

“A Prospective Observational Study Assessing the Morbidity Outcomes of Late Preterm Neonates”

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Abstract

Background & Objectives: To study on early neonatal morbidities in late preterm neonates admitted to neonatal intensive care (NICU).

Methods: All late preterm babies (34 0/7weeks-36 6/7 weeks) admitted to neonates who meet the inclusion criteria were studied for a period of 1st October 2019 to 31st March 2021. The infants in the sample were followed throughout their stay in the neonatal intensive care unit (NICU), up until hospital discharge. All the data was collected from infants' and mothers' medical records and at the time of the discharge. Short-term outcomes such as neonatal morbidities, mortality, hospitalization and also maternity risk factors were assessed. **Result:** A total of 103 late preterm and term neonates were included in the study. Male preponderance was noticed with a ratio of 1.2:1. Majority of the neonates were born with birth weight of more than 2 kg. PROM and previous history of LSCS forms the major maternal risk factor for preterm. This study confirmed that late-preterm infants are a population at risk of increased neonatal morbidity. Neonatal Hyperbilirubinemia requiring phototherapy forms the major one followed by respiratory distress, sepsis and feed Intolerance. Duration of hospital stay also prolonged in late preterm. Majority of late preterm neonates required more than 7 days of hospital duration. Mortality rate and the rate of rehospitalization were also high. **Conclusion:** Late-preterm infants are therefore a high-risk group of children and need special attention. Immaturity is the major factor contributing to adverse morbidities. Further research is required to develop specific guidelines and protocols to reduce neonatal late preterm mortalities and morbidities.

Keywords: India, Late preterm infants, Neonatal morbidity, Outcomes.

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Introduction

Late preterm infants are those delivered between 34 (34^{0/7}) and 37 (36^{6/7}) weeks of gestation period i.e., between 239 to 259 days after the first day of the last menstrual period (1)(2). Globally incidence of late preterm births (LPB) accounts for 75% of preterm births and 9.1% of total births (3). In India, the incidence of LPB was 116 per 1000 live births (11.6%) (2). Neonatal intensive care of LPB is costly, with costs estimated to be 2568 Canadian dollars for the first two years of birth (4) and 1058 USD for late preterm births in India (5). Late preterm births can be due to spontaneous delivery or induced due to maternal and fetus risk factors rendering fetus survival unsafe in the mother's womb (6)(7). Infants born late preterm have a higher chance of being admitted to the neonatal intensive care unit (NICU), being readmitted to the hospital, and having a more extended hospital stay than term infants. They are also more likely to experience neurological morbidities, neonatal and infant mortality, temperature instability, hypoglycemia, sepsis, hyperbilirubinemia, necrotizing enterocolitis, and respiratory morbidities. Late preterm infants are physiologically less developed than term infants and have less compensatory reactions to the extra-uterine environment (8)(9)(10). Despite being the largest category of preterm newborns, late preterm infants have received little attention as they are classified as "near-term," making them appear "nearly mature," with no cause for concern. Given that the late preterm subgroup comprises almost 10% of all births, even a slight rise in morbidity will significantly influence

the availability of comprehensive healthcare resources (11). So, it is not surprising that there has been an increase in the total number of late-preterm infants admitted to NICUs worldwide (12). Only a few retrospective studies were conducted in developed countries to assess the outcomes of NPB (13)(14). Understanding the risk of morbidity in late preterm infants is crucial for newborn care providers to manage potential morbidity during the hospitalization for childbirth and earlier follow-up after hospital discharge. It may also help in deciding whether to perform non-emergency obstetric interventions. The current study aims to examine neonatal morbidities in late-preterm neonates admitted to a tertiary care hospital's neonatal critical care unit.

Materials and Methods

Study location

All late preterm babies (34 0/7weeks - 36 6/7 weeks) admitted to neonates admitted in Basaveshwar Teaching and General Hospital (BTGH) and Sangameshwar Teaching and General Hospital (STGH) attached to MahadevappaRampure Medical College, Kalaburagi who met the inclusion criteria were included in the study for a period of 1st October 2019 to 31st March 2021(18months)

Inclusion criteria

All late preterm babies (340/7 weeks to 366/7 weeks) admitted to NICU between 1st October 2019 to 31st March 2021(18months).

Exclusion criteria

1. Late preterm babies of parents who have not given consent.
2. Late preterm babies who had lethal malformation, chromosomal anomalies.

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Data collection

Data were collected from infants’ and mothers’ medical records and supplemented with additional information collected at discharge using a structured form covering the variables of interest. Variables relating to the mothers and their infants were analysed.

Maternal variables

The maternal studied were: age (years), number of pregnancies, prior history of miscarriages, still births and premature deliveries; type of delivery (normal or caesarean); Previous caesarean section, intercurrent clinical conditions observed during gestation – diabetic, hypertension, Anemia, urinary infections at any point during pregnancy, syphilis, human immunodeficiency virus (HIV), toxoplasmosis, heart disease, hepatitis B; premature rupture of membranes (PROM) for longer than 18 hours; placental abruption.

Neonatal variables

The neonatal variables studied were: age at admission, days in hospital, sex, birthweight, gestation age (calculated from modified

Ballard’s scoring), hypoglycemia (glucose below 40 mg/dL), hyperbilirubinemia requiring phototherapy/exchange transfusion, Feed intolerance, respiratory pathologies – transient tachypnea of the newborn (TTN), hyaline membrane disease (HMD), pneumonia, apnea of prematurity, sepsis, intervention done, deaths andrehospitalization.

Results

Study characteristics

103 neonates who met all the inclusion criteria were included in the study. Mean age of neonates was 2.49± 2.23 with age ranging from 1 day to 10 days. 73.8% neonates were in the age group 1-3 years, 20.4% in the age group 4-6 years and 5.8% neonates in the age group 7-10 years. 64 (62.1%) were males and 39 (37.9%) were females. 62 (60.2%) were late preterm babies born at 34 to 35 gestation weeks and 41 (39.8%) were born at 36 to 37 gestation weeks(**Figure 1**). Birth weight of neonates varied. 4.9% had a birth weight > 1.5 kgs, 26.2% had 1.5 to 2.0 kgs, 28.2% had 2.0 to 2.5 kgs and 40.8% had > 2.5 kgs. Baseline study characteristics were given in **Table 1**.

Table 1: Baseline characteristics of the late preterm and term neonates

Variables	Sub Category	Number of Subjects (%)
Age (days)	1-3	76 (73.8%)
	4-6	21 (20.4%)
	7-10	6 (5.8%)
	Mean ± SD	2.49 ± 2.23
	Median (Min, Max)	1 (1, 10)
Gender	Female	39 (37.9%)
	Male	64 (62.1%)
Gestational age (weeks)	34-35	62 (60.2%)
	36-37	41 (39.8%)
Birth weight (kgs)	<1.5	5 (4.9%)
	1.5 - 2	27 (26.2%)
	2 - 2.5	29 (28.2%)
	>2.5	42 (40.8%)
Duration Of Hospital Stay (days)	<3 days	14 (13.6%)
	4 - 7	22 (21.4%)
	8 - 14	49 (47.6%)
	>14	18 (17.5%)



Figure 1: A 2 days old neonate born at 34 weeks gestation age

Neonates maternal risks

Among the 103 included neonates in the study, 3 (2.9%) were born in maternal younger age > 20 years, 3 (2.9%) were born due to maternal anemia, 1 (1%) neonatal maternal had a prior history of premature delivery and 5 neonates maternal had bad obstetric history (BOH).

10 (9.7%) neonates were born due to premature rupture of membranes (PROM), 3 (2.9%) were born due to antepartum hemorrhage (APH) and 3 (2.9%) neonates maternal were diabetic. 59 (57.3%) were born due maternal vaginal delivery and 44 (42.7%) were born via LSCS(**Table 2**).

Table 2: Cohort neonatal maternal risks associated with the selected group

Variables	Sub Category	Number of Subjects (%)
Maternal risk	Younger age	3 (2.9%)
	Anemia	3 (2.9%)
	PIH	8 (7.8%)
	Previous history	1 (1%)
	APH	3 (2.9%)
	Diabetes	3 (2.9%)
	PROM	10 (9.7%)
	BOH	5 (4.9%)
	Elderly Primi	1 (1%)
	Multiple Pregnancy	4 (3.9%)
	No risk factor	62 (60.2%)
Mode of delivery	Vaginal	59 (57.3%)
	LSCS	44 (42.7%)

Interventions given to neonates

Mainly external oxygen was given to the neonates. 14 (13.6%) neonates received only oxygen supply, 12 (11.7%) received oxygen + phototherapy, 5 (4.9%) intervened with Oxygen + Phototherapy +

Ionotropes + Ventilation and 4 (3.9%) received Oxygen, Ionotropes, Ventilation. The details of the interventions given was graphically presented in **Figure 2**.

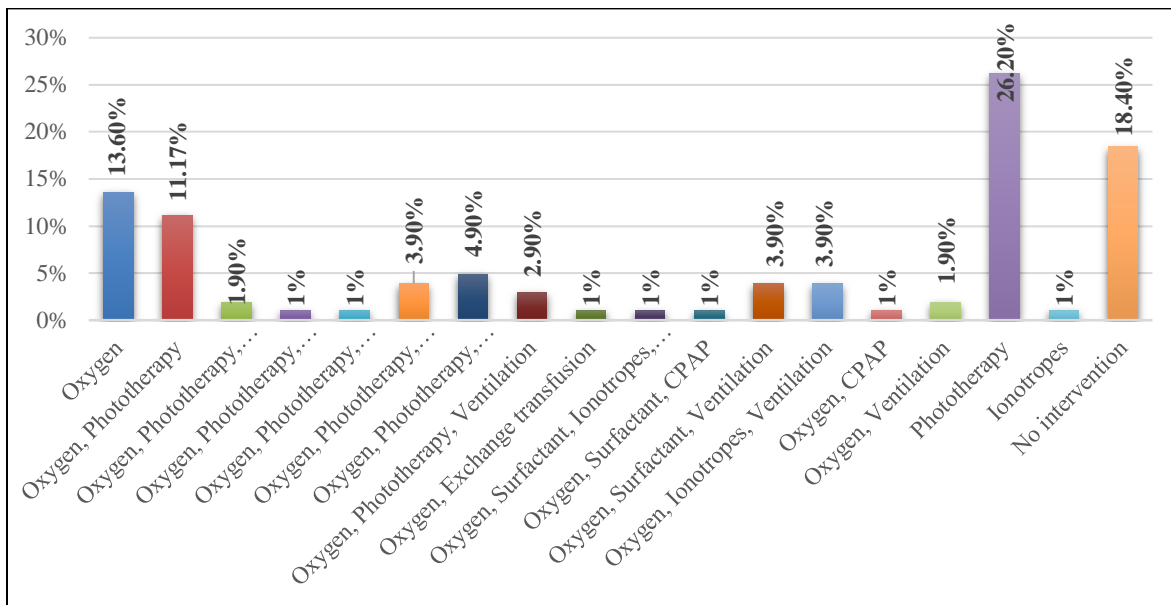


Figure 2: Summary of the interventions done on the selected neonates in the present study

Neonatal outcomes of preterm and term neonates

Based on gestation age 62 neonates were late preterm babies, out of them 59 were discharge and 3 neonates attained mortality. 41 neonates born between 36 to 37 weeks gestation age were categorised as term babies, out of them 40 were discharged and 1 attained mortality. In late preterm babies 17 (68%) were detected with hypothermia, 10 (76.9%) had hypoglycemia (> 40 mg/mL), 35 (61.4%) had hyperbilirubinemia, 16 (55.2%) had feed intolerance, 16 (88.9%) had respiratory disorder syndrome (RDS), 13 (56.5%) had

pneumonia, 7 had birth asphyxia and 3 had intraventricularhemorrhage. Comparatively, term babies had lesser number of complications were observed- hypothermia 8 (32%), hypoglycemia 3 (23.1%), hyperbilirubinemia 22 (38.6%), feed intolerance 13 (44.8%), RDS 2 (11.1%), pneumonia 10 (43.55%) and probable sepsis 7 (63.6%) (**Table 3**). From Chi square test it can be observed that, there is significant association between preterm, term and respiratory system and sepsis. However no significance can be found between preterm, term and any other variables.

Table 3: Neonatal outcomes of late preterm and term neonates

Variable	Subcategory	Late preterm	Term	p-value
		Number of subjects		
Outcome	Discharged	59 (59.6%)	40 (40.4%)	0.537 ^c
	Death	3 (75%)	1 (25%)	
Hypothermia	Absent	45 (57.7%)	33 (42.3%)	0.360 ^c
	Present	17 (68%)	8 (32%)	
Hypoglycemia	Absent	52 (57.8%)	38 (42.2%)	0.187 ^c
	Present	10 (76.9%)	3 (23.1%)	

Hyperbilirubinemia	Absent	27 (58.7%)	19 (41.3%)	0.780 ^c
	Present	35 (61.4%)	22 (38.6%)	
Feed Intolerance	Absent	46 (62.2%)	28 (37.8%)	0.515 ^c
	Present	16 (55.2%)	13 (44.8%)	
Respiratory System	Normal	33 (55%)	27 (45%)	0.018 ^{c*}
	RDS	16 (88.9%)	2 (11.1%)	
	Pneumonia	13 (56.5%)	10 (43.55%)	
	TTN	0	2 (100%)	
Birth Asphyxia	Absent	55 (61.8%)	34 (38.2%)	0.402 ^c
	Present	7 (50%)	7 (50%)	
Intraventricular Hemorrhage	Absent	59 (59%)	41 (41%)	0.153 ^c
	Present	3 (100%)	0	
Apnea Of Prematurity	Absent	59 (59%)	41 (41%)	0.153 ^c
	Present	3 (100%)	0	
Sepsis	Culture proven	7 (100%)	0	0.027 ^{c*}
	Probable sepsis	4 (36.4%)	7 (63.6%)	
	Absent	51 (60%)	34 (40%)	
	Present	0	0	

Discussion

The frequency of preterm births is increasing in many countries and this increase is mainly due to rise in LPB. Many reasons were proposed to explain this increasing trend including increase surveillance of the mother and fetus, increasing maternal age and reproductive technologies which is associated with multiple pregnancies(18). This study demonstrates the importance and magnitude of the risks of intercurrent conditions to infants born at 34^{1/7} to 36^{6/7} weeks gestation are subjected .

In the present study, 103 neonates were selected based on inclusion criteria. Male predominance was observed in this study with 62.1% comprising male child and female child constitute about 37.9% which is comparable with the study conducted by smyrni et al., 2021 (14). Majority of the neonates 76 (73.8%) in the present study were admitted within 3 days of birth which is comparable with the study conducted by Jaiswal et al., 2011 (15). In their study neonates less than 3 days constitute about 65.5%. Birth weight of more than 2.5 kg was found in 40.8% neonates. Birth weight was found to be appropriate according to their gestational age in 51 neonates which constitute about 69%. But in few infants birth weight was less than 1.5 kg which is comparatively less than their gestation age. 3 of the lower weight late preterm neonates attained mortality and other neonates developed morbidities and had longer stay at hospital. Literature reports show low weight infants > 2 kgs have higher risk and incidence of mortality and morbidity. Currently antenatal steroids were given to reduce the mortality and morbidity risks in late preterm infants (19)(20).

Maternal risk for late preterm was elicited in 80 cases which accounts for about 76.5%. There were no recorded indication in 33 of the mother which constitute about 24.3%. Among risk factors studied

PROM and previous LSCS constitute the major one of 25.29% followed by Anaemia and PIH respectively. A prospective research was conducted by Dimitriou et al., 2010 (21) to assess the impact of maternal circumstances on morbidities. The findings were consistent with those of our study that showed that as gestational week increases, the risk of neonatal morbidity reduces, suggesting the fetus's maturation (8). Several other literature studies show association of maternal morbidities such as diabetics and hypertension with premature delivery(22)(23). Another major cause for premature delivery is PROM. In correlation with our study, similar findings 39% PROM births were reported by Lorenzo et al., 2021 (24).

In the present study, hyperbilirubinemia constitute the major group with 57 (55.3%) neonates. All of them required phototherapy and one neonate required exchange transfusion to reduce hyperbilirubinemia along with phototherapy. Respiratory distress constitutes the second most morbidity with 18 (17.5%) neonates affected followed by pneumonia, which highlights the immaturity of the late preterm born respiratory systems. Surfactant was given to all RDS neonates and required mechanical Ventilation during the hospital stay. Leone et al., 2012 conducted a multi-centre retrospective study and compared morbidity outcome of late preterm infants with full-term infants. The study showed late preterm infants had a significant higher morbidity: respiratory distress (34.7% versus 4.6%), hyperbilirubinaemia (47.7% versus 3.4%), hypoglycemia (14.3% versus 0.6%), hypothermia (2.5% versus 0.6%), duration of hospitalization (mean 9.9 days versus 5.2 days). The Study concluded late preterm infants show considerably higher rate of medical complications and prolonged hospital stay compared with matched full-term infants and therefore need more Medical and financial resources(16). A comparison of the present study with the other reported studies is given in **Table 4**.

Table 4: Comparison study of the neonatal short-term morbidity outcomes

Morbidities	Jaiswal et al., 2011 (15)	Leone et al., 2012 (16)	Tuene et al., (17)	Present study
Overall morbidities	70.8%	70%	-	76.5%
Hyperbilirubinemia	55.1%	47.7%	23.5%	55.3%
Respiratory distress	10.5%	34.7%	11%	17.5%
Hypothermia	-	2.5%	-	24.3%
Hypoglycemia	8.8%	14.3%	7.1%	12.6%
Food intolerance	-	8.3%	34%	28.2%

Risk of mortality was nine times greater for late preterm infants compared to full term infants (25). There were 3 late preterm neonates who attained mortality in our study. 2 neonates with RDS died because of pulmonary hemorrhage and 1 neonate died because of IVH. Ying Dong et al., 2011 found that the mortality in the early neonatal (age 0-6 days), late neonatal (age 7-27 days) and post neonatal (age 28-364 days) periods was 6, 3, and 2 times higher respectively in late preterm infants than in term infants. During infancy, late preterm infants were 3 times more likely to die than term

infants (26).

The current study provides an overview of morbidity outcomes in late preterm and term neonates in India in comparison with the other globally reported studies. However, the study is limited due to sample size and involvement of only two centres. The second limitation was most of the data was collected from medical records, which implies some variables are still not known and well studied.

Conclusion

In this study, analysis of the data shows that late preterm neonates suffer a large number of intercurrent problems during the neonatal period contributing to a high neonatal mortality rate. Late-preterm infants are therefore a high-risk group of children and need special attention while in hospital, including delayed discharge and follow-up very soon after discharge. Further evidence based studies are required to establish and evaluate strategies, routines and protocols for premature interruption of pregnancy and reducing preterm complications.

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