

## Original Research Article

# Early health issues in late pre-terms

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### ABSTRACT

**Background:** Rates of preterm birth are increasing worldwide, mostly due to late preterm births (i.e. 34-36 6/7 weeks). The objective of the study is to calculate incidence of early morbidity and mortality in late preterm neonates (within first 7 days of life) compared with term neonates.

**Methods:** It was a prospective cohort study. All live inborn late preterm infants (34 0/7 to 36 6/7 weeks) and term infants (37 0/7 to 41 6/7 weeks) who were born between November 2010 to October 2011. Study was done to find out early morbidity and mortality in late preterm births.

**Results:** Present study included 256 late preterm infants and 498 term infants, amongst whom 95 (37.10%) late preterm and 98 (19.67%) term infants required NICU care ( $p < 0.001$ ). Late preterm infants were at significantly higher risk for overall morbidity due to any cause ( $P < 0.001$ ; Odds Ratio (OR): 2.4; 95% CI: 1.7-3.3), respiratory morbidity ( $P < 0.001$ ; OR: 3.64; 95% CI: 1.7-7.4), neonatal depression ( $p < 0.001$ ; OR: 2.94; 95% CI: 1.00-8.62), any resuscitation/ventilation ( $P < 0.05$ ; OR: 3.1; 95% CI: 1.15-8.31), probable sepsis ( $P < 0.001$ ; OR: 11.2; 95% CI: 2.5-49.8), confirmed sepsis ( $p = 0.05$ ; OR: 7.7; 95% CI: 0.9-63.9), or other problems like jaundice, hypoglycemia, hypothermia and feeding difficulty. The incidence of morbidity increased as gestational age decreases from 19.67% in term infants ( $> 37$  weeks) to 27.8%, 43%, 54.5% at 36, 35 and 34 weeks, respectively ( $P < 0.001$ ).

**Conclusions:** The morbidity risk in late preterm births is 1.3 times more at 36 weeks, 2 times more at 35 weeks and 2.7 times more at 34 weeks as compared with term neonates. The mean cost of stay increased 1.8 times in the late preterm neonates as compared to the term neonates.

**Keywords:** Early health problems, Late preterm, Morbidity

### INTRODUCTION

Preterm birth is defined as births occurring before the completion of 37 week of gestation (259 d).<sup>1</sup> However, there is no uniformity in the use of the phrase near-term. The Workshop panel proposed that infants born between week 34 and 36 (d 239 through 259) of gestation ought to be called late preterm instead near term.<sup>2,3</sup> Because the latter may imply that these infants are almost term and mature, there is the possibility of underestimating their

risks, less diligent evaluation, and poor follow-up. Evidence is emerging that late pre-terms make up a majority of preterm births, take up a significant amount of health care resources, have increased mortality/morbidity, and may even have long-term neuro-developmental consequences secondary to their late prematurity. During the last many years, the proportion of all preterm births has increased. In fact, much of the increase in the preterm birth rate in recent years can be attributed to increases in late-preterm births.<sup>4,5</sup>

Late-preterm births account for more than 70% of all preterm births.<sup>4,6</sup> Because late preterm infants comprise the majority of preterm neonates, caring for such a large population who are prone to have unfavourable outcomes can exert a profound impact on the society. Also, the emotional, personal, and financial costs to individuals, family, and society associated with late-preterm births have not been sufficiently described.<sup>7</sup> However, the total resources and costs associated with late-preterm birth are likely to be a relatively substantial part of the total cost of all preterm births, because the population of late-preterm infants is significantly larger than the population of infants who are born before 34 weeks' gestation. This study focused on health facets of late preterm infants to help readers understand this significant health problem, of late preterm neonates better and re-evaluate our obstetric and neonatal practice.

The study was conducted with the following aims and objectives: to calculate incidence of morbidity and mortality in late preterm infants and to estimate the magnitude of increased risk associated with late preterm births (within first 7 days of life) compared with term neonates.

## METHODS

This hospital-based prospective cohort study was conducted at Choithram Hospital and Research Centre, Indore, M.P., an urban tertiary care hospital. The study was approved by the hospital ethics committee.

### Inclusion criteria

- All live inborn late preterm infants (34 0/7 to 36 6/7 weeks) and term infants (37 0/7 to 41 6/7 weeks) born between November 2010 to October 2011 were eligible for enrolment in the study.

Gestational age was assessed by maternal last menstrual period, by first trimester ultrasound scan and new Ballard's score. In case of discrepancy in the assessment of gestational age by more than 2 weeks, gestational age by mother's EDD was considered the correct gestational age. A suitable case reporting form (CRF) mentioning infant's particulars, antenatal history, family history, maternal disorders and risk factors, labor details, neonatal history, and neonatal morbidity was developed for the study. All infants enrolled in study were followed daily, till their duration of hospital stay, for any morbidity by clinical evaluation. Record was maintained for infants who were discharged and later got readmitted for various morbidities.

### Outcome variables

Any medical condition resulting in post-delivery inpatient hospital admission or readmission in first 7 days of life was studied. Some of the known complications which were studied were:

- Respiratory distress: decided on the basis of Silverman's score/Downe's score by the attending paediatrician. Various respiratory morbidities studied were:
  - a. Respiratory distress syndrome- diagnosis made on basis of chest X-ray.
  - b. Transient tachypnoea of newborn (wet lung) characterized by tachypnoea with signs of mild respiratory distress including retractions and cyanosis.
  - c. Apnoea-defined as cessation of airflow for 20 seconds or more or accompanied by bradycardia (heart rate <100 beats/minute) or cyanosis.
  - d. Pulmonary artery hypertension-Primary (sustained increase in pulmonary vascular resistance at birth (PVR) at birth; or Secondary-to meconium aspiration syndrome, cardiovascular causes.
  - e. Pneumonia
- Perinatal asphyxia-Clinical syndrome preceded by at least one of the following three antecedents:
  - a. Evidence of fetal hypoxia/distress,
  - b. Apgar score of three or less at 5-minutes or later,
  - c. metabolic acidosis (cord blood pH<7)<sup>8,9</sup>
- Hypoglycemia: In healthy infants (roomed in)-40mg/dl; after 24 hrs 45 mg/dl; infant with abnormal signs and symptoms-45 mg/dl. Blood sugars were monitored in the IUGR (intrauterine growth restriction) (12 hourly), IDM (Infant of diabetic mother) (as per protocol) and LGA (Large for gestation, birth weight >2SD) (12 hourly) infants. Random blood sugar estimation was also done in all symptomatic infants as per the clinician's discretion.
- Jaundice: Clinically visible jaundice requiring phototherapy/exchange transfusion as per age appropriate hour-specific total serum bilirubin (TSB) nomogram (AAP chart).
- Feeding problem-Delay in initiating and maintaining adequate direct breast feeding is considered as feeding difficulties in the absence of sepsis and respiratory distress. Causes being inadequate output in mother (measured by manual milk expression and weighing baby daily); weak NNR (neonatal reflexes-rooting; sucking); number of neonates not accepting feeds due to other causes like illness/ventilation/kept nil by mouth/requiring gavages feeding/ katori spoon feeding.
- Sepsis: Probable sepsis: Positive septic screen (two of the four parameters namely, TLC <5000/mm<sup>3</sup> or 15000/ mm<sup>3</sup>, absolute neutrophil count less than 1800/mm<sup>3</sup> or >7200/mm<sup>3</sup>, C-reactive protein >0.5mg/dL, platelets <1 lac/mm<sup>3</sup>); or Proven sepsis: Isolation of pathogens from Blood or CSF or Urine.<sup>10,11</sup>
- Hypothermia: Rectal temperature of less than 35.5 degree Celsius.<sup>12</sup>
- Readmission: Any admission after discharge from hospital.
- Average cost of stay as calculated from patients' medical bill on discharge.

### Statistical analysis

All collected data was analysed using SPSS software. Neonatal morbidities were compared between late preterm and term infants. Chi-square test was applied for discrete variables and p value <0.05 was considered significant. Chi-square for trends was done for comparing morbidities across gestational age groups. Relative risk was calculated to describe the ratio of the probability of the event occurring in the late preterm group versus term group. The odds ratio was calculated to describe the strength of association or non-independence between the two groups.

### RESULTS

There were 869 live births in hospital during study period. Of these, 256 (29.45%) late preterm and 498 (57.3%) term births were included in the study. All included infants were followed for 7 days of life/till they are discharged. On comparing the two groups, there was significant difference in mean birth weight, weight for gestation and mode of delivery (Table 1). Ninety-five (37.10%) of late preterm and 98 (19.67%) of term infants had at least one of the neonatal morbidities requiring inpatient hospital admission during the first 7 days of life ( $p < 0.0001$ ; Relative Risk (RR)=1.88).

**Table 1: Baseline variables of the study population.**

Variable	Late preterm (n=95)	Term (n=98)	P value
Gestation (weeks) mean (SD)	35.2 ( $\pm 0.68$ )	>37 (-)	
Birth weight (kg) mean (SD)	2.08 ( $\pm 0.44$ )	2.73 ( $\pm 0.43$ )	
<b>Weight for gestation</b>			
AGA	79 (83.15)	89 (90.81)	
SGA	16 (16.84)	8 (8.16)	
LGA	-	1 (1.02)	
Total LBW infants	79 (83.15)	33 (33.67)	
<b>Mode of delivery</b>			
Vaginal	31 (32.63)	70 (71.42)	<0.0001
Cesarean	64 (67.36)	28 (28.57)	
Elective	24 (37.5)	1 (3.57)	<0.001
Emergency	40 (62.5)	27 (96.42)	

P <0.05-Significant and P >0.05-Not significant

**Table 2: Comparison of morbidity in late preterm and term infants.**

Variable	Late preterm (95) (%)	Term (98) (%)	P value	Odds Ratio
Any morbidity	95 (37.1)	98 (19.67)	<0.001	2.4 (1.7-3.3)
Respiratory morbidity	34 (35.78)	13 (13.26)	<0.001	3.64 (1.7-7.4)
Neonatal depression	13 (13.68)	5 (5.01)	<0.05	2.94 (1.0-8.62)
Jaundice	69 (72.63)	69 (70.40)	0.73	1.11 (0.59-2.08)
Probable sepsis	18 (18.94)	2 (2.04)	<0.001	11.2 (2.5-49.8)
Confirmed sepsis	7 (7.36)	1 (1.02)	0.058	7.7 (0.9-63.9)
Resuscitation	16 (16.84)	6 (6.12)	<0.05	3.1 (1.15-8.31)
Oxygen requirement	40 (42.10)	26 (26.53)	<0.05	2.01 (1.09-3.69)

P <0.05-Significant and P >0.05-Not significant

On comparing the neonatal morbidity in the two groups, late preterm infants were at significantly higher risk for overall morbidity due to any cause, respiratory morbidity, neonatal depression, any resuscitation/ventilation, jaundice, hypoglycemia, probable sepsis, and confirmed sepsis (Table 2 and 3). Most of the neonates were referred to NICU within 6 hours of their birth but the number was just twice in the late preterm neonates as compared to the term neonates (62% and 30% respectively;  $p < 0.001$ ; RR=2.02).

Authors recorded a bimodal peak in the age of presentation to NICU, first within 6 hours of birth and second after 48 hours of life. Most common cause being

jaundice in both the groups, but other peculiar causes seen in the late preterm neonates included sepsis, feeding intolerance and hypothermia.<sup>13-17</sup>

**Table 3: Respiratory morbidity distribution.**

Disease	Late preterms n=95 (%)	Terms n=98 (%)	RR	p value
TTN	17 (17.89%)	13 (13.26%)	1.349	0.37
HMD	12 (12.63%)	-		
Pneumonia	5 (5.26%)	-		
MAS	2 (2.10%)	7 (7.14%)	0.294	0.12
PAH	2 (2.10%)	2 (2.04%)	1.03	0.97

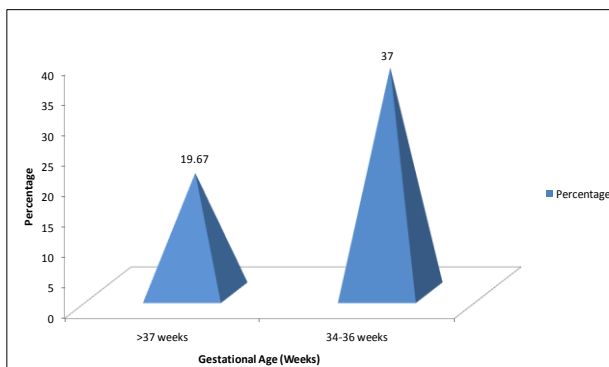
Six (6.31%) late preterm infants required readmission in the first 7 days of life, most common cause being sepsis (Table 4). Late preterm neonates were found to have 24-28% risk of receiving top feeding. Authors found that the rate of aggregated morbidity increased weekly as the gestational age decreases (Table 5), from 19.67% in term neonates to 27.8% at 36 weeks, to 43 % at 35 weeks, to 54 % at 34 weeks (Figure 1 and Figure 2) i.e. 1.3 times more at 36 weeks, 2 times more at 35 weeks and 2.7 times more at 34 weeks as compared with term neonates ( $p<0.001$ ).

**Table 4: Cause of readmission in the late preterm infants.**

Variable	Late preterm (n=6/95) (6.31%)
Sepsis	3 (50%)
Sudden respiratory arrest	1 (16.66%)
Respiratory morbidity	1 (16.66%)
Feeding intolerance	1 (16.66%)

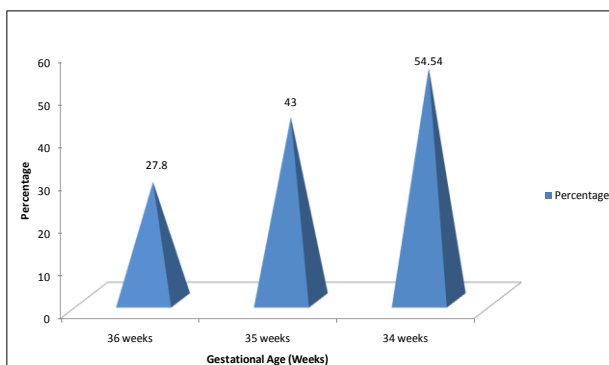
**Table 5: Gestation wise morbidity distribution.**

Morbidity	Total	34week (n=44) %	35 week (n=79) %	36 week (n=133) %
Transient tachypnoea of newborn	17	0	9 (52.94)	8 (47.05)
Hyaline membrane disease	12	7 (58.33)	5 (41.66)	0
Birth asphyxia/ depression	13	7 (53.84)	4 (30.76)	2 (15.38)
Sepsis	18	9 (50)	4 (22)	5 (27.77)



**Figure 1: Incidence of early (<7 day) morbidity in newborns (late preterm versus term).**

In this study, authors found that the late pre-term neonates form a very vulnerable group. They are not comparable to term infants and are prone to various morbidities at birth and later in life.



**Figure 2: Incidence of early (<7 day) morbidity in late preterm at various gestational age.**

The late preterm neonates are prone to have prolonged hospital stay due to their morbidities, and this adds to the financial burden on the family. Thus, authors found that average cost of stay was much more in late preterm neonates, i.e. Rs.12200 as compared to that of Rs.7100 in the term neonates, in NICU.

## DISCUSSION

In the present study, 37.1% of late preterm and 19.67% of term infants had at least one neonatal morbidity requiring inpatient hospital admission during the first 7 days of life ( $p<0.001$ ). Respiratory morbidity (35.78%), neonatal depression (13.68%), and jaundice (72.63%) were the frequently identified morbidities in late preterm infants while neonatal jaundice (70.04%) was the most frequently identified morbidity in term infants. Caesarean delivery significantly contributed to neonatal morbidities ( $p<0.0001$ ). Compared with term infants, the maternal risk factors are more common in late preterm infants ( $p<0.001$ ), most common of which were PIH, PROM, GDM and previous LSCS. Compared with term infants, late preterm infants were at 2 times higher risk for overall morbidity due to any cause, 2.5 times higher risk for respiratory morbidity, 2.8 times higher risk for requiring resuscitation at birth, 9 times higher risk for acquiring sepsis. Peculiar causes for morbidity in late preterm group were hypoglycaemia, hypothermia and feeding intolerance. Shapiro-Mendoza et al reported that late-preterm infants were 7 times more likely to have newborn morbidity than term infants (22% vs 3%).<sup>17</sup> The newborn morbidity rate doubled in infants for each gestational week earlier than 38 weeks. Late-preterm infants who were born to mothers with any of the maternal conditions assessed were at higher risk for newborn morbidity compared with similarly exposed term infants.



Melamed et al also found that compared with full-term infants, spontaneous late preterm delivery was independently associated with an increased risk of neonatal morbidity, including respiratory distress syndrome, sepsis, intraventricular hemorrhage, hypoglycemia, and jaundice requiring phototherapy.<sup>18</sup> Another study by Tomashek et al found that late preterm infants were 1.5 times more likely to require hospital-related care and 1.8 times more likely to be readmitted than term infants.<sup>19</sup> In present study authors found that, forty four percentage of late preterm neonates did not receive breast feeding within first hour of their birth due to various morbidities and weak reflexes and were found to have 24-28% risk of receiving top feeding whether or not they are shifted to NICU. Because of prematurity late preterm infants are prone to have other complications like hypothermia (15%), hypoglycemia (7%) and feeding intolerance due to incoordination between sucking and swallowing or N.E.C (5%), subsequently leading to poor weight gain, and dehydration during early postnatal weeks.<sup>14,20-21</sup> Similar results were found in the study by Santos IS et al, where as compared to the term births, late preterm births showed increased risk of depression at birth (relative risk (RR) 1.7 (1.3, 2.2)), perinatal morbidity (RR 2.8 (2.3, 3.5)), and absence of breast feeding in the first hours after birth (RR 0.9 (0.8, 0.9)).<sup>22</sup> RRs for neonatal and infant mortality were, respectively, 5.1 (1.7, 14.9) and 2.1 (1.0, 4.6) times higher than that observed among term newborns. In the only published Indian study by Jaiswal et al, late preterm infants were found to be at significantly higher risk for overall morbidity due to any cause ( $P<0.001$ ; adjusted Odds Ratio (OR): 5.5; 95% CI: 4.2-7.1), respiratory morbidity ( $P<0.001$ ; adjusted OR: 7.5; 95% CI: 4.2-12.3), any ventilation (non-invasive or invasive) ( $P=0.001$ ; adjusted OR: 4.2; 95% CI: 2-8.9), jaundice ( $P<0.001$ ; adjusted OR: 3.4; 95% CI: 2.7-4.4), hypoglycemia ( $P<0.001$ ; adjusted OR: 4.5; 95% CI: 2.6-7.7), and probable sepsis ( $P<0.001$ ; adjusted OR: 3.2; 95% CI: 1.6-6.5).<sup>23</sup> The incidence of morbidities increased from 23% at 40 weeks to 30%, 39.7%, 67.5%, 89% and 87.9% at 38, 37, 36, 35 and 34 weeks, respectively ( $P<0.001$ ).

Authors found that morbidity was more in late preterm neonates leading to prolonged hospital stay, and thus lead to increase in financial burden to 1.8 times more as compared to the term neonates. Similarly, Lubow JM et al found that rates of neonatal intensive care unit admission, length of stay, and neonatal morbidities are significantly higher in late preterm as compared with term births.<sup>24</sup> The present study is one of the few attempts to obtain actual data on late preterm births and associated neonatal morbidities from India. As the present study was designed to assess early neonatal morbidities, it did not address morbidities after 7 days of life, and also whether outcomes studied had long-term implications. No consensus has yet been reached on the contributing factors of the increase in late preterm births. Because the actual indication for delivery is recognized as a determinant in neonatal outcome, more attention should

be devoted to examine the etiology of late preterm births.<sup>25,26</sup> The results in present study show that late preterm infants have 2 times higher risk for overall morbidity due to any cause relative to term infants and the morbidity risk increases approx. 1.5 times with each decreasing gestation.

## CONCLUSION

Late preterm infants are physiologically and metabolically immature; thus, are at higher risk for developing various morbidities. The late preterm neonates are prone to have prolonged hospital stay due to their morbidities; and this adds to the excessive utilization of health care resources and increase financial burden on the family.

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