gestation are called as "late-preterm" infants. Even though physically resembling infants born at term gestation (37⁰⁷–41⁶⁷ weeks) they are developmentally immature and are at higher risk of morbidity and mortality. **Objective:** The objective of the study was to study the etiology and burden of late-preterm infant (34⁰⁷–36⁶⁷ weeks) birth. **Material and Methods:** This prospective observational study was conducted over 11 months in a tertiary care Level III neonatal intensive care unit in an urban city of India to elucidate the burden and etiology of late-preterm infant birth. **Results:** In our study, 17.5% (160, n=916) of total admissions were late-preterm infants. The most common underlying cause of late-preterm infant birth in this cohort was a previous lower segment caesarian section (LSCS) 27.5% (44, n=160) and pregnancy-induced hypertension 25% (40, n=160) followed by preterm labor 15.6% (25, n=160). Median gestation was 35 weeks with IQR (34–36 weeks). The median birth weight was 2100 grams with IQR (1900–2400 g). **Conclusion:** Late-preterm infants account for a significant proportion of preterm births and major burden on the neonatal intensive care workload. The most common reason of late-preterm births was an elective LSCS, done due to an earlier LSCS delivery.

Key words: India, Late-preterm infants, Morbidities, Outcome

Infants born at 34⁰⁷ through 36⁶⁷ weeks' gestation are called as "late-preterm" infants [1]. It is now well established that due to their physiological and metabolic immaturity, late-preterm infants are at higher risk of developing medical complications during the birth hospitalization [2–8]. In addition, late-preterm infants have higher rates of hospital readmission during the neonatal period than do term infants [9]. As the late-preterm subgroup accounts for nearly 10% of all births, even a modest increase in any morbidity will have a huge impact on the overall health-care resources [2]. In India, very little data are available till now on mortality, morbidity, and burden of late-preterm infants.

Worldwide the reason for the increase in late-preterm births during the past decade is not well understood.[10,11] One hypothesis is that it may be attributable to increased use of reproductive technologies and resulting increase in multifetal pregnancies [12]. Another hypothesis is that advances in obstetric practice have led to an increase in surveillance and medical interventions during pregnancy [13,14]. Rates of labor induction and cesarean delivery have also increased during the past decade. Furthermore, there is an increase in the incidence of late-preterm births secondary to increase in the provider initiated preterm birth at 34⁰⁷–36⁶⁷ weeks gestation carried out in the absence of a strong medical indication [15]. Unintended preterm birth also can occur

with the elective delivery of a baby thought to be term due to errors in gestational age (GA) assessment [16].

It is important to understand why these infants are being born early as well as the unique problems that this growing population of infants may experience. A clearer understanding of the underlying risk factors, associated etiologies and their relative effects on delivery at 34⁰⁷ through 36⁶⁷ weeks' gestation on the mother and fetus is needed to develop interventions to prevent unnecessary late-preterm births and to improve the management of infants who are born late preterm [14,15].

MATERIALS AND METHODS

This prospective observational study was conducted over a duration of 11 months from August 1, 2014 to June 30, 2015. All late-preterm infants (34⁰⁷–36⁶⁷ weeks of gestation) admitted to the tertiary care Level III neonatal intensive care unit (NICU) during the study period. All late-preterm infants with congenital abnormalities and chromosomal syndromes and late-preterm infants admitted after 7 days of life or those who were readmitted were excluded. The Institutional Ethics Committee approval was obtained. The primary objective was to elucidate burden and etiology of late-preterm infant birth among infants admitted to NICU.

Sample Size

From earlier studies, it was found that 70% of late-preterm infants had any morbidity requiring admission to NICU [17]. We calculated a sample size of 164 infants with the power of 80% ($\beta=0.20$) and Type I error of 5% ($\alpha=0.05$). The sample size was determined using formula $\{n=Z^2pq/d^2\}$ where $Z=1.96$, $p=70$ (morbidity in late-preterm), $q=30$, $d=7$ so after calculation $n=164$.

All live inborn and outborn (delivered in other hospital and infant admitted in our NICU) late-preterm infants (34^{0/7}–36^{6/7} weeks) admitted to the NICU were enrolled for the study after obtaining parent's consent. GA was determined by best obstetric estimate and new modified Ballard's score. When there was discrepancy of 2 or more weeks, then new Ballard's score was taken as criteria for GA over other methods. Antenatal and postnatal data were recorded in a predetermined study pro forma.

Antenatal steroid coverage includes mothers who received antenatal steroids in 1 week before delivery. This definition was adapted to document steroid usage in late-preterm births. Clinical conditions were predefined as per unit protocol, and same was recorded in case form. At the end of the hospitalization cost of hospital care was obtained and recorded in pro forma. However, cost of medicines and laboratory tests were excluded.

Statistical methods: The data collected were analyzed statistically using Microsoft Excel and SPSS 20. Baseline variable data were compared using student t-test for continuous and nonparametric as appropriate. Chi-square test used to analyze categorical data.

RESULTS

During the study period of 11 months, late-preterm infants accounted for 17.5% ($n=916$) of all admissions. Of 160 late-preterm infants recruited 79 ($n=160$, 49.3%) were inborn. On comparison of baseline variables, median maternal age was 25 years with IQR (21–28 years). There were 51 primi (31.8%) mothers and 10 set of twins which constituted 12.5% of all admissions, but there were no triplets. Complete antenatal steroids (2 doses) were given in 66 (41.2%) mothers, single dose in 9 (5.6%) mothers, and 85 (53.2%) mothers did not receive antenatal steroid.

A total of 143 (89.3%) were delivered by lower segment cesarean section (LSCS) while 17 (10.7%) by vaginal delivery. In 124 (77.5%) mothers, labor was absent while 25 (15.62%) mothers had preterm labor and in 11 (6.88%) mothers, labor was induced. The most common indication of delivery leading to late-preterm birth was previous LSCS 44 (27.50%) and pregnancy-induced hypertension (PIH) (40, 25%) followed by preterm labor 25 (15.62%) as shown in Table 1.

In this cohort of late-preterm infant, the median gestation was 35 weeks with IQR (34 to 36 weeks). The median birth weight was 2100 grams (IQR - 1900–2400 g). A total of 120 (75%) babies were appropriate for age, 26 (16.25%) were small for GA, and 14 (8.75%) were large for date. There were 96 (60%) male and 64 (40%) females and the median age at admission was

at 1 h (IQR - 0–2 h). A total of 71 (44.37%) infants were born from 34^{0/7} to 34^{6/7} weeks, 10 (6.25%) in 35^{0/7} to –35^{6/7} weeks, and 79 (49.38%) in 36^{0/7} to –36^{6/7} weeks gestation. Reasons for NICU admission were transient tachypnea of the newborn (TTNB) (71, 44.39%) followed by congenital pneumonia (33, 20.62%), probable sepsis (13, 8.12%), and respiratory distress syndrome (RDS) (10, 6.25%) as shown in Table 2.

A total of 120 (75%) babies had respiratory morbidities; of which, 71 (59.16%) had TTNB, 33 (27.5%) had congenital pneumonia followed by RDS in 10 (8.34%), persistent pulmonary hypertension in 4 (3.34%), and meconium aspiration syndrome in 2 (1.3%) babies. A total of 131 (81.9%) infants were discharged to home while 25 (15.6%) left against medical advice (LAMA) and 4 (2.5%) died in NICU during the study period. The median

Table 1: Indications of late-preterm birth

Indication of delivery	n=160 (%)
Previous LSCS (scar tenderness)	44 (27.50)
PIH	40 (25.00)
Preterm labor	25 (15.62)
GDM	11 (6.88)
PROM	11 (6.88)
Induction	11 (6.88)
Twins	10 (6.25)
APH	04 (2.50)
Fetal distress	02 (1.25)
MSL	01 (0.62)
Transverse lie	01 (0.62)

LSCS: Lower segment cesarean section, PIH: Pregnancy-induced hypertension, GDM: Gestational diabetes, PROM: Premature rupture of membrane, APH: Antepartum haemorrhage, MSL: Meconium stained liquor

Table 2: Reasons for NICU admission

Reasons for admission	n=160 (%)
TTNB	71 (44.39)
Congenital pneumonia	33 (20.62)
Probable sepsis	13 (8.13)
RDS	10 (6.25)
NNJ	6 (3.75)
PPHN	4 (2.50)
IDM	4 (2.50)
Hypoglycemia	3 (1.88)
Low birth weight care (<1800g)	3 (1.88)
MAS	2 (1.25)
Perinatal depression	2 (1.25)
Polycythemia	2 (01.25)
Twins	2 (1.25)
Seizures	2 (1.25)
Meconium ileus	1 (0.62)
CHD	1 (0.62)
Cardiomyopathy	1 (0.62)

TTNB: Transient tachypnea of the newborn, RDS: Respiratory distress syndrome, NNJ: Neonatal jaundice, PPHN: Persistent pulmonary hypertension, IDM: Infant of diabetic mother, MAS: Meconium aspiration syndrome, CHD: Congenital heart disease

duration of NICU stay was 3.5 days (IQR - 2–5 days). A total of 128 (80%) babies required some form of respiratory support. Oxygen was used most commonly in 63 (49.21%) infants while 39 (30.46%) required bubble CPAP and 14 (10.95%) required mechanical ventilation. The median duration on CPAP was 24 h (IQR - 24–48 h), and for mechanical ventilation, it was 48 h (IQR - 21–72 h). In this study, 5 (50%) babies required surfactant administration.

Blood cultures were sent in 104 (65%) infants of which 94 cultures were sterile, and 10 had blood culture growth. A total of 109 (68.12%) infants had been treated with antibiotics. The median antibiotic treatment duration was 5 days (IQR - 3–5 days). Around 151 (94.3%) infants required intravenous fluid and median time to reach full feeds was of 3 days (IQR - 2–4 days). There was a significant discrepancy in the assessment of GA by the antenatal and postnatal method. It was found that the median GA by antenatal (dates) was 36 weeks (IQR - 35–36 weeks) versus postnatal GA assessment by Ballard's method [26] 35 weeks (IQR - 34–36 weeks) with $p < 0.05$.

DISCUSSION

In this observational study, late-preterm infants accounted for 17.5% of total NICU admissions, and nearly half of late-preterm infants admitted were outborn. The most common reasons for late-preterm births were previous LSCS (scar tenderness) in 27.5%, followed by PIH and preterm labor. This is in accordance with an earlier retrospective study, where LSCS rates among late-preterm deliveries were reported as high as 70–80% [25]. In earlier studies on late-preterm infant births done in India, it was found that the major indications for late-preterm births were preterm labor, preterm premature rupture of membrane, and PIH [17–20]. None of the earlier studies documented previous LSCS as a major indication of preterm birth. This difference in our results as compared to other studies could be explained on the basis of the difference in the nature of late-preterm infants admission to NICU, as our NICU had both inborn and outborn infants which reflect the common scenario in our country while earlier studies were done in centers dealing with inborn infants. Thus, a significant proportion of late-preterm birth and hence, morbidities can be prevented by restricting primary LSCS and enhancing practice of vaginal birth after cesarean section [18].

In our study, 41.2% of mothers received the complete course of antenatal steroids while 5.6% received only a single dose. This number is surprisingly low considering the anticipated benefits and recommendation of antenatal steroid use being till 34 weeks of gestation. In an earlier study, it was found that 14% mothers received incomplete course and 28% received the full course [17]. It was found that there was a significant discrepancy in antenatal and postnatal GA estimation in late-preterm infant births ($p < 0.05$). This error can also contribute to decision-making in delivery by obstetricians; thus, better and accurate methods of GA assessment are required.

In this study, an overall 75% of late-preterm infants had respiratory morbidities. Other studies found neonatal jaundice

requiring phototherapy as the most common morbidity followed by respiratory morbidity and hypoglycemia in late-preterm infants [21,22]. Nearly 80% of late-preterm infants required some form of respiratory support. Higher requirement of respiratory support in our study can be explained by the fact of being a tertiary center for outborn, only critically sick late-preterm infants were referred often without proper neonatal transport facility, and also there is a high incidence of respiratory morbidity in late-preterm infants. During the study period after suspecting sepsis, blood culture was sent in 65% infants of which only 9.6% had positive blood culture growth. The median antibiotic treatment duration was 5 days. In an earlier study, 32% of late-preterm infants were evaluated for sepsis and received empirical antibiotics while the incidence of blood culture-proven neonatal sepsis was 9.6% [17]. Thus, late-preterm infants with their associated morbidities form a significant indication for empirical use of antibiotics which, in turn, will increase antibiotics misuse and hence resistance.

In this study, 81.9% of infants were discharged, 15.6% LAMA due to financial constraints and 2.5% died in NICU. Similar results were found in earlier studies with nearly 98% discharge and 2% mortality [22,23]. High LAMA rates could be because of the predominant poor socioeconomic status of parents in this cohort. The median duration of NICU stay in our study was 3.5 days (IQR - 2–5 days). Another previous study found hospital stay < 3 days in 10.4%, 4–7 days in 25%, 7–14 days in 45.8%, and > 14 days in 18.8% of the late-preterm infants [22].

Against the backdrop of average per capita health spending per annum of Rs. 7000/- (\$109) and total health-care spending of 5% of country's gross domestic product [24], late-preterm infant care is a significant economic burden both on individual and society. Till date major segment of neonatal health care is provided by private and semi-private institutions thus cost of late-preterm infants care will be ever increasing. In the current scenario, a major cause of neonatal mortality rate is preterm births accounting for 27% of total neonatal deaths; however, very little data are available in India about late-preterm births [20]. Current efforts to reduce neonatal mortality to single digit value will be effective only if both preterm and late-preterm births can be prevented and also sufficient beds and infrastructure are made available for late-preterm infants.

This study is an initiative toward highlighting the need to analyze factors responsible for late-preterm births and to introduce necessary interventions to reduce late-preterm infants birth such as by educating health personnel and general public on hazards of LSCS. Furthermore, there is an urgent need for uniform evidence-based guidelines on the use of antenatal steroids in late-preterm infant's births. However, a study being conducted in a tertiary care unit with nearly equal inborn and outborn admissions, these results might be applicable to centers with similar profile. Only short-term outcomes were studied, but there is a need to document long-term neurodevelopmental and cognitive outcome in this cohort.

CONCLUSIONS

Late-preterm infants account for a significant proportion of preterm births and major burden on the neonatal intensive care

workload. The most common reason for late-preterm birth was previous LSCS in mother. While respiratory morbidities were most frequently observed in late-preterm infants immediately at birth, significant proportion of late-preterm infants is unnecessarily exposed to antibiotics.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Deshabhotla S, Hussain A, Tandur B. Burden of late-preterm infant at a tertiary care neonatal intensive care unit - A prospective observational study. *Indian J Child Health*. 2018; 5(6):441-444.