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Short-Term Neonatal Outcomes Associated with Late Preterm Deliveries: A Retrospective Study in Sri Lanka

Champika G. Maggonage[1*], Lakshrini Gunarathne[2], Sandya Bandara[2], Sibra R. M. Shihab[1]

Abstract

Background: Increasing morbidity and mortality of late preterm neonates, born between 34 and 36 (+ 6 days) weeks, is a growing global health concern. This study investigated the incidence and severity of late preterm birth (LPB) and associated early neonatal complications in a Sri Lankan cohort of late preterm neonates.

Methods and Findings: A total of 138 subjects were retrospectively included in the study following strict inclusion and exclusion criteria. Short-term neonatal complications developed in the first two weeks of life or during the hospital stay were collected from hospital records. The incidence of LPB of the total preterm births (n=445) was 31%. A total of 49.3% (68/138) of subjects experienced at least one measured complication; jaundice (34.8%), infection (27.7%), respiratory distress (23.9%), hypothermia (17.4%), feeding problems (15.9%) and hypoglycemia (5.1%), while 42.8% (59/138) were admitted to the neonatal unit. The mean birth weight of the subjects was 2334.6 g, whereas 63.8% (88/138) had low birth weight and admitted to neonatal unit due to severe complications (p=0.0001). Moreover, vaginal delivery had significantly fewer complications than other modes of delivery (p<0.0001).

Conclusion: The presence of neonatal morbidity in the study cohort was significant. Therefore, obstetric practice regarding the timing of delivery after 34 weeks of gestation and antenatal management strategies should be re-assessed to reduce late preterm morbidities.

Keywords: Late-preterm neonates; Neonatal complications; Neonatal outcomes; Short-term complications

Introduction

Globally, the incidence of preterm birth is increasing despite the remarkable endeavor of research and clinical efforts for its prevention [1]. Approximately 15 million babies are born prematurely, as if one in ten, either as a spontaneous onset or an iatrogenic preterm birth [2]. There are various reasons for the unremitting rise in spontaneous preterm labour such as advances in maternal age, increasing obesity rates, more multiple gestations and increasing fertility treatment [3]. Iatrogenic preterm births are mainly due to maternal medical disorders such as hypertensive disorders, cardiac diseases and diabetes in pregnancy [4]. Moreover, culture may also influence the rising preterm births as maternal use of recreational drugs and opioids are commonly seen in some parts of the world, whereas it is a trend less prevalent in Sri Lanka [5].

Affiliation:

[1]Department of Obstetrics and Gynaecology, Faculty of Medicine University of Peradeniya, Sri Lanka

[2]Neonatal Intensive Care Unit, Teaching Hospital Peradeniya, Sri Lanka

***Corresponding author:**

Champika G. Maggonage, Department of Obstetrics and Gynaecology, Faculty of Medicine University of Peradeniya, Sri Lanka.

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A rapid increase in late preterm births have also increased the rate of preterm births; approximately 74% of all preterm births and 8% of total births are late preterm births [6]. Late preterm neonates are born between 34 weeks and 36 weeks + 6 days of gestation and were previously named as near-term neonates [7]. In early clinical practice, late preterm infants were presumed to be physiologically and developmentally mature. However, physiological maturation among neonates born at similar gestation varies appreciably [8]. Therefore, there is a considerable biological disparity in physiological maturation between late preterm and term neonates. However, in 2005, the workshop "optimizing care and outcome of the near-term pregnancy and near-term newborn infant" organized by the National Institutes of Health discouraged the use of "near-term" as it can be misleading that these infants are fully matured and will lead to underestimating the inherent risk to these infants [9].

Preterm and late preterm births are associated with higher rates of neonatal morbidities and mortalities [10,11]. A study has reported that late preterm infants are four times more likely to have at least one medical condition [12] and at higher risk of developing early neonatal complications leading to high morbidity and mortality [13]. Currently, limited published evidence available regarding diverse morbidities found in late preterm infants [1]. The existing evidence suggests that these late preterm neonates are at increased risk for transient tachypnea, respiratory distress [14-16], temperature instability [17,18], hypoglycemia [8,19], feeding difficulty, jaundice [8,20], longer hospital stay and higher rates of hospital readmission due to these complications [8,11,21-27]. Moreover, due to these complications in late preterm births, there is a relatively high rate of admission to the neonatal intensive care unit (NICU), which amounts to the high cost of late preterm births. The total cost of late preterm births is derived not only from neonatal care but also from antenatal care, intrapartum care and long-term medical, educational and social services [25,28].

The management of preterm labour remains a challenge for the obstetrician as it is encountered with a lot of anticipated risk for both mother and foetus [29]. In the recent past, obstetricians have become increasingly comfortable with late preterm deliveries. Therefore, many obstetricians have had a low threshold for labour induction during this late preterm period, and minimal efforts are taken to extend the pregnancy beyond 34 weeks of gestation. The low threshold for labor induction after 34 weeks of gestation can be attributed to two main factors: the consideration of physiological similarity between term and late preterm neonates and the findings of low neonatal morbidity and mortality in late preterm infants from previous studies [30,31]. However, this is no longer accepted as an unanticipated rate of complications are demonstrated in the late preterm neonates.

Neonatologists are now considering biological differences among late preterm neonates and evidence is upcoming for increased perinatal morbidity and mortality. It is imperative to appreciate the complications that this cohort is facing. If the gravity of the problem is severe, it is essential to develop interventions to prevent unnecessary late preterm births and need to improve management facilities for late preterm neonates. Additionally, further studies are required to determine the optimal timing for delivery in the late preterm period, balancing the risk of intrauterine fetal death against early neonatal complications. In Sri Lanka, this cohort has not yet been evaluated. Therefore, the present descriptive study is designed to identify and evaluate the gravity of late preterm birth, early neonatal complications, and outcomes in a Sri Lankan cohort of late preterm infants.

Methods

Study design and sample collection

This is a retrospective, descriptive study performed on late preterm infants born between 34 weeks and 36 weeks + 6 days between January and July 2017 at Teaching Hospital, Peradeniya, Sri Lanka. Peradeniya Teaching Hospital is a prime tertiary care hospital affiliated with the University of Peradeniya, Sri Lanka. The neonatal unit (NICU + special care baby unit (SCBU)) here is a level IV unit; a regional neonatal unit. The total number of deliveries, preterm deliveries and late preterm deliveries during the study period were collected. Baseline characteristics of pregnancies that are known or potential predictors of the outcome were measured. The effects of confounding variables were considered. Socio-demographic characteristics of late preterm neonates, maternal age, parity, mode of delivery, gender and birth weight (obtained within one hour of birth) of neonates were recorded. Birth weight less than 2500 g was defined as low birth weight according to the World Health Organization [32].

Short-term neonatal complications including respiratory distress, hypothermia, hypoglycemia, hyperbilirubinemia, infection, sepsis and feeding difficulties developed in the first two weeks of life or hospital stay were described. Furthermore, the mode of management and admission to the neonatal unit were recorded. All information was collected from the bed head tickets and other hospital records, retrospectively and authors had no access to information that could identify the individual study participants during or after collection of data. The data were accessed on 19th October 2017. The study was carried out adhering to the principles and ethical guidelines of 1975 Helsinki declaration. Ethical clearance for the study was approved by the Ethics Review Committee, National Hospital Kandy, Sri Lanka. The permission to trace hospital records was obtained from the director of Teaching Hospital, Peradeniya and in-charges of relevant units at the hospital.

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Inclusion and exclusion criteria

Late premature neonates were diagnosed by their gestational age at the time of delivery and neonates delivered between 34 weeks and 36 weeks + 6 days were included in the study. Pregnancies which are dated ultrasonically between 11 weeks to 13 weeks + 6 days by the crown to rump length and between 14 weeks to 20 weeks by head circumference and only low risk, uncomplicated singleton pregnancies up to the time of delivery were selected for the study.

Pregnancies that were not dated ultrasonically as mentioned above were excluded from the study even though those neonates were delivered in the late preterm gestation period according to the maternal last menstrual period. Furthermore, neonates who were born following complicated pregnancies like gestational hypertension, diabetes, pre-labor premature rupture of membranes, major congenital anomalies and multiple pregnancies were also excluded from the study.

Statistical analysis

The sample size (n) was calculated using the following formula according to the criteria described elsewhere.

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

(t =1.96; confidence level at 95%, p = 9%; estimated prevalence, m = 10%; relative precision)

The calculated final sample size was 31. The data were summarized into a Microsoft office excel worksheet and the statistical analysis was performed using Statistical Software for Social Sciences (SPSS version 20.0®). The descriptive statistics of the variables were calculated. The numerical and categorical variables were presented as mean ± standard deviation and frequency/percentage, respectively. The categorical variables were compared using the chi-square test. A post hoc analysis was performed to determine the difference between categorical variables. A p-value < 0.05 was set as statistically significant.

Results

During the course of the study period, 4642 neonates were born in this tertiary care hospital, of which 4197 were term and 445 were preterm (9.6%) babies. Of the total preterm neonates, 341 (76.6%) were late preterm and this was 7.3% of all newborns delivered in the study setting. According to inclusion and exclusion criteria, the purposive sample of 138 late preterm neonates were selected for the present study.

Characteristics of late preterm neonates

The baseline characteristics of the study subjects and their mothers were summarized in Table 1. In brief, majority (56.5%) of the late preterm neonates were born in 36th gestational week with an average age of 251 (35 weeks and 6 days) ± 6 days and comprised an equal number of males and females. A large proportion (46%) of neonates were born through emergency caesarian section, followed by normal vaginal delivery (40%) and elective caesarian section (14%). Almost 2/3rd of the subjects had low birth weight and 42.8% were admitted to neonatal unit. The mothers of the neonates were approximately 30 years old on average and had a median parity of 2 (range: 1–6).

Short-term neonatal complications

Of the total subjects, only one death occurred and 68 (49.3%) experienced at least one of the measured neonatal complications (Table 2), of which 59 (86.8%) were admitted to the neonatal unit. The neonatal unit stay on average was 14 days, ranged 3–42 days. Jaundice was the highest prevalent complication, followed by infection and sepsis and respiratory distress. Neonates with low birth weight was more likely to develop more complications (p=0.0001) and be admitted to neonatal unit (p=0.0001). Vaginal delivery caused significantly fewer short-term neonatal complications than other modes of delivery (p<0.0001).

Table 1: Baseline characteristics of the study population.

Variables	Descriptive statistics
Neonatal age (Mean±SD), *days*	251 ± 6
Births in following weeks of gestation, *n*	
·34 weeks	19
·35 weeks	41
·36 weeks	78
Gender of the neonates, *n*	
·Male	69
·Female	69
Birth weight (Mean±SD), *g*	2334.6 ± 586.17
·< 2500 g, *n*	88
·> 2500 g, *n*	50
Admissions to	
·Neonatal unit (NICU+SCBU), *n*	59
·Postnatal ward, *n*	79
Maternal age (Mean±SD), *years*	29.8 ± 5.3
Parity (Median), *n*	2
Modes of Delivery, *n*	
·Emergency caesarian section	63
· Elective caesarian section	20
· Normal vaginal delivery	55

Note: *n*; frequency, SD; standard deviation

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Table 2: Short-term neonatal complications of the study population.

Short-term complications	Frequency
Neonatal unit admission	59
Jaundice	48
Infection and sepsis	38
Respiratory distress	33
Hypothermia	24
Feeding problem	22
Hypoglycemia	7
Death	1

The neonatal complications were stratified based on the gestational age of the neonates; Category 1: 34 weeks to 34 weeks and 6 days, Category 2: 35 weeks to 35 weeks and 6 days, Category 3: 36 weeks to 36 weeks and 6 days and assessed (Figure 1).

It was evident that there is a significantly higher risk of developing short-term neonatal complications in late preterm neonates born between 34 weeks and 34 weeks + 6 days. The risk of getting admitted to neonatal unit, developing jaundice, infection and hypothermia is significantly higher in the neonates born in 34 weeks than those born later.

Management of short-term neonatal complications

Further, we analyzed different management modes practiced in the setting to overcome short-term neonatal complications (Table 3).

The majority (81.2%) of late preterm neonates with jaundice were treated with single phototherapy. Of the neonates with infection and sepsis, 31.6% had severe infection as they were treated with third-line antibiotics. Supplementary oxygen treatment via nasal prone (30.3%) and incubator care (62.5%) were the most used methods to manage respiratory distress and hypothermia, respectively. Moreover, only 5.1% (7/138) was reported with hypoglycemia and were managed with dextrose bolus followed by infusion. A total of 22 (15.9%) neonates had feeding difficulties and the mean number of days to establish full feeds was 3.11 days.

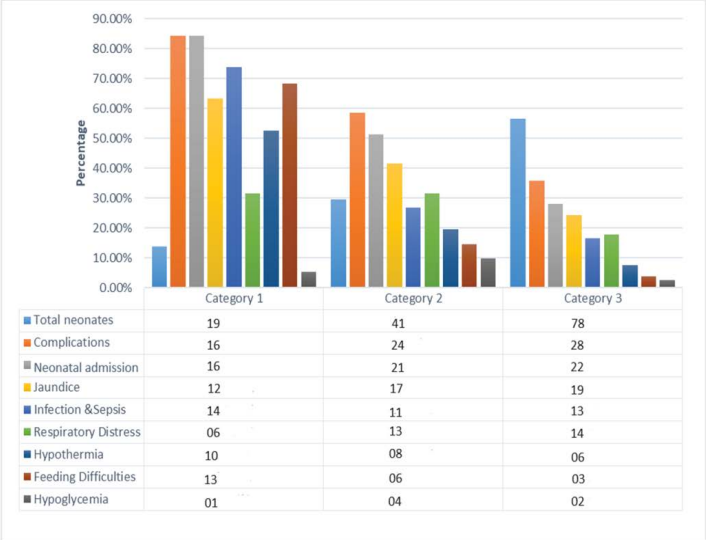

Figure 1: Incidence of short-term neonatal complications stratified by gestational age.

Table 3: Modes of management for short-term complications in late preterm neonates.

Short-term complications	Mode of management	Frequency	Percentage
Hyperbilirubinemia (n = 48)	Single Phototherapy	39	81.2
	Double Phototherapy	9	18.8
	Exchange Transfusion	0	0
Infection and Sepsis (n = 38)	First-line antibiotics	13	34.2
	Second-line antibiotics	13	34.2
	Third-line antibiotics	12	31.6
Respiratory Distress (n = 33)	Oxygen Via face mask	7	21.2
	Oxygen via a head box	5	15.2
	Oxygen via Nasal prone	10	30.3
	Oxygen via CPAP	9	27.3
	IPPV	2	6
Hypothermia (n = 24)	Warmer care	9	37.5
	Incubator Care	15	62.5

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Discussion

The foremost reason for the ever-rising incidence of preterm labour is the increasing number of late preterm births which are responsible for three fourth of entire preterm births [3]. Despite that studies done on late preterm neonates were sparse until the recent past. That is because neonatologists thought that those neonates are physiologically and metabolically mature enough to survive extra uterine. But in the recent past, there was emerging evidence confirming higher morbidity and mortality among late preterm neonates. However, there is significant dissimilarity in the morbidity and mortality in this group between countries which may reflect the quality of neonatal care. Especially in developing countries, neonatal morbidity and mortality tend to be higher than in developed countries [2]. Among other developing countries and neighboring countries, Sri Lanka has the best figures for perinatal morbidity and mortality.

In this study, magnitude of short-term neonatal morbidity among late preterm neonates was assessed. It was found that 49.3% of late preterm neonates developed at least one or more measured complications and also 42.8% of late preterm neonates got admitted to the neonatal unit. It was evident that complications such as jaundice, infection, respiratory distress, hypothermia, feeding problems, and hypoglycemia were fairly common among late preterm neonates.

A study done in neighboring country, India, found that 13.3% prevalence of preterm deliveries, of which 95.5% were late preterm births [11]. Altogether late preterm births have accounted for 12.7% of all newborn deliveries. In that study, 13.8% has born between 34 weeks and 34 weeks + 6 days, 25.8% has born between 35 weeks and 35 weeks + 6 days and 60.4% has born between 36 weeks and 36 weeks + 6 days. These figures are in agreement with the present study. In this Indian study, mean birth weight has been 2.56 kg while it is 2.33kg in the present study. They also analyzed the same neonatal complications except for feeding problems and the incidences of complications are different from the present study. Furthermore, in that study authors found a significant association between the period of gestation and the development of hypothermia and respiratory distress in late preterm neonates. In that study, the early neonatal complication with the highest incidence is respiratory distress (23.5%) while in the present study it is neonatal jaundice (34.8%) and respiratory distress is the third commonest complication with 23.9% incidence.

Another study done in the region has found that 10.7% of preterm deliveries and out of them, late preterm births have been responsible for 72.7% [22]. Altogether late preterm births have accounted for 7.8% of all newborn deliveries. In that study, all studied neonatal complications i.e. respiratory distress, hypoglycemia, sepsis, feeding difficulties, and admission to the hospital have been significantly higher in late preterm infants than in term infants ($p<0.001$).

Similar significant clinical importance in late preterm neonates has been found in studies done in the Western world as well. A study done in Texas over 18 years analyzed 250,000 live-born singleton late preterm neonates and found that late preterm neonates accounted for 76% of preterm neonates [9]. In another study done in the United States authors assessed Apgar scores, clinical diagnoses like temperature instability, jaundice, hypoglycemia, suspicion of sepsis, apnoea and bradycardia, respiratory distress, treatment with an intravenous infusion, length of hospital stay, and delay in discharge to home. In addition to that and hospital costs also have been assessed [8]. The median length of stay has been similar for both late preterm and full-term neonates. Both groups have had comparable 1-minute and 5 minutes Apgar scores. However, all other clinical outcomes analyzed have differed significantly between late preterm and full-term neonates. Late preterm neonates have been four times more likely to be diagnosed with at least one neonatal complication compared to term infants and have been three and half times more likely to be diagnosed with more than one neonatal complication.

There are a few other relevant entities that have not been assessed in the present study. Assessment of possible long-term complications among late preterm neonates was not the scope of the present study. Risks of late preterm births do not confine to the neonatal period and also extend beyond the first month of life. Those are not only morbidities but also related to mortality. In one study authors have concluded that long-term neurodevelopmental consequences are higher even in infants born at 34 to 36 weeks [23]. In another study, authors have shown an association between low birth weight and poor mental and emotional well-being [33]. The average birth weight of late preterm neonates is lower than that of full-term neonates and it was proved in the current study as well.

A study done in the United States over 8 years has focused on the mortality of late preterm neonates during infancy [10]. Their infant mortality rate has been three times higher in late preterm infants than in term infants (7.9 versus 2.4 deaths per 1000 live births). And authors have suggested using these findings in obstetrical and pediatric decision-making.

Other than the unfavorable clinical sequelae linked with late preterm infants, the financial cost to the family and the country cannot be neglected. It has been proven that late preterm birth is associated with significantly increased economic costs over the first two years of life [24]. Authors have suggested using their economic estimates to inform budgetary and service planning by clinical decision-makers.

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There were several strengths associated with this study. There was a uniformity of obstetric and neonatal care as data was gathered from an obstetric unit and a neonatal unit. As complicated and high-risk pregnancies like gestational hypertension, diabetes, and multiple pregnancies were excluded, confounding factors are minimal.

This study also has several limitations. As all subjects were recruited only from a single center, the generalizability of results will be a question. Another limitation may be a failure to categorize subjects according to maternal race, body mass index, and administration of antenatal corticosteroids. Sub-group analysis was not done according to these factors and these may have an impact on the outcome. As the study is retrospective, diagnosis of neonatal complications was done by the attending neonatologist at that particular time. However, all were using unit protocol or guidelines for the diagnosis. This must have minimized the inter-practitioner variability. Similarly, this study did not focus on long-term outcomes of late preterm births and hospital re-admissions, and at the same time, it was not objective. Also, current study did not look into mortality beyond the first month of life.

Conclusion

This study concludes the presence of significant neonatal morbidity within this late preterm cohort. Nearly 50% of neonatal morbidity and 42.8% of admissions to neonatal unit deserve re-examination of obstetric practice regarding the timing of delivery after 34 weeks of gestation. With these results can be hypothesized that late preterm neonates are behaving differently from their term counterparts. A more conservative approach should be considered in managing these pregnancies, especially between 34 weeks and 34 weeks + 6 days as complication rates were highest in this category.

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Conflicts of interests

The authors declare that they have no competing interests.

Authors' contributions

Champika G. Maggonage**:** conceptualization, formal analysis, data curation, methodology, writing – original draft preparation

Lakshrini Gunarathne: conceptualization, formal analysis, methodology, writing – original draft preparation

Sandya Bandara: Investigation, methodology, writing – review & editing

Sibra R. M. Shihab: software, writing – critical review & editing

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