EARLY TERM DELIVERY AT 37 WEEKS GESTATION – WHAT ARE THE RISKS?

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Abstract: *Early term birth - compared to term delivery - is associated with increased rate of perinatal complications. The authors evaluated the short term prognosis of infants delivered at 37 weeks gestation compared to term neonates using a retrospective case control study, controlling also the birth weight. SPSS 10.0 for Windows was used for statistical analysis. The study included 343 delivered at 37 weeks gestation and 343 term infants. Early term infants had lower Apgar scores at 1 and 5 minutes (p=0.000, p=0.006), increased rates of respiratory distress (9.9% vs. 0%, OR 2.11[CI 1.94-2.39]), persistent pulmonary hypertension (23.7% vs. 4%, p=0.003, OR 7.45[CI1.64-23.72]), jaundice (47.5% vs. 22.2%, p=0.000, OR 3.18[CI2.28-4.43]), anemia (30.7% vs. 15.9%, p=0.014, OR 2.34[CI1.17-4.70], and neonatal intensive care unit admission (10.5% vs. 1.2%, p=0.000, OR 9.94[CI3.49-28.24]). An analysis of the epidemiology of early term birth is mandatory in order to decrease their rate and better neonatal prognosis.*

INTRODUCTION

The definition of term newborn has been recently changed in order to more accurately underline that between $37^{0/7}$ and $41^{6/7}$ weeks gestation the neonatal prognosis is not uniform and differs for every week of gestation. Therefore we are speaking now about early term infants if they are born at $37^{0/7}$ - $38^{6/7}$ weeks, full term infants if delivery occurs at $39^{0/7}$ - $40^{6/7}$ weeks, late term infants if birth takes place between $41^{0/7}$- $41^{6/7}$ weeks, and postterm if they are delivered at 42 or after 42 weeks of gestation.(1) The best neonatal outcome is registered if delivery occurs at 39-40 weeks gestation.(1,2)

Early term delivery rate is increased worldwide and in Romania in the latest years due to multiple factors including increased maternal age and more complicated pregnancies, increased number of multiple pregnancies, improved pregnancy management, and increased number of deliveries induced for maternal and fetal medical complications, gestational age estimation errors, demographic changes etc. Early term birth - compared to term delivery - is associated with increased rate of perinatal complications as revealed by data published in the literature. Research published in the recent years is revealing that every week of gestation is important for the neonatal health since maturation of the brain and lung occurs during the last weeks before the 40^{th} week of gestation.(1)

The first studies regarding early term birth focused on the presence of labor and delivery mode, less on the neonatal prognosis but recent data are showing that early term delivery is associated with increased risks for the newborn. The study published by Consortium on Safe Labor (3) showed that neonates born at 37 weeks have increased rates of respiratory failure (OR 2.8[2.0-3.9]), respiratory distress syndrome, transient tachypnea of the newborn, pneumonia, and ventilator use compared to infants born at 39 weeks gestation. Increased rates of neonatal intensive care unit (NICU) admission were observed also by Sengupta et al. (2) and by Clark et al. (4) at 37 weeks versus 39 weeks deliveries. At 37 weeks gestation, compared to 39 weeks, hypoglycemia, increased need for respiratory support, oxygen, parenteral fluids, low Apgar scores, antibiotic usage, feeding difficulties were more often reported.(2,3,5-14) Also, neonatal and infantile mortality rates are significantly higher at 37 weeks versus 39 weeks - neonatal mortality of 1.7/1000 newborns at 37 weeks compared to 0.8/1000 newborns at 39 weeks; infantile mortality 4.1/1000 at 37 weeks newborns compared 2.1-2.2/1000 newborns at 39 weeks.(15)

Therefore, based on these reports, international professional organizations are discouraging non-medically indicated deliveries before 39 weeks gestation (5,16,17) admitting that when the evidence regarding the optimum delivery moment is scarce or based on expert opinion, the management of the pregnancy should be individualized and complex decisions must be based on the accurate estimation of the gestation age, maternal and fetal risks, available obstetrical facilities, and patient preferences. Early term deliveries without medical indication are discouraged.(1,5,16,18)

PURPOSE

The authors aimed at evaluating the short term prognosis of infants delivered at 37 weeks gestation compared to infants delivered at term.

MATERIALS AND METHODS

In order to evaluate the short term prognosis of infants delivered at 37 weeks gestation versus infants delivered at term, a retrospective case control study was developed. In order to exclude birth weight bias, for each infant born at 37 weeks a pair case, term infant, having a birth weight ± 100 g was identified in the database of the Maternity Hospital Sibiu during the study period, 1 January 2013 - 30 June 2015. Only neonates surviving at discharge were included in the analysis.

Epidemiological data - birth weight (BW), gestational age (GA), gender, area of residence, maternal social, demographic and medical characteristics -, labor and delivery information, and data regarding perinatal complications - need for resuscitation at birth, Apgar score, respiratory distress, persistent pulmonary hypertension, jaundice, anemia, weight

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loss, hospitalization in the intensive care unit, feeding type etc. - were extracted from the database of the unit and from neonatal medical records. The term respiratory distress (RD) was used to describe the neonatal respiratory conditions diagnosed at birth and comprised respiratory distress syndrome due to surfactant deficiency, transient tachypnea of the newborn, amniotic fluid aspiration syndrome, and pneumonia; RD was classified as minor if only oxygen was used to treat the condition, of medium severity if continuous positive airway pressure (CPAP) support was needed, and severe if intubation and ventilation were necessary to treat the disease. The severity of persistent pulmonary hypertension was determined after the severity of tricuspid insufficiency - mild if tricuspid insufficiency was evaluated as grade I, moderate if it was grade II, and severe if the assigned grade was III or worse. Jaundice was considered if phototherapy was needed but we excluded pathological jaundice (blood type and Rh sensitization, infection, resorption of haematomas etc.). Anemia at birth was defined by hemoglobin levels less than 15.0 mg/dL. Gestational age was determined using the best obstetrical estimates, last menstrual period, and earliest prenatal ultrasound scans. Where such data were not available, new Ballard score was used to determine the gestational age. Gestational age was expressed in complete weeks of gestation.

Statistical analysis was performed using SPSS 10.0 for Windows, p was considered statistically significant at values below 0.05 (confidence interval - CI - 95%). Data are reported as values, mean values, standard deviations (SD), and percentages, the Independent T-test was used to compare the scale variables and Fischer's exact test or chi square test were used (where appropriate) for the analysis of the categorial variables. Odds ratio was calculated, also using 95% confidence intervals.

RESULTS

During the study period - 1 January 2013 - 30 June 2015 - a total number of 346 newborns were delivered at 37 weeks gestation, representing 5.23% of the total number of admissions registered - 6558 newborns admitted in the unit, 5068 of them being born full term (39-40 weeks of gestation). There was no difference between the proportions of the neonates delivered at 37 weeks gestation between the years of study although the rate tended to decline: 5.66% in 2013, 5.36% in 2014, and 5.18% in 2015. We registered 3 deaths at 37 weeks gestation and 4 deaths in the group of full term infants. The mortality rate was significantly higher in the group of newborns delivered at 37 weeks – 8.7/1000 live neonates - compared to those born at full term – 0.8/1000 live neonates. Deaths were excluded from the analysis since 2 of the neonates born at 37 weeks gestation had severe malformations incompatible with life (the other one died due to cardiac and respiratory failure secondary to amniotic fluid aspiration and severe pulmonary hypertension of the newborn). After excluding the deaths, the study groups comprised 343 neonates born at 37 weeks gestation and 343 matched full term newborns.

Table no. 1. Demographic characteristics of the study groups

	37 weeks	Term	P
GA (weeks)	37	39.6 ± 0.7	0.000
BW (g)	2953.7 ± 415.6	2957.4 ± 406.2	0.904
PI	1.89 ± 0.7	1.86 ± 0.7	0.506
Male gender	168 (49)	168 (49)	1
Twin pregnancy	28 (8.2%)	12 (3.5%)	0.009

Every newborn delivered at 37 weeks was matched with a full term neonate (gestational age 39-41 weeks gestation) having a birth weight of ± 100 g compared to its pair. Mean gestational age, birth weight, and ponderal index (PI) of the study groups are presented in table no. 1. Even though a match of the cases based on gender was not intended, the distribution according to gender was similar in the study groups (table no. 1). It should be noted that the group of newborns delivered at 37 weeks gestation comprised significantly more twins (table no. 1).

Maternal demographic, social, and medical characteristics of the infants in both study groups are presented in table no. 2. Compared to term deliveries, the mothers that delivered at 37 weeks gestation were significantly older, highly educated, more commonly living in urban areas, and more often benefited from prenatal care. Also, the parity of the mothers delivering at 37 weeks gestation was significantly lower than that of those who delivered at term. Pregnancies after assisted reproductive techniques were seen more often in the group of neonates born at 37 weeks.

Table no. 2. Maternal baseline characteristics

	37 weeks (mean ± SD or n/%)	Term (mean ± SD or n/%)	*P*
Maternal age (years)	27.6 ± 6.6	26.5 ± 6.4	0.025
Maternal education			0.001
No education	17 (5)	27 (7.9)	
Elementary school	85 (24.1)	115 (33.5)	
High school	130 (37.9)	121 (35.3)	
Higher education	111 (32.4)	80 (23.3)	
No of pregnancies	2.2 ± 1.6	2.3 ± 1.9	0.351
Parity	1.7 ± 1.0	1.9 ± 1.3	0.019
Urban area	190 (55.6)	154 (45.0)	0.006
ART pregnancy	18 (5.2)	1 (0.3)	0.000
Monitored pregnancy	293 (85.4)	266 (77.6)	0.008
No antenatal pathology	306 (89.2)	329 (95.9)	NS
No pathology during pregnancy	238 (69.4)	270 (78.7)	NS

*ART - assisted reproductive techniques

An interesting observation was the highly increased rates of cesarean section and cesarean section in absence of labor in the group of newborns delivered at 37 weeks compared to term ones (table no. 3).

Table no. 3. Labor and delivery data

	37 weeks (n/%)	Term (n/%)	*p*
C-section	136 (39.7)	93 (27.1)	0.000
Absent labor	95 (27.8)	57 (16.7)	0.000
Abnormal presentation	22 (6.4)	29 (8.5)	0.309

Table no. 4. Comparison of Apgar scores, need for resuscitation, and respiratory and cardiac conditions

Condition	Study groups	No cases	Value	*p*; OR (95%CI)
Apgar at 1 min (mean ± SD)	37 weeks	343	9.2 ± 0.7	0.000
	Term	343	9.6 ± 0.8	
Apgar at 5 min (mean ± SD)	37 weeks	264	9.7 ± 0.6	0.006
	Term	226	9.8 ± 0.6	
Resuscitation at birth (n/%)	37 weeks	343	11 (3.2)	0.655 1.23[0.50-2.99]
	Term	343	9 (2.6)	
RDS (n/%) - minor - 20 (58.8%) - medium - 12(35.3%) - severe - 2 (5.9%)	37 weeks	343	34 (9.9)	0.000 2.11[1.94-2.29]
	Term	343	0 (0)	
PPHN (n/%) - minor - 11 vs 2 - major - 6 vs 0	37 weeks	343	18 (23.7)	0.003 7.45[1.64-33.72]
	Term	343	2 (4.0)	

Tables no. 4 and 5 illustrate the comparison of the short term outcomes between the neonates delivered at 37 weeks as compared to those delivered at term. Newborns delivered at 37 weeks gestation had lower Apgar scores but the need for resuscitation at birth was not different between the study groups (table no. 4). Respiratory and cardiac adaptation difficulties were significantly more often seen and more severe at 37 weeks compared to term (table no. 4). Infants born at 37 weeks gestation had a more complicated postnatal course (table no. 5), needing more often care in the neonatal intensive care unit (NICU).

Table no. 5. Postnatal conditions - comparison between study groups

Condition	Study groups	No cases	Value	*p*; OR (95%CI)
Maternal-fetal infections	37 weeks	343	24 (7.0)	0.265 0.73[0.42-1,27]
	Term	343	32 (9.3)	
Anemia at birth (n/%)	37 weeks	137	42 (30.7)	0.014 2.34[1.17-4.70]
	Term	82	13 (15.9)	
Hemoglobin (g/dL)(mean ± SD)	37 weeks	137	16.1 ± 0.22	0.000
	Term	82	17.3 ± 0.23	
Jaundice (n/%)*	37 weeks	343	163 (47.5)	0.000 3.18[2.28-4.43]
	Term	343	76 (22.2)	
Weight loss (g) (mean ± SD)	37 weeks	343	175.3±57.2	0.000 9.94[3.49-28.24]
	Term	343	153.1±52.8	
NICU admission (n/%)	37 weeks	343	36 (10.5)	0.000 9.94[3.49-28.24]
	Term	343	4 (1.2)	
NICU hosp. length (days) (mean ± SD)	37 weeks	36	3.6 ± 2.8	0.138
	Term	4	6.5 ± 8.5	
NICU hosp. length (days) (mean ± SD)**	37 weeks	36	3.6 ± 2.8	0.453
	Term	3	2.3 ± 2.3	
Exclusive breastfeeding at discharge	37 weeks	343	81 (23.6)	-
	Term	343	96 (28)	
Exclusive formula at discharge	37 weeks	343	4 (1.2)	-
	Term	343	5 (1.5)	
Hospitalization length (days) (mean ± SD)	37 weeks	343	5.2 ± 4.3	0.006
	Term	343	4.3 ± 3.9	

*Except pathological jaundice; **Except a severe HIE case in a term baby with prolonged NICU hospitalization

DISCUSSIONS

Our case-control study demonstrated that delivery at 37 weeks gestation significantly increases the risk for postnatal complication compared to term delivery, similar with most of the data published in the literature. Since the mean birth weight and ponderal index of the newborns in the study groups were not different (table no. 1) biases related to birth weight were excluded. Also, the similar distribution according to gender (table no. 1) excluded any association between neonatal outcomes and gender. The significantly higher proportion of twins in the group of newborns delivered at 37 weeks (table no. 1) may contribute to the worse neonatal outcome of this group.

Newborns delivered at 37 weeks gestation had Apgar scores significantly lower compared to term infants (table no.4). Despite this, the need for resuscitation at birth was not different between the study groups. Clark et al. (4) showed that the rates of Apgar scores < 7 are decreasing from 1.01% at 37 weeks to 0.61% at 39 weeks. Another study, published by Seikku et al. (9) on a large birth cohort from Finland showed also an increased risk for Apgar scores < 7 at 1 and 5 minutes in newborns delivered at 37 weeks compared to full term infants - OR 1.03 [95% CI 1.03-1.04], and OR 1.24 [95% CI 1.04-1.49] respectively. This finding may have implications on long term, since the study of Seikku et al. (9) also demonstrated an increased risk for neonatal mortality, cerebral palsy, intellectual disabilities, and neurosensorial deficits for infants born at 37 weeks gestation compared to term ones.

Newborns delivered at 37 weeks gestation had, in our study, a 2-fold increased risk for postnatal respiratory conditions, similar with data published by the Consortium on Safe Labor (3) who also identified increased rates of respiratory distress syndrome, transient tachypnea of the newborn, pneumonia and respiratory failure at 37 weeks versus 39 weeks gestation. Also, even though almost 50% of the newborns that developed respiratory conditions at birth had minor problems, requiring only oxygen therapy, in the other 40% of the cases pressure support and mechanical ventilation was needed (table no. 4). An increased risk for surfactant deficiency at 37 weeks gestation was shown also by data published by Cheng et al. (6) - OR 3.12 [95% CI 2.90-3.38]. The need for respiratory support was increased - OR 1.93 - and intubation and mechanical ventilation was needed 6 times more often in early term versus term neonates in the study published by Sengupta et al. (2) Similar results were published in 2012 by Ghartey et al. (7), who found a 2-fold increased risk for respiratory distress syndrome, oxygen therapy, CPAP support and by Tita et al. (8) who identified respiratory morbidities in 8.2% of the early term infants compared to 3.4% in term newborns, and 48% increased risk for respiratory morbidities at 37 weeks versus 39 weeks gestation. Pulmonary immaturity is the main pathophysiological explanation for the increased risk for respiratory conditions at 37 weeks. In our cohort, other explanations might be the increased rate of cesarean section deliveries and absence of labor in almost one third of these cases (table no. 3). As underlined by Salemi and his colleagues (19), elective early term delivery increases the risk for neonatal adverse outcomes by 13-66%, the absence of labor being associated with more unfavorable neonatal prognosis. Other authors identified increased risks for unfavorable outcome in association with elective cesarean section in absence of labor.(5,8) Also, other authors have showed that early term newborns delivered by cesarean section have an increased risk for NICU admission compared to vaginal delivery.(2,20)

We have not found data in the literature regarding the rate of persistent pulmonary hypertension of the newborn but often, respiratory difficulties immediately after birth are associated with persistence of fetal circulation and cardiac failure, a condition that occurs more frequently in late preterm and term newborns. In our study groups, we have found that both the rate and severity of this condition was increased at 37 weeks compared to term infants (table no. 4). Similar, no data in the literature are published related to maternal-fetal infections except a study that found an increased use of antibiotics in newborns delivered early term versus term neonates (2.6% versus 1.6%, OR 1.62).(2) There was no difference between the incidences of maternal-fetal infection between the study batches in our study (table no. 5).

The incidence of anemia at birth was significantly increased and the mean value of hemoglobin at birth was significantly lower in newborns born at 37 weeks compared to those delivered at term (table no. 5). No data were found in the literature to be compared to our results but these findings are also explained by the physiological immaturity of newborns at 37 weeks compared to term.

A significantly increased weight loss during birth hospitalization at 37 weeks (table no 5) compared to term is

explained both by the higher water body content and by the more complicated postnatal course of these infants.

Jaundice, intense enough to necessitate phototherapy, was seen significantly more often in newborns delivered at 37 weeks (table no. 5) and this is also explained by a grade of immaturity of bilirubin metabolism at this gestational age compared to term and possibly was associated with a greater physiological weight loss.

The more complicated postnatal development of the newborns in the 37 weeks gestation group explains the higher rate of NICU admission of this infants (table no.5) and this is also in accordance with the data published by other authors.(2,4,5,8,10,21) Although in our study the NICU admission rate was significantly higher at 37 weeks compared to term, the length of NICU hospitalization wasn't significantly different even after removing from the analysis a term newborn with severe hypoxic-ischemic perinatal encephalopathy. However, newborns delivered at 37 weeks gestation had a significantly increased hospitalization length compared to term newborns (table no. 5), similar with data in the literature.(2,8,10)

Feeding difficulties are also flagged by other authors in early term versus term infants.(2,3,13,14,21) These difficulties may be explained by increased rate of postnatal morbidities. In our study, even though the rate of exclusive breastfeeding was higher in term newborns, the differences weren't significant (table no. 5).

Even though it was beyond the aim of this study the evaluation of neonatal mortality – the number of deaths is small – we cannot overlook the significantly increased neonatal mortality associated with birth at 37 weeks gestation compared to term delivery. This is in accordance with data published in the literature by other authors, as for example Reddy at al. (15) who identified a neonatal mortality rate of 1.7/1000 live births at 37 weeks gestation compared to 0.8/1000 live births at 39-40 weeks gestation, and an increased risk for neonatal mortality at 37 weeks gestation of 2.3 (95% CI 2.1-2.6].

Our study has several limits. The first one is the retrospective design of the study. Gestational age is prone to biases since different methods were used for its evaluation and 15% and 23%, respectively, of the pregnancies in the study groups did not benefit of prenatal care (table no. 2). Also, no investigation was done in order to evaluate if the cesarean section were medically indicated or not in order to evaluate specifically if the postnatal pathology of the neonates born at 37 weeks gestation is associated with the delivery mode or to the absence of labor prior cesarean section. The aim of our study was not the evaluation of the neonatal outcome in relation to maternal characteristics and delivery mode but our results are suggesting that such an analysis may be helpful in order to develop policies that would decrease the early term delivery rates and the incidence of unfavorable outcomes of these infants. But our study brings new data on neonatal outcomes as anemia at birth, pronounced jaundice, and weight loss in infants born at 37 weeks gestation, data that suggests that at 37 weeks a functional immaturity of organs and systems may interfere with a normal transition to extra-uterine life.

CONCLUSIONS

Our results are contributing to the growing body of evidence demonstrating that early term delivery is associated with increased risks for neonatal morbidity and mortality in comparison with term delivery and that every week gestation is important for the full maturation of the fetus and for a better neonatal outcome. Studies are showing now that not only the short term prognosis is worse in early term born infants but the long term outcome may be also influenced. Early term delivery increases the risk of rehospitalisation (10,22,23), may negatively influence academic performances and the general development of the child (9,24,25), increases the risk for respiratory infections needing hospitalization in childhood, mainly bronchiolitis (26) and the risk for bronchitis and asthma at 3-5 years.(27)

All these data are supporting the need to reinforce the recommendation of obstetrical societies to discourage non-medically indicated deliveries before 39 weeks of gestation.(5,16,17,28) Decisions regarding the optimum moment for delivery must be individualized in all the cases balancing between the maternal and neonatal risks in the case of delivery versus maternal and neonatal risks if pregnancy is continued. Unfortunately, educational policies addressed to the future mothers are not as efficient as medical policies instituted by hospital and health insurance house.(28)

Our results are demonstrating that we need a re-evaluation of our data in order to more clearly identify the etiology and epidemiology of early term birth in our unit in order to develop policies that may reduce the rate of early term births and, consequently, diminish the rate and severity of unfavorable neonatal outcomes. Postnatal conditions, their therapies, care and treatment in the NICU, and increased length of hospitalization are significantly increasing the costs. All these are enough reasons for a better and more individualized decision of the delivery mode and moment whenever delivery must be considered before 39 weeks of gestation.

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