

## Original Research Article

# Early neonatal morbidities in late preterm compared to term neonates born in a tertiary care private hospital

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### ABSTRACT

**Background:** Late preterm babies, born between 34 completed weeks of gestation through 36 weeks 6/7 gestation, tend to be physiologically less mature than term infants, subjecting them to an increased risk of developing various morbidities. Limited information is available regarding the current scenario in India. Therefore, the objective of this study was to understand and compare the early morbidities in late preterm newborns with those in full term babies in a tertiary hospital in India.

**Methods:** The current prospective, observational study consisted of total 150 babies divided into two groups equally; late preterm neonates born between 34 and 36 weeks of gestation and full-term neonates. Weight (at birth, at 72 hours), heart rate, temperature and respiratory parameters were noted of all babies. The newborns were examined for respiratory morbidities, ability to breastfeed, hypoglycemia, hypothermia, neonatal jaundice and signs of sepsis. The need for resuscitation, admission to neonatal intensive care unit (NICU) and parenteral nutrition was also assessed. Data was expressed as mean±SD and was analyzed using the Student 't' and Mann Whitney U tests.

**Results:** The mean length and weight at birth in late preterm babies was significantly lesser than term newborns. Late preterm babies were found to have significantly higher incidence of complications like hyperbilirubinemia (62.7% vs 13.3%), respiratory morbidities (16% vs 4%), poor feeding, hypothermia, hypoglycemia, and sepsis compared to term newborns ( $p < 0.01$ ).

**Conclusions:** Late preterm infants are at a higher risk than term infants for a number of neonatal complications. Initiatives imparting special care to late preterm infants are required in order to lower the morbidities endured by this population.

**Keywords:** Hyperbilirubinemia, Late preterm, Morbidities, Neonate, Neonatal intensive care

### INTRODUCTION

The usual length of pregnancy ranges between 39 to 41 completed weeks of gestation. However, a landmark study conducted by Blencowe et al, across numerous countries worldwide revealed that nearly 15 million children are born preterm annually.<sup>1</sup> Preterm birth, which is defined as delivery before 37 weeks of gestation, is the second most common cause of death in children less than

5 years old.<sup>1</sup> A decrease in the duration of gestation is known to abruptly increase the risks of an adverse outcome in preterm infants. This, therefore, makes preterm birth an important determinant of neonatal morbidity and mortality.

Based on the recommendation by the National Institute of Health (NIH) in July 2005, late preterm neonates are defined as babies who are born between 34 completed

weeks of gestation through 36 weeks and 6 days of gestation. They tend to be less mature physiologically as well as metabolically. When compared to term infants, their compensatory responses to the extra-uterine environment are also limited.<sup>2</sup> The annual number of late preterm deliveries is increasing steadily worldwide. The rate of preterm births in the United States increased from 9.1% in 1981 to 12.3% in 2003, most of which was accounted for by an increase in the proportion of late preterm births. However, the evidence emerging from the United States seems to be the part of a much larger global trend. The late preterm birth rate was 5.9% in Canada in 2006 while in Denmark, a 22% increase in the rate of moderate to late preterm births (32-36 weeks gestation) was observed between the years 1995 to 2004.<sup>3,4</sup> A study conducted in Portugal, too, estimated a late preterm birth rate of 5.4% in the country.<sup>5</sup>

The upsurge in the rate of late preterm births has been attributed to two factors. Both, the rise in the number of successful artificial reproductive techniques; as well as increased surveillance and medical interventions leading to early deliveries in high-risk pregnancies may have contributed to this trend.<sup>2</sup>

Late preterm neonates, being generally larger than the usual preterm infants, are assumed to be 'near term' and therefore, mature physiologically. This assumption has, however, led to an underestimation of the inherent risks to these infants. Despite forming the largest subgroup of preterm infants, limited research has been carried out on this cohort until recently. Moreover, they have a higher rate of hospital readmission compared to the term babies.<sup>2,6</sup> The economic burden involved in caring for late preterm neonates is also enormous and adds more strain to the overburdened system of health care delivery.<sup>7</sup>

Recent research has revealed that while serious morbidities are rare, the late preterm group has 2 to 3 fold increased rates for mild to moderate morbidities, such as hypothermia, hypoglycemia, delayed lung fluid clearance and respiratory distress, poor feeding, jaundice, infection and neuronal injury and disruption of normal brain development.<sup>8,9</sup>

Despite the late preterm subgroup accounting for nearly 10% of all births in India, there is a dearth of data on the short term and long term implications of late preterm birth.<sup>8</sup> Such vital information pertaining to the racial and demographic variation can provide substantial data which could then significantly influence the overall outcome of this population. Therefore, deemed it worthwhile to study and compare the early morbidities in late preterm newborns with those in full-term babies in a tertiary hospital in India.

## **METHODS**

The present prospective, observational, comparative study was conducted in L.H Hiranandani Hospital,

Mumbai. The study duration was of 1 year and the study population included term and late preterm neonates born in the hospital.

The inclusion criteria comprised of late preterm neonates born between 34 0/7 and 36 6/7 weeks of gestation; and neonates born after 37 completed weeks of gestation. The exclusion criteria included all infants with major congenital abnormalities, infants with chromosomal syndromes, early pre-terms, babies born to mothers with gestational diabetes mellitus, mothers having placental abruption and babies of mothers having chronic hypertension or eclampsia and per vaginam leaking for >18 hours.

A total sample size of 150, comprising of 75 subjects in each group, was determined using standard formula based on the prevalence of neonatal morbidities in the late preterm and term neonates. Informed parental consent was obtained prior to enrolment in study. Consecutive babies that were delivered in the hospital during the study period were subjected to gestational assessment which was done based on the maternal menstrual history, if reliable, or by new Ballard score.

The information collected included maternal data consisting of the age of the mother and mode of delivery, details of the baby including birth weight, sex and vital parameters. Heart rate, respiratory rate and oxygen saturation were noted half hour after birth while temperature was recorded 8 hourly until discharge. Other respiratory morbidities were looked for and the need for resuscitation was assessed. An exclusive breastfeeding rate at discharge was recorded and babies requiring formula feed or expressed breast milk were identified. Hypoglycemia, hypothermia, neonatal jaundice (based on American Academy of Pediatrics guidelines), standard signs of sepsis and weight loss at 72 hours after birth were observed. The need for admission to neonatal intensive care unit (NICU) and intravenous fluid admission was determined and recorded.

## **Statistical analysis**

Data was statistically described in terms of mean ( $\pm$ SD), frequencies (number of cases) and percentages where appropriate. Student 't' test was used to assess normally distributed data, while non parametric data was analyzed using Mann Whitney U test. Categorical data was assessed using Chi square test. A "p" value less than 0.05 was considered as statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 21.

## **RESULTS**

A total of 150 neonates were included in two study groups; term (n=75) and late preterm (n=75).The mean

gestational age (GA) in the group with term neonates was 38.62±0.96 weeks according to the mothers' last menstrual period (LMP) and 38.68±0.93 according to Ballard score while in the late preterm neonates group, it was 35.56±0.96 and 35.49±0.64 weeks based on LMP and Ballard score respectively.

The mean birth weight in the term babies was 3.08±0.42kg and in the late preterm group was 2.11±0.42kg. However, the mean percentage weight loss at 72 hours of life was noted to be 4.93±0.96% in term neonates compared to 6.78±1.22% in late preterms which was found to be statistically significant (p<0.01). A statistically significant difference was also found in the mean length at birth between both the groups. However, the same was not seen with respect to head circumference (Table 1).

**Table 1: Anthropometric data of late preterm and term neonates.**

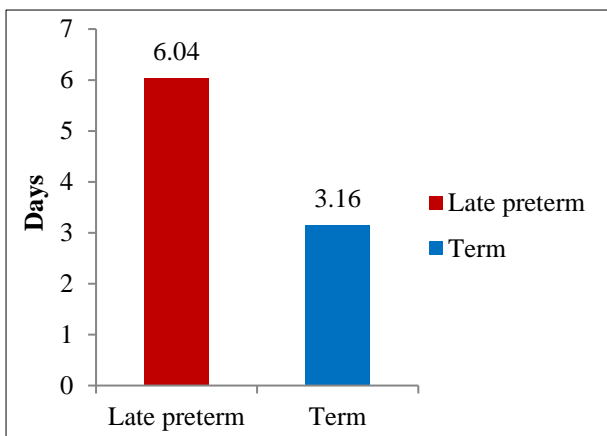
Variables	Group	N	Mean	SD	P value
Birth weight (kgs)	LPTI	75	2.11	0.31	<0.01
	Term	75	3.08	0.42	
Weight at 72 hrs (kgs)	LPTI	75	1.97	0.31	<0.01
	Term	75	2.92	0.42	
Weight loss (in %)	LPTI	75	6.78	1.22	<0.01
	Term	75	4.93	0.96	
Length (in cm)	LPTI	75	42.33	2.35	<0.01
	Term	75	49.17	1.51	
Head circumference (in cm)	LPTI	75	31.99	0.82	0.426
	Term	75	34.55	0.66	

LPTI= late preterm infants; Term = term infants

**Table 2: Comparison of temperature, respiratory parameters and feeding between late preterm and term neonates.**

Variables	LPTI (n=75) (%)	Term (n=75) (%)	Total (n=150)	p value
Temperature	Hypothermia	15 (20%)	1 (1%)	<0.01
	Normal	60 (80%)	74 (99%)	
Respiratory rate	Tachypnea	8 (11%)	3 (4%)	0.209
	Normal	67 (89%)	72 (96%)	
SpO <sub>2</sub> > 95%	No	4 (5%)	2 (3%)	0.681
	Yes	71 (95%)	73 (97%)	
Feeding at discharge	Not Breastfeeding	9 (12%)	0 (0%)	<0.01
	Breastfeeding	66 (88%)	75 (100%)	

LPTI= late preterm infants; Term = term infants



**Figure 1: Comparison of mean duration of hospital stay between late preterm and term neonates.**

Hypothermia was observed to be significantly higher in late preterm infants (n=15) compared to 1 term infant. Variation in the respiratory rate and oxygen saturation were found to be comparable in both groups. Among the late preterm babies, 88% (n=66) were on direct breast feeding at discharge from NICU, while the others

received supplemental feeds in the form of expressed breast milk or formula feeds through bottle. Feeding difficulties were not encountered in term neonates at discharge (Table 2).

Figure 1 depicts the comparison between mean duration of hospital stay in late preterm and term neonates. The duration of hospital stay was found to be significantly longer in the late preterm group (6.04±4.27 days) compared to the term neonates (3.16±0.52 days) (p <0.01). Moreover, out of total 75 LPTI, 40% required NICU admissions compared to 5.3% term newborns (p<0.01).

The LPTI had frequent episodes of hypoglycemia (12% vs 0%) with statistically significant differences in relation to the term newborns as depicted in (Table 3). Similarly, other complications like poor feeding (32% vs 0%), icterus (62.7% vs 13.3%) and sepsis were also significantly more in preterm babies (p<0.01) compared to term newborns. The need for parenteral nutrition (16% vs 4%) and incidence of respiratory morbidities (16% vs 4%) was found to be higher in late preterm babies compared to term newborns.

**Table 3: Comparison of morbidities between late preterm and term neonates.**

Comorbidities	Group		Total	p value
	LPTI (n=75) (%)	Term (n=75) (%)		
NICU admission	30 (40%)	4 (5%)	34	<0.01
Hypoglycemia	9 (12%)	0 (0%)	9	<0.01
Poor feeding	24 (32%)	0 (0%)	24	<0.01
Jaundice	47 (56%)	10 (13%)	57	<0.01
Sepsis	9 (12%)	1 (1%)	10	0.02
Parenteral nutrition	12 (16%)	3 (4%)	15	0.026
Ventilator support	5 (7%)	2 (3%)	7	0.44
Respiratory morbidity	12 (16%)	3 (4%)	15	0.026

LPTI= late preterm infants; Term = term infants

There was no mortality and the survival outcome was found to be 100% in both the groups of the study.

## DISCUSSION

The last 6 weeks of gestation signify a critical period in the growth and development of the fetal brain, lungs and other systems. Evidence accumulated in recent times has stated that the risks for health complications, including serious morbidities are higher in late preterm infants compared with term infants.<sup>2</sup> Besides, there is also a reported three-fold higher infant mortality rate in this group.<sup>10</sup>

In the current study, authors aimed at comparing the early morbidities in late preterm infants compared to term infants in a tertiary care hospital in Mumbai, India. It has been proposed that increased risk of neonatal morbidity in the late preterm period could additionally be related to the pregnancy complications leading to premature delivery.<sup>11</sup> In order to overcome this dilemma, we included only low risk pregnancies in order to ensure that our results reflect the net effect of late prematurity on the neonatal outcome.

In the present study, we found that late preterm babies had significant weight loss by 72 hours of life and also decreased mean length compared to term babies. Hence, although previous studies have suggested that the size and weight of late preterm and term infants are comparable, our findings are in accordance with those of Modi et al, who observed that the mean weight in late preterm neonates was significantly lower than term neonates.<sup>2,8,12</sup>

A significantly large number of newborns (20%) in the late preterm group had episodes of hypothermia compared to the term newborns (1%) in our study. This finding was similar to that of Binarbasi et al, who stated that hypothermia was noted in 14.5% of late preterm neonates in their study.<sup>13</sup> A decrease in the brown adipose tissue stores and in the hormones necessary for their

breakdown probably predisposes late preterm infants to increased heat loss. Moreover, the reduced insulation in the form of white adipose tissue and increased body–surface area to body-weight ratio may subject them to the risk of hypothermia.<sup>14</sup>

This study also indicated a significantly decreased ability to breastfeed in the group with late preterm neonates. This finding was analogous to that of Kao et al, who compared various aspects of breastfeeding behaviour between late preterm and full term neonates.<sup>15</sup> Binarbasi and Abu Salah et al, too, observed in their studies that the incidence of feeding difficulty in late preterm neonates was 19.1% and 15.8% respectively compared to 0.5% and 1.2% in term babies.<sup>13,16</sup> It has been suggested that late preterm neonates probably have poor suck and swallow coordination as a result of neuronal immaturity and reduced oromotor tone. This could lead to inadequate caloric intake, and dehydration may therefore ensue.<sup>14</sup>

NICU admission was required in significantly higher number of late preterm babies in the study. Haroon et al, too, observed that compared to 2% of term babies, nearly 19% of late preterm infants required NICU admission.<sup>17</sup> Similar findings were also reported by Wang and Yvonne Cheng et al.<sup>18,19</sup> Tomashek et al, suggested that late preterm infants were 1.8 times more likely to be admitted than term infants.<sup>10</sup>

In the current study, neonatal hyperbilirubinemia was the most commonly occurring morbidity in late preterm infants followed by poor feeding. This finding is consistent with those observed by Tamil Selvan and Melamed et al, who also suggested that neonatal hyperbilirubinemia was seen more commonly in late preterm babies.<sup>20,21</sup> This is possibly due to developmental immaturity of the liver and brain in late preterm infants. Sarici et al, reported that late preterm infants had significantly higher bilirubin levels on days 5 and 7, demonstrating that these infants have a relatively delayed bilirubin peak with a tendency to persist for a longer duration.<sup>22</sup> Hence, this immaturity is also contributory to



the severity and duration of neonatal jaundice in the late preterm infants compared to their term counterparts.<sup>23</sup>

Hypoglycemia and sepsis each accounted for 12% in late preterm group while no case of hypoglycemia was detected in term babies in this study. This finding concurs with that observed in the prospective study conducted by Selvan showing significantly higher incidence of hypoglycemia and sepsis in late preterm newborns.<sup>20</sup> This finding may be explained by the fact that hepatic glycogen stores normally accumulate in the third trimester and are hence lesser in late preterm babies. Moreover, they have immature hepatic enzymes for gluconeogenesis and glycogenolysis. This combined with impaired hormonal regulation and insulin secretion by immature pancreatic beta cells predisposes these infants to severe hypoglycemia.<sup>14</sup>

In view of poor feeding (32%) and hypoglycemia (12%), more late preterm babies received parenteral fluid (16%) in the current study. A study by Gianni et al, showed that late preterm infants are at relatively high risk of requiring nutritional support during hospital stay.<sup>24</sup> Wagh et al, observed that late preterm babies had greater requirement of intravenous fluids when compared to term controls (57.8% vs. 2.1%).<sup>25</sup> The present findings add to the knowledge of late preterm infants' feeding issues and may contribute to modifying nutritional approaches for these infants.

Respiratory morbidity and the need for ventilator support was found to be higher in late preterm babies as compared to term infants. Likewise, Selvan et al, showed that respiratory distress was seen in 17.5% of late preterm compared to 1.3% of term babies.<sup>20</sup> Findings are also corroborated by those of Hibbard et al, who observed respiratory distress in 10.5% of late preterms compared to 1.13% of term infants.<sup>26</sup> Respiratory concerns are related to delayed transition to air breathing, delayed fluid clearance and surfactant deficiency. The delay in fluid clearance probably stems from the fact that epithelial sodium channels (ENaC), that are required for transepithelial movement of fetal lung fluid attain peak expression at term. Therefore, late preterm infants manifest decreased ability to clear lung fluid.<sup>14</sup>

The duration of hospital stay was greater in late preterm compared to term babies in view of the morbidities. This finding confirms that of Modi et al, who also observed that while 42% of late preterm neonates required admission for 3 to 7 days, only 28% of term infants needed the same duration. Moreover, nearly 17% of late preterm neonates required NICU admission for more than 7 days compared to 8% of term babies.<sup>12</sup>

Though the overall survival outcome was 100% in both the groups of this study, Selvan and Zullini et al, found that late preterm babies had higher mortality compared to term babies.<sup>20,27</sup> Young et al, also stated similar findings and suggested that a weekly increase in estimated

gestational age was associated with a decreasing risk of death.<sup>28</sup>

In the present study, 76% of late preterm neonates had at least one morbidity compared to 20% of term babies. This observation is similar to Wang et al who noted that nearly 78% of near-term infants compared with 45% of term infants had at least one clinical problem and almost all outcomes differed significantly between late preterm and full term neonates.<sup>18</sup>

In a retrospective study, Modi et al, found that the risk of morbidity was nearly 3 times higher in late preterm compared to term neonates, also accompanied by an increased NICU stay.<sup>12</sup> Shapiro-Mendoza et al, too, observed that the risk of morbidity among LPTI doubled with every week that the gestational age (GA) reduced.<sup>29</sup> Thus, study revealed significantly increased morbidity in the late preterm population compared to the term newborns.

## CONCLUSION

Late preterm infants are at a higher risk than term infants for a number of neonatal complications including hyperbilirubinemia, hypothermia, hypoglycemia, feeding problems, sepsis and neonatal intensive care admission. Initiatives imparting special care to late preterm infants are required in order to lower the morbidities endured by this population. There is a pressing need to document the health and economic impact of these initiatives and to take appropriate preventive and therapeutic measures for this condition.

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