Original Article

# A Comparison of the Short-term Morbidity and Mortality Between Late Preterm and Term Newborns

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**Abstract**

**Introduction: Late preterm babies are defined as those born between 34 to 36 completed weeks. There has been a recent increased awareness that this group of babies has a higher incidence of morbidity as compared to term babies. The aim of this study was to evaluate the short-term morbidities occurring in this group of babies managed in the neonatal unit at Singapore General Hospital (SGH). Materials and Methods: A retrospective study was done of babies managed in the neonatal unit at SGH from January 2005 to December 2008. Maternal, perinatal and neonatal data were obtained from the departmental database. The outcomes of late preterm infants were compared with term infants. Results: A total of 6826 babies were admitted. Ten percent (681 out of 6826) of babies were late preterm babies, making up 63% (681 out of 1081) of all preterm babies. Late preterm babies had significantly greater need for resuscitation at birth. They also had statistically significant increased risks of developing hyaline membrane disease (2.5% vs 0.1%), transient tachypnoea of the newborn (TTN) (8.1% vs 1.7%), pneumonia (7.0% vs 2.8%), patent ductus arteriosus (PDA) (4.3% vs 1.1%), hypotension (0.7% vs 0%), apnoea (3.7% vs 0%), gastrointestinal (GI) bleeding (1.5% vs 0.3%), polycythaemia (2.2% vs 1.0%), anaemia (3.4% vs 1.2%), thrombocytopenia (3.2% vs 0.6%), hypoglycaemia (6.6% vs 1.7%), neonatal jaundice requiring phototherapy (41.1% vs 12.2%) and sepsis (1.7% vs 0.6%). Conclusion: Late preterm infants are indeed a vulnerable group of infants with significant morbidities that need to be addressed and treated. Despite their relatively large size and being almost term, the understanding that late preterm infants are not similar to term infants is important to both obstetricians and neonatologists.**

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**Key words: Moderate preterm, Near term infants, Outcome, Prematurity, Preterm birth**

## Introduction

Late preterm infants are defined as those who are born between the gestational age (GA) from 34 weeks and 0/7 days through 36 weeks and 6/7 days.

Worldwide, late preterm birth has increased since the last decade. In the United States (US), there are approximately 500,000 preterm births annually.[1] These account for 12.5% of all live births in the US every year. Of these preterm births, three-quarters are late preterm births.[1] The rate of late preterm birth in the US has increased nearly 15% since the last decade. The World Health Organization (WHO) reported an estimated 12.9 million preterm births worldwide annually.[2] Out of these, 54% occurred in Asia.[2] Therefore, we believe that Asia has the largest group of late preterm infants worldwide. However, to date, little has been reported with regards to the outcome of this group of infants in Asia. It is important to know whether we observe similar morbidity and mortality amongst our late preterm infants in Asia as compared to those in other continents. There are various reasons for the increase of late preterm births. The increase is largely due to the increase in obstetric interventions, either as a result of pregnancy-related complications or maternal pre-existing medical

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conditions. The increase in obstetric interventions is also due to the advancement in obstetrical technology resulting in early detection and surveillance of foetal abnormalities or foetal distress, consequently leading to earlier delivery of the baby. The advancement of reproductive technologies over the decade has also contributed to the increase of late preterm births due to the increase of multiple pregnancies.

Why have late preterm infants become a huge concern for many perinatologists, obstetricians and neonatologists worldwide over the last decade? We observe vast publications on late preterm infants over the last 5 years. These publications do not merely focus on the morbidity or mortality during the neonatal period but also the long-term outcome of this group of infants. Why are late preterm infants more vulnerable as compared to their 'term' infants? Late preterm infants are believed to be vulnerable due to the immaturity of their body system, either physiologically or metabolically. The decision to deliver should be prioritised in delivering babies who are physiologically mature and capable of transition to extrauterine life without compromising the health of the mother. Hence, the decision to deliver early should always be made conscientiously after balancing the risks of prematurity versus those of continuing the pregnancy.

The aim of this study was to ascertain the incidence of late preterm births in our institution, to determine the maternal, antenatal and intrapartum factors associated with late preterm births as well as to compare the neonatal morbidity and mortality of the late preterm babies with the term infants.

## Materials and Methods

Singapore General Hospital (SGH), established in 1821, is a public restructured hospital in Singapore with 1600 beds, providing mainly adult tertiary care services. A retrospective review of infants managed in the neonatal unit at SGH between 1 January 2005 to 31 December 2008 was performed. The infants were identified from the departmental database, and relevant antenatal, intrapartum and postnatal data were retrieved. The departmental database was approved by SingHealth Centralised Institutional Review Board (CIRB).

For all infants managed in our unit, GA was confirmed at the time of delivery. GA was usually based on the mother's last menstrual period (LMP) together with early ultrasonographic dating information in the first trimester. All preterm infants (less than 37 weeks GA), with the exception of infants conceived by in vitro fertilization (IVF), were scored clinically using the Dubowitz or modified Ballard score. GA scoring was also done if the mother's LMP was uncertain and there was no early dating scan done or there was clinical suspicion about the GA of the infant. If there was a discrepancy of more than 2 weeks between the scored dates and the maternal dates, the GA determined by scoring was taken, after confirmation by an independent scorer.

For the analysis, infants were categorised as late preterm infants (those between 34 to 36 weeks GA) and term infants (those between 37 to 41 weeks GA). Gestational size was classified based on revised intrauterine growth curves by Kitchen et al.[3] Small for gestational age (SGA) was defined as birth weight for GA below the 10$^{th}$ percentile. Appropriate for gestational age (AGA) was defined as birth weight for GA below the 10$^{th}$ to 90$^{th}$ percentile. Large gestational age (LGA) was defined as birth weight for GA above the 90$^{th}$ percentile. Factors which were compared between the 2 groups included general characteristics like birth weight, GA and ethnicity, maternal factors such as parity, pre-existing medical conditions and obstetric complications and intrapartum factors like mode of delivery, level of resuscitation and Apgar score. Neonatal outcomes studied included various respiratory outcomes and the level of respiratory support required, cardiovascular, neurological, gastrointestinal (GI), haematological, metabolic and infective morbidities as well as birth-related injuries. These outcomes included pneumonia, feeding intolerance, GI bleeding, necrotising enterocolitis (NEC), anaemia, thrombocytopenia, polycythaemia, hypocalcaemia, hypoglycaemia, soft tissue injuries etc. Pneumonia was diagnosed based on the presence of clinical features and radiological evidence consistent with pneumonia for which the infant was treated with a course of antibiotics. Feeding intolerance included infants who had feeding difficulties like vomiting and high gastric residuals. GI bleeding included both upper and lower GI bleeding with evidence of blood in the gastric aspirate, vomitus or stool. NEC was diagnosed using the Modified Bell Staging Criteria for Necrotizing Enterocolitis. Anaemia was defined as haemoglobin less than 14 g/dL. Thrombocytopenia was defined as the platelet count of less than 150,000/mm$^3$. Polycythaemia was defined as a haematocrit greater than 65%. Hypocalcaemia was defined as a total serum calcium concentration <2 mmol/L or an ionised calcium concentration <1 mmol/L. Hypoglycaemia was defined as a plasma glucose level ≤2.5 mmol/L. Soft tissue injuries included abrasions, lacerations, etc. while scalp injuries included those with cephalhaematomas, subaponeurotic bleeds, etc.

We also compared the resource usage required such as need for lumbar puncture, umbilical vessel catheterisation and central venous catheterisation as well as highest level of care and length of hospitalisation stay.

All data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software version 16 (SPSS, Chicago, IL). Differences between categorical

variables were analysed using the Chi-square test or Fisher's exact test. Continuous variables were compared using the student's t test for normally distributed data and Mann-Whitney U test for nonparametric data. A *P* value of less than 0.05 was considered significant.

## Results

Between 1 January 2005 and 31 December 2008, a total of 6826 babies managed at SGH were admitted to one of these units — nursery, high dependency or intensive care unit. Out of these babies, 5721 (83.8%) were term infants, 1081 (15.8%) were preterm and 24 (0.4%) were post-term. Of the preterm babies, 681(63%) were late preterm (Fig. 1).

The mean birth weight for late preterm infants was significantly lower compared with the term infants (2545 ± 470 grams vs 3134 ± 409 grams, *P* <0.001) (Table 1).

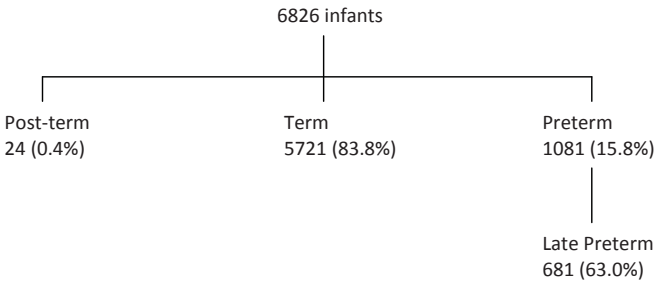


Fig. 1. Concept map showing the cohort profile.

There were significantly fewer late preterm infants who were appropriate for GA (85% vs 88.6%, *P* = 0.007). More late preterm infants were either SGA or LGA compared with the term infants (10.1% vs 8.8%, *P* = 0.001 and 4.8% vs 2.6%, *P* = 0.001 respectively). There were slightly more males in the late preterm group.

Out of the late preterm babies, 36.4% of them were born to mothers who had parity of 3 and above compared to 31.8% who were born to mothers who were primigravida. In contrast, more term babies were born to primip mothers compared to those born to mothers who had parity of 3 and above, 43.7% vs 23.8% (*P* <0.001) respectively.

Mothers with pre-existing medical problems of any type were noted to deliver earlier. Out of the late preterm babies, 43% of them were born to mothers with pre-existing medical problems of any type compared to 27.4% in term babies (Table 2). Pre-existing hypertension and diabetes as well as pre-eclampsia and gestational diabetes were significantly more prevalent in mothers of late preterm infants. Pre-eclampsia and gestational diabetes mellitus (GDM) were the 2 most frequently reported antenatal conditions among mothers of late preterm and term infants.

Pregnancy conceived via IVF was associated with significantly higher incidence of late preterm deliveries as compared to term deliveries, 10% vs 2% (*P* <0.001). Other antenatal conditions such as oligohydramnios, polyhydramnios and antepartum haemorrhage were significantly more common with more late preterm births.

Table 1. General Characteristics

| | Late Preterm, % (n = 681) | Term, % (n = 5721) | *P* Value |
|---|---|---|---|
| Birth weight* | 2545 ± 470 | 3134 ± 409 | <0.001 |
| Gestational size | | | |
| LGA | 4.8 | 2.6 | 0.001 |
| SGA | 10.1 | 8.8 | 0.001 |
| AGA | 85.0 | 88.6 | 0.001 |
| Gender | | | |
| Male | 55.4 | 51.2 | 0.04 |
| Ethnic group | | | |
| Chinese | 43.0 | 45.2 | >0.05 |
| Malay | 41.6 | 39.2 | >0.05 |
| Indian | 9.5 | 9.5 | >0.05 |
| Others | 5.9 | 6.1 | >0.05 |
| Maternity parity | | | |
| 1 | 31.8 | 43.7 | <0.001 |
| 2 | 31.8 | 32.5 | <0.001 |
| 3 and above | 36.4 | 23.8 | <0.001 |

LGA: Large for gestational age; SGA: Small for gestational age; AGA: Appropriate for gestational age
*Mean ± SD

Table 2. Maternal/Antenatal Factors

| | Late Preterm, % (n = 681) | Term, % (n = 5721) | *P* Value | Odds Ratio |
|---|---|---|---|---|
| Medical problems of any type | 43.0 | 27.4 | <0.001 | 2.0 (1.7,2.4) |
| Pre-existing hypertension | 2.6 | 1.1 | <0.001 | 2.5 (1.5,4.3) |
| Pre-existing diabetes | 4.7 | 0.8 | <0.001 | 6.0 (3.8, 9.4) |
| Pre-eclampsia | 13.9 | 3.1 | <0.001 | 4.6 (3.5, 6.0) |
| Gestational diabetes | 12.9 | 6.5 | <0.001 | 2.1 (1.7,2.7) |
| IVF | 10.0 | 2.0 | <0.001 | 5.3 (3.9,7.2) |
| Multiple pregnancy | 16.0 | 0.5 | <0.001 | 35.0 (23.2,52.6) |
| Antenatal foetal anomaly | 2.9 | 3.8 | 0.281 | 0.8 (0.5,1.2) |
| Oligohydramnios | 5.1 | 3.3 | 0.012 | 1.6 (1.1,2.3) |
| Polyhydramnios | 0.9 | 0.2 | <0.001 | 5.6 (2.0,15.9) |
| Antepartum haemorrhage | 4.3 | 1.0 | <0.001 | 4.6 (2.9,7.2) |

IVF: In vitro fertilisation

Intrapartum factors such as maternal pyrexia and meconium stained liquor were more common in term deliveries. However, mothers with prolonged rupture of membrane requiring antibiotics tended to deliver earlier (Table 3).

Late preterm infants had significantly more major malformations and chromosomal abnormalities as compared to the term infants.

More late preterm infants were delivered via caesarean section. They also required more resuscitation at birth and had poorer Apgar scores (Table 4).

*Respiratory Outcome*

Out of the late preterm infants, 28.5% of them had respiratory disorders of any type after birth compared to 14.5% in the term infants (Table 5). Transient tachypnoea of the newborn (TTN) was the most common respiratory morbidity in our late preterm cohort (8.1%). This was followed by pneumonia (7.0%) and apnoea of prematurity (AOP) (3.7%). There was no significant difference in the incidence of air leak and meconium aspiration syndrome (MAS) between the 2 groups.

The late preterm infants needed significantly more respiratory support as compared to the term infants. Comparing the late preterm and the term group, 1.7% vs 0.7% required oxygen therapy, 6.8% vs 1.1% required continuous positive airway pressure (CPAP) and 0.3% vs 0.1% required mechanical ventilation.

*Cardiovascular Outcome*

In terms of cardiovascular outcome, 4.3% of the late preterm infants had patent ductus arteriosus (PDA) compared to 1.1% in the term group ($P$ <0.001). Late preterm infants had a significantly higher rate of hypotension (0.7%).

*Neurological Outcome*

There was no significant difference in the rates of hypoxic ischaemic encephalopathy (HIE), intraventricular haemorrhage (IVH), periventricular leucomalacia (PVL) and seizures between the 2 groups.

*Gastrointestinal Outcome*

The late preterm infants had higher rates of GI complications; 26.4% had GI problems of any type compared to 14.9% in the term group. There were more late preterm infants who had GI bleeding and feeding intolerance. We did not find any statistical difference in NEC between the 2 groups. More late preterm infants had neonatal jaundice requiring phototherapy compared to the term infants, 41.1% vs 12.2% ($P$ <0.001).

*Haematological, Metabolic and Infection Outcome*

Late preterm infants were at higher risk for anaemia, polycythaemia and thrombocytopenia as compared to term infants. They were also at higher risk for hypocalcaemia, metabolic acidosis and hypoglycaemia. There was no difference in the rate of hypothermia between the 2 groups. There was also more late preterm infants who had infection of any time as compared to term infants, 10% vs 4.8% ($P$ <0.001). Out of our cohort of late preterm infants, 1.7% of them had sepsis (clinical or culture positive) compared to 0.6% in the term infants.

*Birth-Related Injuries*

There was no difference in the rates of birth-related injuries such as soft tissue injuries, nerve injuries and fractures between the groups. Nevertheless, there was a greater tendency for term infants to suffer from scalp injuries than late preterm infants (3.6% vs 1.3%, $P$ = 0.002) (Table 6).

Table 3. Intrapartum Factors

| Intrapartum Factors | Late Preterm % (n = 681) | Term % (n = 5721) | Odds Ratio | *P* Value |
|---|---|---|---|---|
| Maternal pyrexia | 1.3 | 3.3 | 0.4 (0.2 – 0.8) | 0.004 |
| Prolonged rupture of membrane requiring antibiotics | 7.0 | 3.4 | 2.0 (1.5 – 2.7) | <0.001 |
| Fetal distress | 5.1 | 4.0 | 1.3 (0.9 – 1.9) | 0.166 |
| Meconium stained liqour | 2.6 | 12.0 | 0.2 (0.1 – 0.3) | <0.001 |

Table 4. Mode of Delivery, Resuscitation at Birth and Apgar Scores

| Intrapartum Events | Late Preterm, % (n = 681) | Term, % (n = 5721) | *P* Value |
|---|---|---|---|
| Mode of delivery | | | |
| Vaginal | 46.7 | 66.8 | <0.001 |
| Instrumental | 4.4 | 8.9 | <0.001 |
| Caesarean | 48.9 | 24.3 | <0.001 |
| Resuscitation at birth | | | |
| No resuscitation | 73.3 | 89 | <0.001 |
| Oxygen/stimulation | 17.9 | 7.7 | <0.001 |
| Bag and mask | 8.1 | 3.0 | <0.001 |
| Intubation/external cardiac massage/drugs | 0.7 | 0.3 | <0.001 |
| Apgar scores | | | |
| <5 at 1 min | 2.5 | 0.4 | <0.001 |
| <7 at 5 min | 0.6 | 0.2 | 0.029 |

*Mortality*

The rate of mortality was 0.1% in the late preterm group compared with no mortality in the term group ($P = 0.004$).

*Resource Utilisation*

Late preterm infants required significantly more interventions and had greater rates of admission to the neonatal intensive care unit as compared to term infants (Table 7). Out of the late preterm infants, 11.9% of them required intensive care as compared to 1.9% in term infants ($P < 0.001$). Late preterm infants also required longer hospital stay with median of 4 days (range, 1 to 42 days) as compared to term infants who had a median stay of 2 days (range, 1 to 101 days) ($P < 0.001$).

## Discussion

In our cohort of 6826 infants, 681 (10%) of them were born late preterm and this accounted for 63% of all preterm births. These figures are similar to those reported in the US where, in 2005, there were 377,000 late preterm births which accounted for 9.1% of all births and 70% of all preterm births.

In a study carried out by Carrie et al, late preterm birth and maternal condition exposure were independent risk factors for newborn morbidity.[4] The risk for neonatal morbidity was higher if both risk factors were present. Comparing both, late preterm birth was the stronger risk. Mothers with medical problems of any type are at higher risk of late preterm births. These medical problems include pre-existing hypertension or diabetes or even common antenatal conditions such as pre-eclampsia or gestational diabetes. Other antenatal conditions like oligohydramnios, polyhydramnios and antepartum haemorrhage often lead to premature deliveries as well.

In our cohort, more late preterm infants were delivered via caesarean section as compared to the term infants, likely due to indications for earlier delivery such as maternal medical/antenatal conditions, multiple pregnancy or intrapartum events like premature rupture of membrane, foetal distress etc. However, we were not able to determine whether there were cases of caesarean section being performed without clear medical indications. Reddy et al recently reported that 23% of late preterm births had no clear recorded indications for delivery in the birth certificate.[5]

Respiratory morbidity is one of the most important health

Table 5. Neonatal Morbidity

| | Late Preterm, % (n = 681) | Term, % (n = 5721) | Odds Ratio | *P* Value |
|---|---|---|---|---|
| **Respiratory** | | | | |
| Any type | 28.5 | 14.5 | 2.3 (2.0 – 2.8) | <0.001 |
| Hyaline membrane disease | 2.5 | 0.1 | 24.4 (9.6 – 62.1) | <0.001 |
| TTN | 8.1 | 1.7 | 5.2 (3.7 – 7.3) | < 0.001 |
| MAS | 0.3 | 0.7 | 0.4 (0.1 – 1.6) | 0.188 |
| Pneumonia | 7.0 | 2.8 | 2.4 (1.7 – 3.3) | <0.001 |
| Air leak | 0.3 | 0.2 | 1.7 (0.4 – 7.7) | 0.498 |
| Persistent pulmonary hypertension | 0.7 | 0.1 | 10.6 (2.8 – 39.5) | <0.001 |
| AOP | 3.7 | 0.0 | | <0.001 |
| **Respiratory support** | | | | |
| Oxygen | 1.7 | 0.7 | 2.5 (1.3 – 4.9) | <0.001 |
| CPAP | 6.8 | 1.1 | 6.5 (4.4 – 9.6) | <0.001 |
| Mechanical ventilation | 0.3 | 0.1 | 2.8 (0.5 – 13.9) | <0.001 |
| **Cardiovascular** | | | | |
| PDA | 4.3 | 1.1 | 4.1 (2.7 – 6.4) | <0.001 |
| Hypotension | 0.7 | 0.0 | | <0.001 |
| **Neurological** | | | | |
| HIE | 0.0 | 0.1 | | 0.490 |
| Seizures | 0.0 | 0.1 | | 0.490 |
| IVH/PVL | 0.0 | 0.0 | - | - |
| **Gastrointestinal** | | | | |
| Any type | 26.4 | 14.9 | 2.1 (1.7 – 2.5) | <0.001 |
| Feeding intolerance | 23.5 | 14.9 | 1.7 (1.4 – 2.1) | |
| NEC | 0.3 | 0.1 | 2.1 (0.4 – 9.9) | 0.337 |
| GI bleeding | 1.5 | 0.3 | 5.0 (2.3 – 11.0) | <0.001 |
| **Neonatal jaundice** | | | | |
| Neonatal jaundice requiring phototherapy | 41.1 | 12.2 | 5.0 (4.2 – 5.9) | <0.001 |
| Neonatal jaundice requiring exchange transfusion | 0.1 | 0.1 | 2.8 (0.3 – 27.0) | 0.351 |
| **Haematological** | | | | |
| Anaemia | 3.4 | 1.2 | 2.8 (1.8 – 4.6) | <0.001 |
| Polycythaemia | 2.2 | 1.0 | 2.1 (1.2 – 3.8) | 0.008 |
| Thrombocytopenia | 3.2 | 0.6 | 5.4 (3.2 – 9.3) | <0.001 |
| Metabolic | | | | |
| Hypocalcaemia | 5.7 | 1.9 | 3.2 (2.2 – 4.7) | <0.001 |
| Metabolic acidosis | 1.0 | 0.2 | 6.6 (2.4 – 17.8) | <0.001 |
| Hypoglycaemia | 6.6 | 1.7 | 4.1 (2.8 – 5.8) | <0.001 |
| Hypothermia | 1.2 | 1.2 | 1.0 (0.5 – 2.1) | 0.975 |
| **Infection** | | | | |
| Any type | 10.0 | 4.8 | 2.2 (1.8 – 2.9) | <0.001 |
| Sepsis (clinical/culture positive) | 1.7 | 0.6 | 2.9 (1.5 – 5.6) | 0.001 |
| Meningitis | 0.0 | 0.1 | 0.9 (0.1 – 17.3) | 0.490 |

TTN: Transient tachypnoea of newborn; MAS: Meconium aspiration syndrome; AOP: Apnoea of prematurity; CPAP: Continuous positive airway pressure; PDA: Patent ductus arteriosus; HIE: Hypoxic ischaemic encephalopathy; IVH: Intraventricular haemorrhage; PVL: Periventricular leucomalacia; NEC: Necrotizing enterocolitis; GI: Gastrointestinal

Table 6. Birth-Related Injuries

| Birth-Related Injuries | Late Preterm, % (n = 681) | Term, % (n = 5721) | Odds Ratio | *P* Value |
|---|---|---|---|---|
| Soft tissue injuries | 4.8 | 4.9 | 1.0 (0.7 – 1.4) | 0.956 |
| Scalp injuries | 1.3 | 3.6 | 0.4 (0.2 – 0.7) | 0.002 |
| Nerve injuries | 0.1 | 0.2 | 0.8 (0.1 – 6.6) | 0.868 |
| Fractures | 0.3 | 0.6 | 0.5 (0.1 – 2.1) | 0.321 |

Table 7. Resource Utilisation

| Resource | Late Preterm, % (n = 681) | Term, % (n = 5721) | Odds Ratio | *P* Value |
|---|---|---|---|---|
| Lumbar puncture | 3.2 | 0.6 | 5.4 (3.2 – 9.3) | <0.001 |
| Umbilical artery catheterisation | 2.6 | 0.3 | 8.6 (4.4 – 16.6) | <0.001 |
| Umbilical vein catheterisation | 1.3 | 0.3 | 3.8 (1.7 – 8.4) | <0.001 |
| Central venous line | 1.5 | 0.1 | 12.2 (4.6 – 32.1) | <0.001 |
| Level 3 (Neonatal Intensive Care) | 11.9 | 1.9 | 7.1 (5.3 – 9.7) | <0.001 |

morbidities affecting the late preterm infants. Wang et al from Massachusetts, United States reported that respiratory morbidity occurred in 28.9% of their late preterm cohort.[6] Our findings were similar with 28.5% of our late preterm cohort having respiratory morbidity. Infants born late preterm may have immature lungs which lead to inefficient gaseous exchange resulting in respiratory distress. Escobar et al and Gilbert et al reported that 10.7% and 3.6% of their cohorts respectively had respiratory distress,[7,8] while Judith et al reported a rate of 9% in their late preterm cohort.[9]

In our late preterm cohort, TTN is the commonest respiratory morbidity which accounted for 8.1%. This is likely due to the delayed intrapulmonary fluid absorption.[10] Out of the late preterm babies, 2.5% of them had respiratory distress syndrome (RDS) as compared to 0.1% in the term group. It can be difficult to differentiate between RDS, TTN and pneumonia as these often overlap. Rubaltelli FF et al reported that the incidence of RDS in his cohort was 12% at 33 to 34 weeks, 2% at 35 to 36 weeks and 0.11% at term, while incidence of TTN was 11.6% at 33 to 34 weeks, 5% at 35 to 36 weeks and 0.7% at term.[11]

Previous studies reported the incidence of apnoea in late preterm infants of between 4% to 7% compared to less than 1% in term infants.[12,13,14,15] Our study shows 3.7% of late preterm infants had apnoea while none of the term infants had apnoea. Late preterm infants are at higher risk for developing apnoea as their central nervous systems are structurally immature and generally smaller with less myelination.[16] Apnoea is also more common in the late preterm due to the immature lung volume, feeding-related problems and anaemia.[17]

Late preterm infants are also at higher risk of persistent pulmonary hypertension (PPHN) compared to term infants. Out of the late preterm infants, 0.7% of them developed PPHN while 0.1% of the term infants developed PPHN. Judith et al reported 0.5% of her 34 weeks cohort developed pulmonary hypertension, followed by 0.3% at 35 weeks, and 0.5% at 36 weeks compared to 0.1% in their term cohort.[9] In pulmonary hypertension, there is a maladaptation to the circulatory transition whereby there is reduced responsiveness to vasodilators such as prostacyclin and nitric oxide. This results in vasoconstriction of the pulmonary vasculature, which in turn causes persistent high pulmonary pressure. This is also contributed by a relative surfactant deficiency in this group of infants in addition to the maladaptation.[18] Our late preterm babies required more ventilatory support such as oxygen therapy, continuous nasal positive airway pressure support or mechanical ventilation. Gilbert et al reported that 3.4% of their late preterm infants required mechanical ventilation as compared to 0.9% in the term group.[8]

Out of the late preterm infants, 4.3% of them had patent ductus arteriosus compared to 1.1% in term infants. Late preterms were also at higher risk for hypotension. It has been postulated that late preterm infants do not have adequate cardiovascular reserve to handle stress postnatally.

In our cohort, there was no difference in the rates of HIE, seizures, IVH and PVL between the 2 groups of infants. However, there are reported concerns of the association between late preterm births with long-term adverse neurodevelopmental sequelae. Late preterm infants are at higher risk of cerebral palsy,[19] neurodevelopmental

disability[20] and speech delay.[21] Therefore, there is a need for long-term follow-up for this group of infants.

Late preterm infants tend to have poorer peristaltic functions and sphincter controls compared with term infants.[22] They are less able to achieve effective sucking and swallowing.[23] This often leads to delay in establishing feeds and results in poor weight gain. They also have immature GI function.[24] The GI tract continues to develop with increasing maturity and the more mature infants tend to have less GI problems. In our cohort, 26.4% of the late preterm infants had GI disorders of any type compared to 14.9% in the term cohort which included feeding intolerance and GI bleeding. Wang et al reported that 32.2% of their late preterm infants had feeding difficulties.[6]

In our study, the late preterm infants were also at higher risk for anaemia, polycythaemia and thrombocytopenia. Very few studies have looked at haematological outcomes in late preterm infants. The immaturity of the bone marrow results in ineffective and inadequate erythropoiesis and platelet production. Maternal conditions and intrapartum factors may also have contributed to the increased rates of haematological problems in the late preterm cohort.

The late preterm infants were at higher risk of developing hypoglycaemia, metabolic acidosis and hypocalcaemia. Wang et al found that late preterm infants tend to require more glucose infusion for hypoglycaemia than in term infants.[6] Out of their cohort of late preterm infants, 15.6% had hypoglycaemia compared with 6.6% in our cohort. Preterm infants are at risk of hypoglycaemia due to the immaturity of liver gluconeogenesis and glycogenolysis, and adipose tissue lipolysis. As the GA increases, the incidence of hypoglycaemia decreases.

Our study did not show any difference between late preterm and term infants in the occurrence of hypothermia. Physiologically, however, late preterm infants are at higher risk for hypothermia as they have a larger surface area to weight ratio as well as less adipose tissue for metabolism.

In our cohort, there were significantly more late preterm infants who had neonatal jaundice requiring phototherapy compared to term infants. Due to the immaturity of liver, the ability to conjugate bilirubin is impaired. Co-existing feeding difficulties also result in impairment of the enterohepatic circulation, decreased stool frequency and dehydration which further aggravates hyperbilirubinaemia.[25]

Late preterm infants are at higher risk of infection. Out of our cohort of late preterm infants, 10% had an infection of any type which included documented bacteraemia, skin/subcutaneous infection, meningitis, pneumonia etc. These can be explained by the lower immunity in late preterm infants especially in the maturation of T-cell and granulocyte functions.[26]

Our study did not show any significant difference between the groups in terms of birth-related injuries such as soft tissue injuries, nerve injuries and fractures. There were more term infants who suffered scalp injuries as compared to late preterm infants. This was possibly because more term infants required instrumental deliveries as compared to our late preterm infants, 8.9% vs 4.4% respectively.

Tomashek et al reported that mortality in late preterm infants is approximately 3 times higher than it is among term infants.[27] However, we did not observe a statistical difference in mortality in our cohort. The mortality in the late preterm group was a 36 weeker who was antenatally diagnosed with holoprosencephaly with multiple dysmorphic features. The parents of this infant declined termination of pregnancy antenatally despite dismal prognosis. Conservative management and comfort case was offered postnatally.

Our late preterm cohort required more interventions including lumbar punctures, umbilical artery catheterisations, umbilical venous catheterisations and central venous lines. More interventions mean higher financial costs and greater resource utilisation. They also required more intensive care. Gilbert et al in his population study in 1996 showed that avoiding 'non-medically indicated births' among the late preterm births could have saved $49.9 million in California alone.[8] By preventing unnecessary late preterm births, we could save on our resource utilisation.

## Conclusion

Late preterm infants are indeed a vulnerable group of infants. Despite their relatively large size and being almost term, they should not be regarded as being similar to term infants. This is an important understanding that obstetricians and neonatologists need to have when they decide and plan for late preterm deliveries. Management strategies should be planned based on adequate understanding of the health morbidity which late preterm infants face after birth.

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