International Journal of Research in Medical Sciences
Alam MM et al. Int J Res Med Sci. 2023 May;11(5):1628-1633
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20231327

Original Research Article

Outcome of late preterm infants and the factors associated with neonatal intensive care admission

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Received: 25 February 2023
Accepted: 31 March 2023

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ABSTRACT

Background: Infants born between 34 0/7 and 36 6/7 weeks of gestation are referred to as late-preterm infants (LPI). The study's objective was to examine the prevalence and course of LPI at our institution.
Methods: This single-center prospective observational study was conducted at the level 3 NICU from June 2018 to June 2019 and included LPIs born in the hospital. Both the prevalence of LPI and the reasons for premature births were evaluated. Infants were observed until discharge for complications and outcomes (mortality and NICU admission). The risk factors associated with NICU admission were analyzed using multivariate logistic regression analysis.
Results: LPI constitutes 2.94% of all live births and 40.45% of total preterm births. Pre-eclampsia (15.1%) and premature membrane rupture (9.4%) were the two main causes of preterm birth, while the majority of mothers (37.7%) experienced spontaneous labor. A total of 55 (51.9%) babies developed complications, with respiratory distress (33.9%) being the most common. Three infants died, and 65 infants needed admission to the NICU. NICU hospitalization was independently associated with the existence of maternal risk factors, gestational age of 35 weeks, the requirement for resuscitation, and children whose weight was out of proportion to their gestational age.
Conclusions: LPIs account for a large proportion of premature babies, are prone to complications, and have a high mortality and morbidity rate.

Keywords: Complications, Late preterm infant, Mortality, NICU

INTRODUCTION

Preterm birth, defined as the delivery of an infant prior to 37 completed weeks of gestation, is one of the leading causes of neonatal mortality.[1] About 15 million premature babies are born every year.[2] Premature births have recently increased, owing primarily to an increase in the number of late preterm births. The term "late preterm infants" (LPI) was coined by the National Institute of Child Health and Human Development to define infants born between 34 0/7 weeks and 36 6/7 weeks gestational age, replacing the previous terminology of "near term" in 2007.[3] LPI are a distinct group of premature neonates who are frequently overlooked due to their close proximity to term maturity and good weight, despite the fact that their needs are similar to those of other preterm rather than term infants.

The preterm birth rate has increased by 30% between 1981 and 2003 in the United States, mostly due to the LPI, which has increased to 7.28%, whereas early preterm births remained unchanged.[4] Though there is vast data available on preterm births from all countries, data on late preterm births is scarce, particularly in developing countries. According to the few studies that have been conducted in India, the prevalence of LPI ranged between 9 and 11.6% of all births.[5,6] To address this gap in knowledge, we undertook the study with the aim of

studying the prevalence and outcome of LPI in our center. Risk factors associated with NICU admission in these children were also studied.

METHODS

This single-centre prospective observational study, approved by the institutional ethical committee and review board, was conducted at the level 3 NICU of a tertiary care hospital in India from June 2018 to June 2019. The study included LPI born during the study period after obtaining informed consent from the parents. Babies who were referred from other hospitals were not included. The minimum sample size required was calculated as 94, based on the NICU admission rate for LPI of 37% with a 95% confidence interval and a margin of error of 10%.[7] Gestational age (GA) was assessed using the New Ballard score and further classified as large for gestational age (LGA), appropriate for gestational age (AGA), and small for gestational age (SGA) based on standard intrauterine growth charts. The maternal and perinatal histories were meticulously documented. Babies were closely monitored for any complications until they were discharged. Screening ultrasound of the skull for intraventricular hemorrhage (IVH) and echocardiography to rule out structural heart disease were done based on the decision of the treating consultant.

The primary outcome indicator used in the study was NICU admission. Uncomplicated infants kept in the NICU for observation for less than 8 hours were not considered NICU admissions. Statistical analysis was done using SPSS 24.0 software. The standard deviation and median with range were used to describe continuous data, while frequencies were used to describe categorical data. Early complications in the babies' stays were expressed as a percentage. The mortality rate was also computed. The babies were divided into two groups for further analysis: those who needed NICU admission and those who did not. To determine significant factors responsible for NICU admission, a univariate analysis was performed using the chi-square test, Fisher's exact test, or Mann-Whitney U test, as applicable. A p value of 0.05 or less was considered significant. Determinants found to be significant in univariate analysis were analyzed using multivariate logistic regression to establish the association.

RESULTS

The total number of live births during the study period was 3610. Among them, 3315 (91.83%) were term, 262 (7.26%) were preterm, and 33 (0.91%) were post-term infants. The number of LPIs born during the study period was 106 (2.94% of total babies born and 40.45% of total preterm births). The mean age of the mothers in the study group was 27.0±3.2 years, with the majority being primigravida (n-44; 41.5%). The majority (40; 37.7%) of the mothers did not have any identified cause for preterm delivery and went into spontaneous labour. Among the commonest identified causes were pre-eclampsia (16; 15.1%) and premature rupture of the membrane (PROM) (10; 9.4%). The maternal risk factor for preterm deliveries is shown in table 1. The majority of the babies were born through vaginal delivery (55; 51.9%), whereas 51 (48.1%) required a lower section caesarean section (51; 48.1%). Ten (9.4%) babies required some form of resuscitation effort.

Table 1: Maternal risk factors leading to preterm birth in the current study.

Risk factors	N	%
Pre-eclampsia	16	15.1
Premature rupture of membrane	10	9.4
Polyhydramnios	8	7.5
Oligohydramnios	6	5.7
Cervical incompetence	5	4.7
Urinary tract infection	5	4.7
Gestational diabetes mellitus	4	3.8
Elderly primigravida	3	2.8
Severe anemia	3	2.8
Antepartum hemorhage	3	2.8
Twin pregnancy	2	1.8
Heart disease	1	0.9

Table 2: Complications observed among the late preterm babies in the study.

Complications	n	%
Transient tachypnea of newborn	20	18.9
Neonatal hyperbilirubinemia	14	13.2
Sepsis	8	7.5
Respiratory distress syndrome	7	6.6
Hypocalcemia	6	5.7
Feeding difficulty	6	5.7
Apnea of prematurity	4	3.8
Hypothermia	4	3.8
Hypoglycemia	4	3.8
Pneumonia	3	2.8
Meconium aspiration syndrome	2	1.9
Intraventricular haemorrhage	2	1.9

The study group included 56 (52.6%) males and 50 (47.2%) females, with a median weight of 2.52 kg (range 1.40–3.50 kg). Sixty-nine (65.1%) babies were of AGA age, whereas 29 (27.3%) were SGA, and 8 (7.5%) were LGA. During their hospital stay, 55 (51.9%) babies experienced complications. The most common complication observed in the study was respiratory distress, present in 36 (33.9%) patients, with the majority being transient tachypnea of the newborn (TTN) (20; 18.9%), followed by respiratory distress syndrome (RDS) (7; 6.6%), pneumonia (3; 2.8%), and meconium aspiration syndrome (MAS) (2; 1.8%). Three (2.8%) babies required mechanical ventilation support, whereas 18 (16.9%) required nasal CPAP support. Six (5.6%)

patients received surfactant therapy for RDS. The complications observed in the study are shown in Table 2.

Forty (37.7%) babies were started on direct breast feeding; 20 (18.9%) were on katori spoon/paladai feeding; 15 (14.2%) were on oro-gastric tube feeding and 31 (29.2%) required intravenous fluids immediately after birth. Sixty-five (61.3%) babies required NICU admission, with a median duration of NICU stay of 5 days (range 1-27 days). Eighty-nine (84.0%) babies were normally discharged within 7 days of birth. Fourteen (13.2%) required extended hospital stays (more than 10 days), and three (2.8%) died.

Table 3: Univariate analysis of risk factors associated with NICU admission among late preterm babies in the study.

Variables	NICU admission	No NICU admission	p value
Maternal age (mean±SD)	27.31±3.42	26.56±2.93	0.202
Gravida			
Primi	36 (56.3%)	28 (43.8%)	0.224
Multi	29 (69.0%)	13 (31.0%)	
Maternal risk factor			
Absent	14 (37.5%)	26 (62.5%)	0.001
Present	51 (75.8%)	15 (24.2%)	
Gestational age at delivery			
<35 weeks	15	9	0.013
≥35 weeks	28	54	
Mode of delivery			
Vaginal	26	29	0.002
LSCS	39	12	
Resuscitation efforts required			
Yes	9	1	0.044
No	56	40	
Baby sex			
Male	35 (62.5%)	21 (37.5%)	0.792
Female	30 (60%)	20 (40%)	
Birth weight			
<1.5 kg	20	5	0.028
≥1.5 kg	45	36	
Weight AGA			
Yes	34	35	0.003
No	31	6	

Table 4: Multivariate logistic regression analysis of risk factors for NICU admission among late preterm babies in the study.

Variable	P value	Odds ratio (95% CI)
Presence of maternal risk factor	0.001	5.91 (2.08-16.76)
LSCS delivery	0.061	2.62 (0.92-6.90)
Gestational age <35 weeks	0.038	3.49 (1.43-5.19)
Weight not AGA	0.004	5.94 (1.78-19.86)
Birth weight <1.5 kg	0.130	1.76 (0.73-5.19)
Resuscitation efforts required	0.037	6.72 (1.12-40.24)

On univariate analysis to determine the factors resulting in NICU admission, we found the presence of maternal risk factors (p-0.001), LSCS delivery (p-0.028), need of resuscitation measures (p-0.006), babies with gestation age <35 weeks (0.013), birth weight <1.5 kg (0.028) and weight not AGA (p-0.003) more likely to require NICU admission (Table 3). On multivariate binary logistic regression analysis, the presence of maternal risk factors (p-0.001; OR-5.91), gestational age <35 weeks (p-0.038, OR-3.49), need for resuscitation efforts (p-0.037; OR-6.72) and children whose weight was not AGA (p-0.004; OR-5.94) were significantly associated with NICU admission (Table 4).

DISCUSSION

In the current study, we studied the prevalence of LPI and its mortality and morbidity, especially the need for NICU stay. The current study found that 2.94% of all births were LPI, which is comparable to figures reported in some developed countries such as Canada (4.8%), Denmark (3.6%), Finland (3.3%), Norway (3.8%), and Sweden (3.6%).[8] In the current study, the most common risk factors for preterm labour were pre-eclampsia (15%) and PROM (9.4%), while 38% did not have any identified risk factors and went into spontaneous labour. Pregnancy-induced hypertension (24.7%) and PROM (14.6%) were shown to be the two main risk factors for preterm delivery, according to Giliyaru et al.[9]

The mortality rate among the LPI in the current study was 2.8%, which was higher than the term neonates (0.8%), which is consistent with earlier studies.[10,11] A large systematic review by Teune et al also concluded that LPIs were at high risk of death in the initial 28 days of life, with a relative risk of 5.9.[12] The most common complication in the study was respiratory distress, which was observed in 34% of the patients. The overall incidence of LPIs requiring NICU admission for respiratory issues requiring intervention has been reported to be between 9-28% in different studies.[7] TTN developed in 22.6% of the patients in the study, which is higher compared to other studies, which have reported the incidence in the range of 3.9-9.9%.[13] The incidence of RDS in the study was 6.6%, which was comparable to other studies that reported incidences of between 5.2-6.4%.[14] Six (5.6%) patients received surfactant therapy for RDS in the study. The need for surfactant therapy has been reported at 3.8% among LPI.[15]

In the current study, the incidence of hyperbilirubinemia requiring treatment was 13.2%, with no patients developing kernicterus. Several studies have found that LPI have a higher rate of hyperbilirubinemia, requiring phototherapy, than term infants.[16-20] In a retrospective study, Bhutani et al found that a significant number of LPI treated for hyperbilirubinemia in the same way as term infants developed kernicterus and had higher rates of sequelae.[21]

Feeding problems are also common in LPI and are a leading cause of hospitalisation as reported in a recent meta-analysis of 22 studies.[12] The current study reported feeding issues in 5.7% babies. In the current study, 3.8% of LPIs had symptomatic hypoglycemia that necessitated NICU admission. Wang et al. discovered hypoglycemia in 16% of LPI patients.[20] According to Kalyoncu et al, LPI were 11 times more likely than term neonates to experience hypoglycemia.[11] The overall incidence ranges from 8.7% to 50%.[17,18,21-23] Temperature instability is one of the causes of prolonged hospitalisation among LPI, with a reported incidence of 5-10%.[20,22,24] Reported incidence of hypothermia as a reason for NICU admission was 4% in the current study.

In the current study, 7.5% of the babies developed sepsis and 2.8% developed pneumonia. In the meta-analysis by Teune et al, LPI were reported to have a fivefold higher risk of culture-positive infections, compared with their term counterparts.[12] They also found 21 times higher odds of developing meningitis and 3.5 times higher odds of developing pneumonia than full-term infants.[12] In the current study, two babies (1.8%) experienced IVH (grade 1 and 2). McIntire et al found 0.5% of LPIs had grade 1 or 2 IVH at 34 weeks, 0.2% at 35 weeks, and 0.06% at 36 weeks. In LPIs, the rate of grade 3 or 4 IVH was extremely low (0.01%).[16]

The current study found that 61% of LPIs required NICU admission, which was higher than the 37% reported in developed countries.[7,25] The difference in population and the rate of perinatal complications could explain the high rate of admission. The presence of maternal risk factors, gestational age of 35 weeks, birth weight not AGA, and the need for resuscitation were all found to be significantly associated with prolonged NICU admission. Babies born via LSCS and those weighing less than 1.5 kg were also more likely to require prolonged NICU care, although a significant association could not be established. In a study by Carter et al, premature rupture of membranes was found to have a 9-fold increased risk for NICU admission. No other maternal risk factors were significant in their study.[26]

In the current study, maternal risk factors were positively associated with NICU admission, but we did not evaluate each maternal risk factor separately. In their study, Battarbee et al reported that lower gestational age and foetal growth restriction were the causes of prolonged NICU stay in late-preterm births, which was consistent with the current study.[27]

The major limitations of the study are that it was a single-center study and that it included only babies born in the hospital. The association of the individual maternal risk factors with NIUC admission was not studied. The study was unable to assess the effect of steroid therapy on the prevention of RDS. Long-term follow-up and morbidity were not studied as we followed the infants till NICU discharge only.

CONCLUSION

LPI constitutes a large number of preterm infant births, and they are at high risk of developing complications, with respiratory complications being the most common. The presence of maternal risk factors, such as a gestational age of 35 weeks, birth weight not AGA, and those who required resuscitation at birth, raises the likelihood of NICU admission.

Due to their high morbidity and mortality and similarity to preterm babies, they should be given additional care, and the pediatrician should not get carried away by the good size of these babies.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Alam MM, Alam S, Mazahir R. Outcome of late preterm infants and the factors associated with neonatal intensive care admission. Int J Res Med Sci 2023;11:1628-1633.