

Late-preterm birth in a level III hospital: incidence and associated morbidity

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Abstract

Introduction: Late-preterm infants are physiologically and metabolically immature and have important risk of morbidity and mortality.

Aim: To analyze the incidence of late prematurity and its associated morbidity and mortality at a level III hospital between 2011 and 2013.

Methods: This was a descriptive and retrospective study of infants born between 34^{+0/7} and 36^{+6/7} weeks' gestation and its associated morbidity and mortality. Medical records were reviewed.

Results: In a 3-year period there were 8,458 births of which 513 (6.1%) were late-preterm infants. Of these, 99/513 (19.3%) had 34 weeks' gestation, 145/513 (28.3%) had 35 weeks' gestation and 269/513 (52.4%) had 36 weeks' gestation. Late-preterm birth rate was 5.7% in 2011, 6.9% in 2012 and 5.6% in 2013 ($p = 0.08$).

In relation to birth weight, 269 (52.4%) of late-preterm infants had low birth weight. There was an association between gestational age and birth weight ($p = 0.002$).

Of the 513 late-preterm infants, 177 (34.5%) were admitted to the Neonatal Intensive Care Unit (NICU) and more often at 34 weeks' gestation (69/99, 69.7%) than at 35 (57/145, 39.3%) and 36 (51/269, 19.0%) weeks' gestation ($p < 0.001$). Most frequent clinical diagnoses were hyperbilirubinemia (112/177, 63.3%), feeding difficulties (111/177, 62.7%), transient tachypnea of the newborn (71/177, 40.1%), hypoglycemia (38/177, 21.5%), intrauterine growth restriction (33/177, 18.6%). Average length of hospitalization was 12 days. Newborns of 34 weeks' gestation were longer admitted than newborns of 35 and 36 weeks' gestation (15.3 vs 9.8 vs 10.8 days; $p = 0.002$). There was one death due to sepsis after surgical correction of gastroschisis.

Conclusion: The incidence of late-preterm birth remained stable between 2011 and 2013. Late-preterm hospitalization rate in the NICU was 34.5%. Hyperbilirubinemia, feeding difficulties and respiratory disease were the main diagnosis. Late-preterm of 34 weeks' gestation were admitted more frequently and for longer periods than the remaining newborns. It's important to pay particular attention to this group of infants.

Keywords

Late-preterm infant, birth rate, birth weight, immature, morbidity, mortality.

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Introduction

Preterm birth is defined as birth that occurs until the 37th week (259th day) of pregnancy. Late-preterm infants are premature newborns delivered between 34^{+0/7} and 36^{+6/7} weeks of gestation [1, 2]. In Europe and other developed countries, preterm delivery rates reported are generally 5-9%, and about 60-70% of preterm births occur at 34-36 weeks' gestation. The preterm birth rate has risen in most industrialized countries [2], in many cases caused by an increase in late-preterm birth rate [3]. In Portugal, preterm delivery rate decreased from 8.9% in 2008 to 7.8% in 2013 [4].

Late-preterm infants are physiologically and metabolically immature [5]. Increased morbidities related to physiologic immaturity of respiratory, metabolic, neurologic and immunologic systems have been observed in these infants. As a consequence, late-preterm infants are at high risk of developing medical complications that result in elevated rates of morbidity and mortality during birth hospitalization [5, 6]. In addition, late-preterm infants have high rates of hospital readmission during the neonatal period [7, 8].

It is important to know the epidemiology and the actual neonatal morbidities of late-preterm infants. The aim of this study was to analyze the incidence of late prematurity and its associated morbidity and mortality at a level III hospital between 2011 and 2013.

Methods

This was a retrospective and descriptive study of all late-preterm live births (34^{+0/7} to 36^{+6/7} weeks

of gestation) in Braga Hospital (Braga, Portugal) between January 2011 and December 2013.

The total number of infants born in Braga Hospital in the analyzed period, as well as the respective gestational age and birth weight, was provided by the Statistical Office of Braga Hospital. Demographic features of the newborns including gestational age (calculated from onset of the mother's last menstrual period with confirmatory ultrasonography performed between 11^{+0/7} and 13^{+6/7} weeks' gestation or when last menstrual period was unknown, dating was assigned based on the assessment of fetal characteristics in the earliest ultrasonography) and birth weight (in grams, obtained after delivery within one hour after birth) are inserted in electronic medical records.

Late-preterm birth rate was calculated as follows: number of late-preterm newborns/total number of newborns.

Infants that were born between 34^{+0/7} and 36^{+6/7} weeks of gestation and those that needed hospitalization in the Neonatal Intensive Care Unit (NICU) were identified. Relevant clinical information was collected from electronic medical records, namely diagnosis at discharge, need for mechanical ventilation during admission in the NICU, duration of hospital stay, need for readmission and neonatal death.

Criteria of NICU admission were followed according to the protocols used in NICU in Braga Hospital: birth body weight less than 1,900 g; respiratory distress or requirement for oxygen (transient tachypnea of the newborn [TTN], respiratory distress syndrome, pneumonia); clinically significant apnea (> 15 seconds) or bradycardia episode (nonsleeping heart rate < 80 bpm); hypoglycemia (blood glucose level of less than 40 mg/dL in capillary or venous blood sample); temperature instability (core body temperature of less than 36°C); neurologic complications (convulsion, intraventricular or intracranial hemorrhage); hyperbilirubinemia needing phototherapy; clinical or laboratory alterations consistent with sepsis; other complications requiring intravenous fluid infusion (poor feeding, severe hematologic alterations, electrolytic imbalance); need for close monitoring as assessed by a neonatologist. The diagnoses of TTN and respiratory distress syndrome were made in accordance with the following definitions.

- TTN: oxygen supplement requirement during the first 6 hours of life, which decreases during the subsequent 18 hours, improvement in

clinical condition within 6 hours and chest x-ray either normal or showing reduced translucency, infiltrates and hyperinsufflation of the lungs.

- Respiratory distress syndrome: oxygen dependence increasing during the first 24 hours of life, typical radiological findings, showing reduced air content, reticulogranular pattern of the lungs, bronchogram.

Data analysis was made stratifying data for years, birth weight and gestational age. Statistical analysis was performed using IBM® Statistical Package for the Social Sciences® software, version 22.0. Data analysis was performed with the Pearson chi-square test for categorical variables and ANOVA for quantitative variables. Multiple comparisons were adjusted using the method of Bonferroni. Differences were considered statistically significant when $p < 0.05$. Data are reported by absolute number, mean \pm standard deviation, rate and percentage.

Results

A 3-year period was analyzed: there were 8,458 births and of these 513 were late-preterm infants: 99 (19.3%) had 34 weeks' gestation, 145 (28.3%) had 35 weeks' gestation and 269 (52.4%) had 36 weeks' gestation.

The late-preterm birth rate was 5.7% in 2011, 6.9% in 2012 and 5.6% in 2013 ($p > 0.05$). Late-preterm infants accounted for 74% of all preterm newborns in 2011 and 2012, and 56% in 2013, and this decrease was statistically significant ($p < 0.001$) (Tab. 1).

In relation to birth weight, more than half (269/513, 52.4%) of late-preterm infants had low birth weight: a large group had $\geq 2,000$ g and $< 2,500$ g (203/513, 39.6%) and only 6 (1.2%) had very low birth weight. There were no late-preterm infants

with extremely low birth weight ($< 1,000$ g). Late-preterm infants of 36 weeks' gestation had more often birth weight $\geq 2,500$ g, while late-preterm infants of 34 weeks' gestation had more often birth weight $\geq 1,500$ g and $< 2,000$ g (it refers to the ratio of newborns and not to the absolute number). There was a statistically significant association between gestational age and birth weight ($p < 0.001$) (Tab. 2).

Of the 513 late-preterm infants, 177 (34.5%) were admitted in the NICU. Hospitalization rate in the NICU for each group of gestational age was: 69.7% (69/99) at 34 weeks' gestation, 39.3% (57/145) at 35 weeks' gestation and 19.0% (51/269) at 36 weeks' gestation, and the observed difference had statistical significance ($p < 0.001$) (Tab. 3).

Of the late-preterm infants admitted in the NICU, 3 were readmissions: 2 newborns required readmission within the first week of life for hyperbilirubinemia needing phototherapy; a 32-day-old infant needed hospitalization for closing ileostomy (after necrotizing enterocolitis grade 3).

The global mean days of hospitalization was 12 days. The average hospitalization days of late-preterm infants of 34 weeks' gestation (15.3 days) was longer than the average hospitalization days of late-preterm infants of 35 and 36 weeks' gestation (9.8 and 10.8 days, respectively), and this difference was statistically significant ($p = 0.002$) (Tab. 3).

There was one death due to septic shock in an infant submitted to surgical correction of gastroschisis (Tab. 3).

The most frequent diagnoses at discharge among late-preterm infants admitted in the NICU are listed in Tab. 4. Hyperbilirubinemia was reported in 63.3% of cases, feeding difficulties in 62.7% of cases, TTN in 40.1% of cases, hypoglycemia in 21.5% of cases and intrauterine growth restriction in 18.6% of cases.

Table 1. Total of births, preterm infants and late-preterm infants between 2011 and 2013.

	2011	2012	2013	Total	p-value
Total of births (n)	3,000	2,848	2,610	8,458	–
Total of preterm infants (n)	231	266	261	758	–
Total LPT infants (n)	171	196	146	513	< 0.001
34 weeks' gestation (n)	25	35	39	99	–
35 weeks' gestation (n)	43	63	39	145	–
36 weeks' gestation (n)	103	98	68	269	–
Late prematurity rate (%)	5.7%	6.9%	5.6%	6.1%	0.08

LPT: late preterm infants.

Statistically significant at $p < 0.05$.

Table 2. Birth weight for gestational age of late-preterm infants born between 2011 and 2013.

Gestational age (weeks)	Birth weight (grams)				p-value
	≥ 2,500	≥ 2,000 and < 2,500	≥ 1,500 and < 2,000	< 1,500	
34	15	53	26	5	< 0.001
35	51	72	21	1	
36	178	78	13	0	
Total (n, %)	244 (47.5%)	203 (39.6%)	60 (11.7%)	6 (1.2%)	–

Statistically significant at $p < 0.05$.

Table 3. Incidence of NICU admission and readmission, number of days in NICU and mortality in late-preterm infants.

	Gestational age (weeks)				p-value
	34 (n = 99)	35 (n = 145)	36 (n = 269)	Total (n = 513)	
Admission (n, %)	69 (69.7%)	57 (39.3%)	51 (19.0%)	177 (34.5%)	< 0.001
Readmission (n)	0	1	2	3	–
Mortality (n)	0	0	1	1	–
Days in NICU (mean ± SD, min-max)	15.3 ± 12.0 (2-61)	9.8 ± 5.3 (1-25)	10.8 ± 8.7 (1-40)	12 ± 7.3 (1-61)	0.002

SD: standard deviation.

Statistically significant at $p < 0.05$.

Table 4. Most frequent diagnoses reported at discharge for each gestational age.

Most frequent diagnoses at discharge (n, %)	Gestational age			p-value	Total late-preterm infants admitted in NICU (n = 177)
	34 (n = 99)	35 (n = 145)	36 (n = 269)		
Hyperbilirubinemia	47 (47.5%)	37 (25.5%)	28 (10.4%)	< 0.001	112 (63.3%)
Feeding difficulties	48 (48.5%)	38 (26.2%)	25 (9.3%)	< 0.001	111 (62.7%)
TTN	36 (36.4%)	18 (12.4%)	17 (6.3%)	< 0.001	71 (40.1%)
Hypoglycemia	14 (14.1%)	11 (7.6%)	13 (4.8%)	0.010	38 (21.5%)
Intrauterine growth restriction	16 (16.2%)	10 (6.9%)	7 (2.6%)	< 0.001	33 (18.6%)
Early sepsis	7 (7.1%)	4 (2.8%)	8 (3.0%)	–	19 (10.7%)
Intraventricular hemorrhage grade 1^a	15 (15.2%)	1 (0.7%)	1 (0.4%)	–	17 (9.6%)
Thrombocytopenia	7 (7.1%)	7 (4.8%)	3 (1.1%)	–	17 (9.6%)

TTN: transient tachypnea of the newborn.

Statistically significant at $p < 0.05$.

^aAccording to Volpe's classification of intraventricular hemorrhage in Volpe JJ, 2001 [27], pp. 428-93.

Other diagnoses less frequently reported in admitted newborns were polycythemia (6/177, 3.4%), electrolyte imbalance (6/177, 3.4%), respiratory distress syndrome (5/177, 2.8%), seizures (5/177, 2.8%), hypoxic-ischemic encephalopathy (4/177, 2.3%), acute necrotizing enterocolitis (3/177, 1.7%).

Of diagnoses reported at discharge, hyperbilirubinemia (47/99, 47.5%; $p < 0.001$), feeding difficulties (48/99, 48.5%; $p < 0.001$), TTN

(36/99, 36.4%; $p < 0.001$), hypoglycemia (14/99, 14.1%; $p = 0.010$) and intrauterine growth restriction (16/99, 16.2%; $p < 0.001$) were significantly more frequent at 34 weeks' gestation. Intraventricular hemorrhage grade 1 (15/99, 15.2%) was almost exclusive of late-preterm infants of 34 weeks' gestation (**Tab. 4**).

Mechanical ventilation was required in 10.7% (19/177) of infants: non-invasive ventilation was used in 15 newborns and 4 required invasive

ventilation (**Tab. 5**). Late-preterm that needed invasive ventilation were 2 newborns of 35 weeks' gestation with respiratory distress syndrome, 1 newborn of 34 weeks' gestation due to hypoxic-ischemic encephalopathy and 1 newborn of 36 weeks' gestation with sepsis and meningitis caused by *Listeria monocytogenes*.

Discussion

This study showed that in our hospital with a level III NICU there were 8,458 births in a 3 year period and 513 (6.1%) were late-preterm infants. The incidence of late-preterm birth ranged between 5.7% and 6.9% and did not vary significantly over the three years studied. Otherwise, the absolute number of late-preterm infants significantly diminished from 2011 and 2012 to 2013 ($p < 0.001$), although the total number of preterm infants has increased but in a non significant way over the 3 years. The group of newborns of 36 weeks' gestation was, globally, the most prevalent in the period studied, accounting for more than half of the late-preterm infants.

In Portugal, the number of live births decreased between 2011 and 2013 by about 14.5% (from 96,856 in 2011 to 82,787 births in 2013) and the same trend was observed in the overall number of premature live births, a decrease of about 9.9% (from 7,191 in 2011 to 6,476 in 2013) [4]. In relation to late-preterm there are few data in the literature nationwide. This issue had been studied at a Portuguese level III maternity in 2009, which reported a late-preterm birth rate of 6.4%. More than half of these late-preterm infants were of 36 weeks' gestation [10]. These data are similar to those described in this study.

The Portuguese study [10] also indicated an increase in late-preterm birth rate between 2008 and 2009. This trend was not observed in our study; however, the time period considered is different, and these variations can be justified in a time of rapid and major changes in terms of birth rate.

Worldwide this theme has been discussed. Some studies reported an incidence of late prematurity ranging from 5.9% to 11.4% [3, 11-16]. Incidence of late-preterm births reported in our study (6.1%) is slightly lower than the incidence observed in the United States (US) in the same period (8.1% in 2012) [14], but in line to rates reported by another single centre study performed by a level III unit in Europe (5.9% in 2005-2009) [15]. In the US report, late-preterm birth rate slightly decrease between 2010 and 2012 from 8.5% to 8.1% [14].

The percentage of hospitalization in the NICU was 34.5% in this group of infants and there was a higher rate of NICU admission at 34 weeks' gestation (69.7%). These data are similar to that observed in other series [10, 12, 15, 16, 18]. Late-preterm infants of 34 weeks' gestation were also longer admitted than the remaining late-preterm infants. These data reveal the high morbidity and consumption of healthcare resources associated with late-preterm, which decrease with the increase in gestational age, as previously described in other studies [7, 11-13].

It was observed a decreasing trend in the frequency of morbidities with the increase in gestational age. Hyperbilirubinemia, feeding difficulties, respiratory disease, hypoglycemia and intrauterine growth restriction were the main diagnoses observed, and they were significantly more frequent at 34 weeks' of gestation in our group of study. These are the most frequent causes of morbidity associated with late-preterm birth in other studies [7, 10-12]. This is understood given physiologic immaturity associated with premature birth.

TTN and respiratory distress syndrome are more frequent in this group related with pulmonary dysfunction due to lack of clearance of lung fluid and/or relative deficiency of pulmonary surfactant, respectively [19, 20]. Our study reported a higher incidence of TTN at 34 weeks' gestation comparing with a large retrospective multicenter study in the US (36.4% vs 6.4%) [16]. That study also reported

Table 5. Need for mechanical ventilation during admission in the NICU for each gestational age.

	Gestational age			Total late-preterm infants admitted in NICU (n = 177)
	34 (n = 99)	35 (n = 145)	36 (n = 269)	
Mechanical ventilation (n, %)	9 (9.1%)	8 (5.5%)	2 (0.7%)	19 (10.7%)
Not invasive	8 (8.1%)	6 (4.1%)	1 (0.4%)	15 (8.5%)
Invasive	1 (1.0%)	2 (1.4%)	1 (0.4%)	4 (2.3%)

a high incidence of respiratory distress syndrome at the same gestational age (10.5%) not seen in our group. Other single center study reported incidence of 33.1% for TTN at 34 weeks' gestation [15], similar to our results. On the other hand, requirement of invasive mechanical ventilation at 34 weeks' gestation in our study was substantially lower than reported in the same US study (1.0% vs 9.1%) [16]. Some possible causes are in relation with illness severity, prenatal management and possible different approaches to respiratory morbidity. Our results showed that mechanical ventilation was needed in an important number of late-preterm infants admitted to the NICU, however about 80% of these cases only required non-invasive ventilation.

Late-preterm infants have also higher incidence of prolonged physiologic jaundice and thus remain vulnerable for brain damage from jaundice for longer periods compared with term infants [20, 21]. In late-preterm infants, deglutition, peristaltic functions and sphincter controls are immature, which may lead to difficulty in coordinating suck and swallowing, a delay in successful breastfeeding, poor weight gain and dehydration [20-22]. Also metabolic instability during the first hours of life is more common in this group, showing greater susceptibility to hypoglycemia, probably due to decrease glycogen storages, stress and thermoregulation and feeding difficulties [21].

Intrauterine growth restriction is a frequent co-morbidity in preterm infants and may also contribute to the increased morbidity and mortality observed among these infants. Moreover, these infants are at risk for hypoglycemia, intraventricular hemorrhage, prolonged hospital stay and increased need for NICU treatment, thus demonstrating the greater severity of these cases [23-25].

The observation of intraventricular hemorrhage grade 1 was almost exclusively of late-preterm infants of 34 weeks' gestation and we found a higher incidence comparing to other studies, which published incidence rates between 0.5% and 2.82% [11-13]. In this studies intraventricular hemorrhage was defined according to Papile and colleagues [26]. In our unit the diagnosis of intraventricular hemorrhage is performed by ultrasonography and it is defined according to Volpe's classification of intraventricular hemorrhage [27]. At 34 weeks' gestation, brain volume is about 65% of term infants and is still an immature brain that can be damaged

by adverse conditions [20, 21]. In addition to apparent health concerns, there is growing recognition that this population may have more subtle neurodevelopmental issues. Some studies have demonstrated that late-preterm infants have poorer school performance and increased risk of psychomotor developmental delay [17].

A limitation of this study is related to its retrospective nature. Data were obtained from medical records already made and not designed specifically for this study. Our study was restricted only to the morbidity identified in the neonatal period and not to the long term follow-up. Finally, pregnancy complications associated with late premature births have not been evaluated. These can adversely affect neonatal outcome independently of late prematurity. However, some studies have shown a high risk of neonatal morbidity associated with late-preterm independently of pregnancy complications [28, 29].

Our data show a stability of late-preterm birth rate in the three years studied, although with a decrease in absolute number of late-preterm infants in 2013. More than a third of late-preterm infants required hospitalization in the NICU and more often and for longer periods at 34 weeks' gestation. These data reveal the high frequency of morbidity that occurs in this group of newborns, and which tends to decrease with the increase in gestational age. Hyperbilirubinemia, feeding difficulties, respiratory disease, hypoglycemia and intrauterine growth restriction were the main problems identified and they should be particularly evaluated and carefully managed in these infants.

Late-preterm births constitute a significant proportion of preterm births and it is important to monitor epidemiological trends and study clinical outcomes. Because of significant neonatal complications among these infants, a re-assessment of optimal obstetric and neonatal care is needed so that clinical management can be better directed toward optimal outcomes. The authors highlight the importance of paying particular attention to this group of infants.

Declaration of interest

The Authors declare that there is no conflict of interest.

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