Early-term delivery and adverse neonatal outcomes at a tertiary center in Turkey

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Early-term infants incur higher risks for neonatal morbidities compared to full-term infants. In this study, we investigated the neonatal morbidities in early-term infants admitted to a neonatal intensive care unit (NICU). Early-term (37 0/7 and 38 6/7 weeks of gestation) and full-term (39 0/7 and 41 6/7 weeks of gestation) infants born between January 2013 and December 2014 were enrolled in this study. Early-term deliveries accounted for 8,026 (25.7%) of all live births (n = 31,170). The admission rate of early-term infants to the NICU was 7.5%. The most common diagnoses were jaundice (44.2%) and respiratory distress (37.8%). The cesarean section and small-for-gestational-age rates were significantly higher in early-term infants ($p < 0.001$), as were the mean duration of hospital stay, prolonged hospitalization (> 5 days), and readmission rates ($p < 0.05$). Morbidities, including NICU admission, respiratory distress, jaundice, hypoglycemia, feeding difficulty, and dehydration, were also more common in early-term infants ($p < 0.05$). This is the first Turkish study to report on the association of early-term delivery with poor neonatal outcomes. These results should be evaluated by obstetricians when considering the timing of labor induction or planned cesarean delivery. They should also be considered by neonatologists, who need to be aware of the higher risk of neonatal morbidities.

Key words: early-term infants, neonatal morbidities, NICU.

Full-term infants born between 37 and 41 weeks of gestation have been considered to be a homogeneous and low-risk group. Babies born at 37–38 weeks might appear to be as healthy as those born at 39–41 weeks; however, recent studies have revealed that this is not the case [1-4]. Neonatal morbidities such as respiratory distress, feeding difficulties, hypothermia, sepsis, and neonatal mortality are increased in infants born at 37–38 weeks of gestation compared with infants born after 38 weeks[2,5-7]. Furthermore, the increased risk of several long-term childhood morbidities, including cerebral palsy and mental retardation, problems at school, hospital admission up to 5 years of age, asthma, and wheezing, has been reported[8-10].

The American College of Obstetrics and Gynecology (ACOG) recommended the designation of 37–38 completed weeks of gestation as "early-term"[11]. The potential public health impact of early-term deliveries is great since 24.8% of all deliveries in the United States in 2013 occurred at 37 and 38 weeks of gestation[12]. Many studies have focused on infants born at < 37 weeks of gestation, but much less is known about early-term infants. In this study, we investigated the clinical and demographic characteristics and short-term outcomes of early-term infants who were admitted to a neonatal intensive care unit (NICU) in Turkey.

Material and Methods

A retrospective study was conducted at the NICU of Etlik Zübeyde Hanım Women's Health Training and Research Hospital between January

2013 and December 2014. Early-term (born between 37 0/7 and 38 6/7 weeks of gestation) and full-term (born between 39 0/7 and 41 6/7 weeks of gestation) neonates were enrolled in this study. Clinical and demographic data were retrospectively collected from the patients' medical records. This study was approved by the Local Ethics Committee of our institution.

The demographic characteristics of the patients were collated, including sex, gestational age (GA), birth weight (BW), maternal age, maternal or gestational disease, and mode of delivery. GA was determined according to the maternal last menstrual period, early ultrasonography, or postnatal clinical examination results.

The primary outcome measure was admission to the NICU. Secondary outcome measures included respiratory morbidities, a diagnosis of transient tachypnea of the newborn (TTN), duration of hospital stay, prolonged hospitalization (defined as a neonatal hospital stay > 5 days), need for phototherapy, and readmission to the NICU.

Clinical problems related to admission were defined as follows: *Respiratory distress*: respiratory morbidity that required admission of the infant to the NICU irrespective of any diagnostic test or therapeutic intervention. We further identified cases with TTN, meconium aspiration syndrome (MAS), and pneumonia. *TTN*: a benign disease of infants experiencing respiratory distress shortly after delivery that usually resolves within 3–5 days. *Jaundice*: documented, clinically apparent jaundice with laboratory measurement of the serum bilirubin concentration according to American Academy of Pediatrics guidelines[13]. *Sepsis*: at least three of the following: bradycardia or tachycardia, hypotonia, hypotension, cyanosis, apnea, respiratory distress, tachypnea, poor skin color and perfusion, feeding difficulty, irritability, lethargy, elevated acute phase reactant, and positive blood culture. *Perinatal asphyxia*: an Apgar score of < 5 at 5 min and 10 min, and an umbilical artery pH < 7.0, or a base deficit ≥ 12 mmol/L, or both. *Hypoglycemia*: a serum glucose concentration < 45 mg/dl in the first 24 h and < 50 mg/dl thereafter. *Feeding difficulties*: inability to breast or bottle feed, abdominal distension, or vomiting. *Small-for-gestational-age* (*SGA*): infants with a BW below the 10th percentile for their GA based on the growth curves of Fenton[14]. *Polycythemia*: venous hematocrit > 70% or > 65% with symptoms such as hypoglycemia, feeding difficulty, and hypotonia. *Dehydration*: increased weight loss according to postnatal age with hypernatremia or abnormal renal function.

In addition to the clinical problems listed above, hospital stay, rehospitalization, and mortality were also recorded. Neonates were excluded if they had congenital anomalies and malformations (e.g., diaphragmatic hernia, gastroschisis, atresia of the gastrointestinal tract, meningomyelocele, hydrocephalus, chromosomal anomalies, and complex congenital heart disease) that would require NICU admission for an underlying condition-related intervention irrespective of GA. We also excluded multiple gestations.

Statistical analysis

Table I. Maternal and Neonatal Demographic Characteristics of Early Term and Full Term Infants Admitted to the NICU

	Early term infants (n=608)	Term infants (n=538)	p
Mothers' age, years*	28.2±5.9	27.4±5.8	**0.02**
Maternal risk factors (diabetes mellitus, preeclampsia, prolonged rupture of membrane and others), n %	73 (12%)	45 (8.3%)	**0.01**
Cesarean section (n,%)	345 (56.7%)	261 (48.5%)	**0.006**
Birth weight, (g*)	3041±607	3335±513	**<0.001**
Small for gestational age (n,%)	91 (15%)	24 (4.5%)	**<0.001**
Large for gestational age (n,%)	62 (10.2%)	75 (13.9%)	**0.025**
Gender, male (n, %)	374 (61.5%)	307 (57.1%)	**0.132**

* Values are presented as mean±SD. The bold entries represent statistically significant at the level of p <0.05.

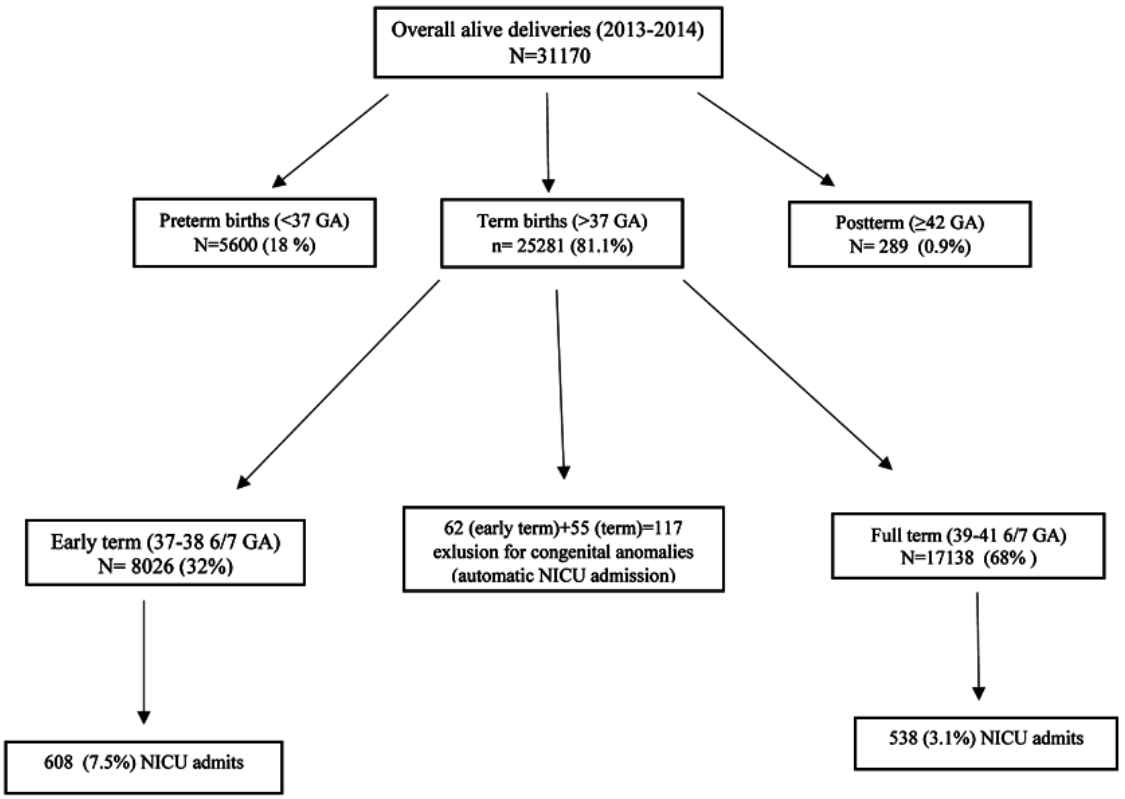

Fig. 1. Cohort Population Flow

Table II. Admission Diagnosis of Early Term and Full Term Infants

Diagnosis (n, %)	Early term infants (n=608)	Full term infants (n=538)	p
Respiratory distress	230 (37.8%)	196 (36.4%)	0.359
Jaundice	269 (44.2%)	262(48.7%)	0.155
Sepsis	12 (2%)	15 (2.8%)	0.437
Perinatal asphyxia	8 (1.3%)	16 (2.8%)	0.092
Feeding difficulty	33 (5.4%)	6 (1.1%)	**0.001**
Dehydration	21 (3.5%)	19 (3.5%)	0.630
Hypoglycemia	30 (4.9%)	15 (2.7%)	0.069
Polycythemia	5 (0.8%)	9 (1.6%)	0.274

The bold entries represent statistically significant at the level of $p<0.05$.

The data were collected and analyzed using the SPSS version 17.0 (SPSS Inc., Chicago, IL). Student t-test and Mann-Whitney u test were used to compare continuous parametric and nonparametric variables. The chi-square ($\chi 2$) test was used to compare categorical variables. Data are expressed as mean± standard deviation, or as percentages; the p-value was considered significant if <0.05 (two tailed).

Results

There were 31,170 births at Etlik Zübeyde Hanım Women's Health Training and Research Hospital during the 2-year study period; these included 5,600 (17.9%) premature births, 289 post-term births (0.9%), and 25,281 (81.1%) term births. During this period, the rate of delivery by cesarean section was 42%, of which 44% were repeated and 56% were primary.

Among all live deliveries, 8,026 (25.7%) were early-term between 37 and 38 6/7 weeks of

Table III. The NICU Morbidities in Early Term Infants and Compared to Full Term Infants

	Early term infants (n=608)	Full term infants (n=538)	p
Duration of hospital stay, days*	3.79±3.8	3,2±3.6	**0.002**
Duration of hospital stay in infants with TTN, days*	5.1±3	4.2±4.1	**0.02**
Prolonged hospitalization (> 5 days), n %	135 (22.2%)	68 (12.6%)	**<0.001**
Readmission to the NICU, n,%	31 (5.1%)	12 (2.2%)	**0.012**
Neonatal death, n,%	4 (0.7%)	2(0.4%)	0.695

* Values are presented as mean± SD. The bold entries represent statistically significant at the level of p<0.05. NICU: neonatal intensive care unit, TTN: transient tachypnea of the newborn.

gestation, while 17,138 (54.9%) were full-term between 39 0/6 and 41 6/7 weeks. The admission rates to the NICU for early-term and full-term infants were 7.5% and 3.1%, respectively. There were 3,809 admissions to the NICU during the study period; these included 608 (15.9%) early-term and 538 (14.1%) full-term infants. Of the term neonates (> 37 weeks), 117 (3.5% of all births) were excluded because of congenital malformations that would have automatically required NICU admission (Fig. 1).

The maternal and neonatal demographic characteristics of early-term and full-term infants admitted to the NICU are listed in Table I. The full-term infants weighed significantly more than the early-term infants ($p < 0.001$). The rate of SGA was significantly higher in early-term infants compared to full-term infants ($p < 0.001$), while the large-for-gestational-age (LGA) percentages were similar in this study. There was a significant difference in the mode of delivery between the two groups, with 56.7% of early-term neonates being born via cesarean section compared with 48% of full-term infants. Maternal risk factors for early-term infants were reported in 73 (12%) neonates, the most common being gestational diabetes (37.5%), pre-eclampsia (21.3%), and preterm rupture of membranes (14.2%).

A significantly greater number of early-term infants (608/8,026; 7.6%) required NICU admission compared with full-term infants (538/17,138; 3.1%). The main diagnoses of the early-term infants were jaundice (n = 269) and respiratory distress (n = 230). Of the patients diagnosed with respiratory distress, 218 were diagnosed with TTN and 12 with pneumonia, MAS, and persistent pulmonary hypertension. The diagnoses of the early-term and term neonates on admission to the NICU are given in Table II.

The mean duration of hospital stay and prolonged hospitalization were both significantly higher in early-term infants compared with full-term infants ($p = 0.002$) (Table III). In addition, the duration of hospitalization in infants with TTN was significantly longer in early-term infants compared with full-term infants ($p = 0.02$). The rates of rehospitalization were significantly higher in early-term infants (5.1%) compared to full-term infants (2.2%), with diagnoses such as jaundice, dehydration, and feeding difficulty ($p = 0.012$). The neonatal mortality rates were similar between the two groups ($p > 0.05$).

The overall morbidity and mortality rates are listed in Table IV. Compared with full-term infants, early-term infants had significantly higher rates of required NICU admission (7.5% vs. 3.1%), respiratory distress (2.8% vs. 1.1%), TTN (2.7% vs. 1%), jaundice (3.3% vs. 1.5%), hypoglycemia (0.2% vs. 0.08%), feeding difficulty (0.16% vs. 0.03%), and dehydration (0.2% vs. 0.1%).

Discussion

There is increasing awareness of the clinical risks and morbidities of early-term infants. Previous studies have shown that early-term infants are associated with a significant increase in neonatal morbidity and poor long-term outcomes compared with full-term infants [2,5,9].

There are approximately 16,000 births every year at our hospital. Of these, 80.8% of inborn infants are term, and 31.7% of term infants are born between 37 and 38 6/7 weeks of gestation. Thus, of all newborn infants delivered, more than two out of every ten (25.6%) are early-term. Our results show that early-term infants had a higher incidence of neonatal morbidity with the risk of being admitted to the NICU, and prolonged hospitalization compared to full-term infants; this is consistent with previously

Table IV. Overall Admission Morbidity and Mortality Rates of Early Term and Full Term Infants

Variable	Early term infants (n=8,026)	Full term infants (n=17,138)	p
% of all births	25.7%	54.9%)	**<0.001**
NICU admission (n, %)	608 (7.5%)	538 (3.1%)	**<0.001**
Respiratory distress (n, %)	230 (2.8%)	197 (1.1%)	**<0.001**
Transient tachypnea of the newborn (n, %)	217 (2.7%)	181 (1%)	**<0.001**
Only oxygen supplement (n, %)	186 (2.3%)	162 (0.9%)	**<0.001**
NCPAP (n, %)	27 (0.3%)	34 (0.19%)	0.059
Intubation, ventilation support (n, %)	10 (0.12%)	8 (0.04%)	0.068
Jaundice (n, %)	269 (3.3%)	262 (1.5%)	**<0.001**
Hypoglycemia (n, %)	19 (0.2%)	15 (0.08%)	**0.011**
Feeding difficulty (n, %)	13 (0.16%)	6 (0.03%)	**0.007**
Sepsis (n, %)	12 (0.14%)	15 (0.08%)	0.203
Dehydration (n, %)	21 (0.2%)	19 (0.1%)	**0.016**
Neonatal mortality (n, %)	4 (0.04%)	2 (0.01%)	0.146

The bold entries represent statistically significant at the level of $p<0.05$.
NICU: neonatal intensive care unit, NCPAP: nasal continuous positive airway pressure

reported findings[2,15,16]. In addition, early-term infants admitted to the NICU experienced a significantly higher readmission rate during the neonatal period compared with full-term neonates.

The rate of cesarean section was significantly higher in early-term infants compared with full-term infants, and this was a contributory factor for prolonged hospitalization and increased respiratory distress on admission in these cases. It is well established that cesarean delivery in term neonates is associated with an increase in neonatal morbidity and admission to the NICU[17,18]. However, in recent studies, GA has been determined to be a strong predictor of neonatal morbidity[2,19]. Our country has one of the world's highest rates of cesarean sections, with the procedure accounting for approximately 48% of all births[20]. In contrast, statistical data from the World Health Organization suggest that the 'ideal rate' of cesarean section deliveries is 15%[21]. The Ministry of Health has recently taken various measures to decrease the number of cesarean sections in Turkey.

Most early-term infants weighed at least 2,500 g at birth and appeared mature, giving false confidence to the clinicians and parents. In fact, these newborns were physiologically immature. Our results support this opinion given the higher rate of NICU admission, significantly greater incidence of TTN and jaundice requiring phototherapy, lower blood glucose levels, and feeding difficulties (Table IV).

The ACOG advises that all elective cesarean sections and non-medically indicated deliveries be deferred until after 39 weeks of gestation, unless medically justified[22]. However, the rate of cesarean sections was higher in early-term deliveries in the present study. Unfortunately, we are not aware of the rates of elective cesareans at our hospital. Although the percentage of elective cesarean sections could not be determined for early-term infants delivered by cesarean section, our results support the recommendation of the ACOG.

More early-term infants than term infants were classified as SGA. The rate of SGA was significantly higher in early-term infants compared to full-term infants, while the percentage of those classified as LGA were similar in our study. Sengupta et al.[2] reported that the percentage of infants classed as SGA or LGA was significantly higher for the early-term group.

Recently, Bates et al.[6] reported that early-term infants had lung immaturity relative to an increase in the incidence of respiratory distress syndrome, the need for respiratory support, and TTN, irrespective of documented fetal lung maturity. In addition, published data suggest that delivery at 37 or 38 weeks of gestation is associated with an increased rate of respiratory morbidity, TTN, and surfactant use compared with pregnancies delivered at > 39 weeks[19, 23]. There was also an increased rate of respiratory distress and TTN among early-term infants in

our study, compared with full-term infants.

Previous studies reported that the risk of sepsis and requirement for antibiotic treatment were significantly higher in early-term infants compared with full-term infants. The culture-positive sepsis rates tended to be higher in early-term infants, although this result was not statistically significant[2,15]. In the present study, the sepsis rates were similar in early-term and full-term infants.

There are several limitations to our study. Firstly, due to its retrospective nature, data on potential confounders such as the elective cesarean rate were not available. Secondly, there was a lack of information on long-term outcomes, including readmission to other hospitals in either the neonatal or infancy period; this limited our ability to accurately assess the long-term consequences and utilization of appropriate healthcare. On the other hand, the strength of this study is its large sample size, and all cases were managed at a single center according to the same clinical protocols. In addition, this is the first study to report the neonatal morbidities associated with early-term delivery in Turkey.

In conclusion, our study shows that early-term delivery is associated with poor neonatal outcomes. These results should be evaluated by obstetricians when considering the timing of labor induction or planned cesarean delivery. They should also be considered by neonatologists, who need to be aware of the higher risk of neonatal morbidities in early-term infants.

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