

Early term infants are at increased risk of requiring neonatal intensive care

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Background: Increasing evidence is demonstrating that infants born early on during the term period are at increased risk of morbidity compared with infants born closer to a complete 40 week gestational pregnancy. The purpose of this study was to compare early term [gestation age (GA): 37-37 6/7 weeks] neonatal outcomes with those of other full term neonatal intensive care unit (NICU) admissions.

Methods: Retrospective chart review of all term infants admitted to the NICU at New York University Langone Medical Center over a 17 month period. Subjects were grouped and analyzed according to their GA at birth: 1) early term infants (GA between 37 0/7 to 37 6/7 weeks) and 2) other term infants (38 0/7 weeks and older).

Results: Early term infants were more likely to require NICU care than other term infants [relative risk: 1.42, 95% confidence interval (CI)=1.07-1.88, $P=0.01$]. In the NICU, they are more likely to manifest respiratory distress syndrome [odds ratio (OR)=5.7, 95% CI=1.6-19.8, $P<0.01$] and hypoglycemia (OR=4.6, 95% CI=2.0-10.4, $P<0.001$). In addition, early term neonates were more likely to be born via elective cesarean section than other term neonates (OR=4.1, 95% CI=2.0-8.5, $P<0.001$).

Conclusions: Being born at early term is associated with increased risk of respiratory disease and hypoglycemia requiring neonatal intensive care. Further efforts directed at decreasing early term deliveries may be warranted.

World J Pediatr 2016;12(1):76-81

Key words: gestational age;
hypoglycemia;
neonatology;
respiratory distress syndrome

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doi: 10.1007/s12519-015-0049-8
Online First November 2015

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Introduction

There has been extensive research in the field of pediatrics describing the morbidity and mortality related to prematurity. It is well established that full term neonates are at lower risk for morbidity and mortality than their preterm counterparts. However, to restrict neonatal health to this dichotomy is an oversimplification. Originally thought to have similar risks as full term neonates, late preterm (LPT) neonates (formally referred as near term neonates) born between 34 weeks and 36 6/7 weeks have been shown to manifest morbidities often times similar to premature neonates.^[1] Common examples include breathing difficulties associated with lung immaturity and hypoglycemia, which have been shown to be the most common reason for LPT admission to the neonatal intensive care unit (NICU).^[2] Therefore, other subgroups, such as early term neonates, should also be investigated.

Early term neonates are defined as those infants delivered at a gestation age (GA) between 37 weeks and 37 6/7 weeks. This group accounts for approximately 27% of all deliveries, a value at least three times that of LPT infants.^[3] This proportion has increased since 1990, when the prevalence was 19%, and is correlated with a general decrease in GA among live births.^[4] There are likely many factors that led to these changes, which includes a rise in elective cesarean sections.^[5] Compared to their full term counterparts, there is growing evidence that early term neonates are predisposed to increased rates of mortality, risk of NICU admissions, and metabolic, neurologic, and respiratory morbidities.^[6-11] They also have been shown to have worse long-term developmental outcomes, including increased utilization of healthcare in the first year of life, and increased risk of asthma, attention deficit hyperactivity disorder, and poor school performance.^[12-16] While some attention has been brought to this population, physicians, nurses, and parents do not always recognize the full ramifications of being born marginally early.^[17]

As stated, there is previous literature investigating issues associated with being born during the first week of the classically defined term period. In order to add

to the knowledge base and determine if this principle can be applied to many different populations, we planned an analysis of our own experience with this age group of infants. Therefore, we set out to compare for any differences between early term neonates and their full term counterparts in regards to rates of NICU admission, prevalence of commonly found morbidities and subsequent interventions, means of admission, maternal and antenatal characteristics, and modes of delivery. Our aims were to determine if our own hospital data supports the findings of previous investigators examining issues related to early term neonates and to also further identify other factors that may be associated with the morbidity associated with this group of infants.

Methods

Study design

We conducted an institutional review board approved retrospective chart review (New York University Institutional Review Board, No. 08782) as part of an overall quality improvement process. The study population consisted of all neonates with an estimated GA of 37 0/7 weeks or more from the institutional census records, delivered at New York University Langone Medical Center and admitted to the NICU over a 17 month period. Additionally, we used data looking at all medical center full term births during this same period. Neonates with major congenital lesions, genetic syndromes, 5 minute Apgar scores of less than 3, and patients transferred from other institutions were excluded. After accounting for the excluded subjects and those who did not have complete chart information, the remaining subjects were grouped and analyzed according to their GA at birth: 1) early term infants (GA between 37 0/7 to 37 6/7 weeks) and 2) other term infants (38 0/7 weeks and older).

Odds ratios were calculated to compare the odds of specific factors associated with the early term group and with the two older full-term groups. Relative risk ratios and Chi-square statistics were also performed for select variables. Factors studied included respiratory disease and hypoglycemia, which had been found previously to be the two most common reasons for NICU admission in our NICUs. In addition, the NICU course for each subject was also analyzed based on the type of delivery preceding the NICU admission. Confidence intervals and *P*-values for the odds ratios and relative risks were calculated; *P*-values <0.05 were considered significant.

Clinical definitions

Respiratory distress was defined as the need for oxygen supplementation due to tachypnea, grunting, nasal flaring, retractions, or cyanosis as noted by the admitting

neonatologist. Respiratory distress syndrome (RDS) was defined as infants with respiratory distress requiring some form of supplemental oxygen and/or ventilatory support, along with a chest radiograph officially read as being consistent with RDS by a pediatric radiologist. In addition, labeling a patient with this diagnosis was based on the documentation noted by the admitting neonatologist. Transient tachypnea of the newborn was diagnosed in infants with clinical signs of respiratory distress in the first few hours of life that resolved within 18 hours of life and radiographic findings of fissure edema. Meconium aspiration syndrome (MAS) was diagnosed if neonates demonstrated respiratory distress in conjunction with a history of meconium being present at birth. In addition those infants needed to have a chest radiograph demonstrating patchy infiltrates, and a clinical diagnosis of MAS in the chart. Hypoglycemia was defined as an infant with a plasma glucose concentration of less than 40 mg/dL.

Results

NICU admissions

During the study period, 5979 term births occurred at NYU Langone Medical Center and 7% of those, 415, were admitted to the NICU. Of those admitted to the NICU, 63 were excluded based on the criteria previously described and 43 charts were not fully available. Of the remaining 303 subjects, 57 (19%) were early term, and the remaining 246 neonates (81%) were 38 0/7 weeks or older at birth. Early term neonates were admitted to the NICU at a higher rate than other full term neonates (6.8% vs. 4.8%) (Table 1). This is equivalent to a relative risk ratio of 1.42 [95% confidence interval (CI)=1.07-1.88, *P*=0.01].

Patient demographics

The largest percentage of full term NICU admissions were male and of Caucasian ethnicity (Table 2). Birth and discharge weight significantly increased, as expected, with increasing GA. In addition, a significantly greater percentage of early term neonates were twins. Otherwise, there were no other statistically significant baseline characteristic differences between the early term and other term subjects.

Table 1. Rates of hospital births and NICU admissions for early term vs. term neonates

Variables	GA 37 0/7-37 6/7 wk	GA ≥38 0/7 wk
Proportion of all term births, %	14.0 (839/5979)	86.0 (5140/5979)
Proportion of term NICU admissions, %	18.8 (57/303)	81.2 (246/303)
Proportion requiring NICU care, %	6.8 (57/839)	4.8 (246/5140)

NICU: neonatal intensive care unit; GA: gestation age.

Respiratory and glucose issues: diagnosis and intervention

Early term neonates in the NICU had greater odds of having respiratory distress syndrome (RDS) [odds ratio (OR)=5.7, 95% CI=1.6-19.8, $P<0.01$] and hypoglycemia (OR=4.6, 95% CI=2.0-10.4, $P<0.001$) compared to other term NICU admissions (Table 3). There was a trend demonstrating that early term neonates could be more likely to demonstrate transient tachypnea of the newborn, but the OR was not statistically significant. There was no statistically significant association for pneumonia. There was a trend showing that full term neonates had higher rates of pneumothorax, but this was not statistically significant.

In terms of respiratory interventions, early term neonates had greater odds of needing oxygen (OR=2.2, 95% CI=1.2-4.0, $P=0.01$) and receiving nasal cannula (OR=2.2, 95% CI=1.2-4.1, $P=0.01$) or continuous positive airway pressure (CPAP) (OR=5.6, 95% CI=2.0-15.5, $P<0.01$) treatment compared to other full

term neonates (Table 3). There were no statistically significant associations for the other respiratory interventions. There was also no statistical difference in regards to mean length of stay in the NICU.

Table 2. Baseline subject demographics

Characteristics	GA 37 0/7-37 6/7 wk (n=57)	GA \geq 38 0/7 wk (n=246)	P value
Sex			
Male, %	51 (29/57)	59 (146/246)	NS*
Female, %	49 (28/57)	41 (100/246)	NS*
Ethnicity			
White, %	82 (47/57)	71 (175/246)	NS*
Black, %	4 (2/57)	5 (13/246)	NS*
Hispanic, %	5 (3/57)	7 (17/246)	NS*
Asian, %	5 (3/57)	14 (35/246)	NS*
Others, %	4 (2/57)	2 (6/246)	NS*
Birth weight (kg)	2.88 \pm 0.06	3.38 \pm 0.03	<0.001 [†]
Discharge weight (kg)	2.88 \pm 0.06	3.36 \pm 0.03	<0.001 [†]
5 min Apgar score	9	9	NS [†]
Twin birth, %	16 (9/57)	2 (5/246)	<0.001*

GA: gestation age; NS: not significant. *: Chi-square test; †: Student's *t* test.

Table 3. Prevalence of respiratory disease and hypoglycemia during neonatal intensive care unit course

Variables	GA 37 0/7-37 6/7 wk (n=57)	GA \geq 38 0/7 wk (n=246)	Prevalence odds ratio (95% CI)	P value
RDS, %	11 (6/57)	2 (5/246)	5.7 (1.6-19.8)	0.006*
TTN, %	19 (11/57)	15 (36/246)	1.3 (0.6-2.8)	NS*
Pneumonia, %	0 (0)	1 (3/246)	N/A	N/A
Pneumothorax, %	2 (1/57)	6 (14/246)	0.3 (0.04-2.4)	NS*
Oxygen, %	47 (27/57)	29 (72/246)	2.2 (1.2-4.0)	0.01*
CPAP, %	16 (9/57)	3 (8/246)	5.6 (2.0-15.5)	<0.01*
NC, %	46 (26/57)	27 (67/246)	2.2 (1.2-4.1)	0.01*
HFV, %	0 (0)	0 (0)	N/A	N/A
Surfactant, %	2 (1/57)	0 (0)	N/A	N/A
Hypoglycemia, %	23 (13/57)	6 (15/246)	4.6 (2.0-10.4)	<0.001*
Mean length of stay (d)	3.5 \pm 0.4	3.4 \pm 0.2		NS [†]

GA: gestation age; RDS: respiratory distress syndrome; TTN: transient tachypnea of the new born; CPAP: continuous positive airway pressure; NC: nasal cannula; HFV: high frequency ventilation; CI: confidence interval; NS: not significant; N/A: not applicable. *: Chi-square test; †: Student's *t* test.

Table 4. Maternal history and delivery characteristics of early term and term NICU admissions

Variables	GA 37 0/7-37 6/7 wk (n=57)	GA \geq 38 0/7 wk (n=246)	Prevalence odds ratio (95% CI)	P value
Mean age (y)	33.5 \pm 0.7	32.7 \pm 0.3	N/A	NS [†]
Mean gravida	2.5 \pm 0.2	2.0 \pm 0.0	N/A	NS [†]
Mean para	0.8 \pm 0.2	2.0 \pm 0.6	N/A	NS [†]
PROM, %	9 (5/57)	14 (34/246)	0.6 (0.2-1.6)	NS [‡]
Induction, %	0 (0)	4 (9/246)	N/A	N/A
Chorioamnionitis, %	16 (9/57)	47 (116/246)	0.2 (0.1-0.5)	<0.001 [‡]
Preeclampsia, %	11 (6/57)	3 (8/246)	3.5 (1.1-10.8)	0.03 [‡]
Diabetes, %	11 (6/57)	4 (10/246)	2.8 (0.9-8.1)	NS [‡]
Overall rate of C/S*, %	37 (309/839)	29 (1480/5140)	1.4 (1.2-1.7)	<0.001 [‡]
Previous C/S, %	18 (10/57)	8 (19/246)	2.5 (1.1-5.9)	0.03 [‡]
C/S NICU admissions, %	60 (34/57)	49 (120/246)	1.6 (0.9-2.8)	NS [‡]
Elective C/S, %	30 (17/57)	9 (23/246)	4.1 (2.0-8.5)	<0.001 [‡]
Emergency C/S, %	14 (8/57)	20 (48/246)	0.7 (0.3-1.7)	NS [‡]
Other C/S, %	16 (9/57)	20 (49/246)	0.8 (0.3-1.7)	NS [‡]

GA: gestation age; C/S: cesarean section; PROM: premature rupture of the membranes; NICU: neonatal intensive care unit; CI: confidence interval; NS: not significant; N/A: not applicable. *: overall hospital cesarean section rate for gestational age group based on total hospital births; †: Student's *t* test; ‡: Chi-square test.

Antenatal factors

Table 4 demonstrates antenatal factors that were studied. In regards to maternal characteristics of the neonates admitted to the NICU, mothers of early term neonates were more likely to have had a previous cesarean section (OR=2.5, 95% CI=1.1-5.9, $P=0.03$) or preeclampsia (OR=3.5, 95% CI=1.1-10.8, $P=0.03$) compared to other term neonates. They also tended to more often present with diabetes, but this association was not found to be statistically significant. Furthermore, mothers of early term neonates had much lower odds of having chorioamnionitis compared to the other term neonates. There was no statistically significant association for induction or premature rupture of membranes.

Modes of delivery

Of all neonates born in the study time period, early term neonates were more likely to be delivered via cesarean section (OR=1.4, 95% CI=1.2-1.7, $P<0.001$) (Table 4). Specifically, of the full-term neonates admitted to the NICU, the early term neonates were four times more likely to be born via elective cesarean section than other term neonates (OR=4.1, 95% CI=2.0-8.5, $P<0.001$).

Means of admission: direct admission versus from the newborn nursery

Direct admission was the most prevalent mode of NICU admission in all NICU admission age cohorts. However, early terms NICU admissions were much more likely to be admitted to the newborn nursery first, and then admitted to the NICU, compared to older full term NICU admissions (OR=4.1, 95% CI=2.0-8.5, $P<0.001$).

Discussion

We believe this to be the first study that compares early term neonates to other full term neonates analyzed from a strictly neonatal intensive care setting. The information reported here demonstrates that early term infants (GA 37 0/7-37 6/7 weeks) make up a significant proportion of NICU admissions and supports previous research that shows that this group of infants is at some increased health risks when compared to other term infants. Our findings illustrate that close to one quarter of full term NICU admissions and around 10% of all NICU admissions were comprised of early term neonates. Furthermore, early term infants had twice the risk of being admitted to the NICU as other full-term neonates, a finding of increased risk which has been also demonstrated in other studies.^[18,19]

Our study also shows that early term neonates had

a greater chance of having respiratory morbidities, including manifesting RDS and requiring oxygen and nasal cannula or CPAP support. While early term infants have a lower incidence of RDS than premature infants, RDS in the former group can sometimes be more severe.^[18,20] Although considered mature, infants born in the first week of the term period appear to often still have lung immaturity. This most likely explains the higher rates of respiratory issues.^[21,22]

In regards to the morbidities we were focused on based on our previous LPT research; this study illustrates the fact that early term neonates have a greater chance of manifesting hypoglycemia. Our results are consistent with findings from previous studies examining this population of infants.^[20,23] Such hypoglycemia may have significant effects on both short-term and long-term neurodevelopmental outcomes.^[24-26]

Even with this increased likelihood of morbidities, early term neonates are currently being classified and treated similarly to other full term neonates. Many times they are admitted to the newborn nursery and then later admitted to the NICU. Our findings showed that early term neonates were four times more likely to be admitted to the NICU from the newborn nursery than the other full-term neonates. This finding represents the inconsistent and widely deviating standard of care for the early term population that may exist in many hospital settings. It demonstrates that infants in this age group are often managed just like older full term neonates, but perhaps this policy needs further evaluation and analysis, because they appear to be at much higher risk for needing a NICU admission. Fortunately, there have been some efforts at standardizing and improving the management of this deceptively immature population. For example, Trembath et al^[27] have suggested future quality improvement efforts towards respiratory maintenance, nutrition, and discharge preparation for early term neonates.

In addition to improving the standard of care of these early term infants, much effort also needs to be made to decrease the incidence of early term births. Our data highlight several factors associated with early term births. First, there were significantly increased odds of multiparity, history of cesarean sections, maternal diabetes, and elective cesarean sections in the early term group of infants compared to the other full term infants. The increased likelihood of elective cesarean sections is a particularly notable finding.

This data highlight some of the controversy surrounding early term elective deliveries. Even though the incidence of early term elective deliveries remains substantial, many experts in obstetrics including the American Academy of Obstetricians and Gynecologists have recommended the prevention of

such births.^[16,28,29] Many efforts have been made to decrease the incidence of these early term births,^[30-32] however these improvements have led to ambiguous perinatal outcomes,^[28,33,34] and further research and improvement is needed.

There are some limitations to this study which need to be considered. First, this was a retrospective chart review study of one NICU center at a single hospital. However, this is a large tertiary care hospital with many births annually and cares for a very diverse patient population. In addition, although we had strict definitions we followed for diagnosis of neonatal disease and indications for deliveries, it is based on medical records filled out by physicians and other healthcare providers. In addition, we only studied a specific period of time, and if the study was expanded and included additional subjects, more statistical power could be achieved. We have plans to further study this population and expand the current research.

In summary, this research demonstrates that infants born during the first week of what has traditionally been considered the full term period (GA: 37 0/7-41 6/7 weeks) may actually have not achieved full maturity and are likely to still be at risk of morbidities that can affect premature and LPT infants, specifically in regards to breathing difficulties and hypoglycemia. The data presented shows that these infants are subsequently more likely to require intensive care. In addition, it appears that some deliveries of infants born during the early term period could be avoided if the number of cesarean sections during this time was somehow decreased. Based on these results, previous studies, and estimates of how many early term infants are born each year, it seems apparent that more research looking at this population is required, and that continued strong efforts need to be directed at decreasing early term delivery rates.

Funding: This research was supported by the Division of Neonatology within the Department of Pediatrics at the New York University School of Medicine.

Ethical approval: This was a retrospective chart review study that did require a clearance from the hospital's ethical committee. This study was approved by the New York University Institutional Review Board (No. 08782).

Competing interest: None declared.

Contributors: Mally PV proposed the study and wrote the first draft, is also the guarantor. Agathis NT analyzed the data. All authors contributed to the design and interpretation of the study and to further drafts.

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Received September 15, 2014

Accepted after revision December 18, 2014