Does Cesarean Section before the Scheduled Date Increase the Risk of Neonatal Morbidity?

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ABSTRACT:

Background: Previous studies led to the recommendation to schedule planned elective cesarean deliveries at or after 39 weeks of gestation and not before 38 weeks. The question is whether this practice is appropriate in face of possible risks to the newborn should the pregnancy have to be ended by cesarean section before the scheduled date.

Objectives: To compare the outcomes of newborn infants who were delivered on their scheduled day by elective cesarean section versus those who required delivery earlier.

Methods: This single-center retrospective study was based on medical records covering a period of 18 months. We compared the neonatal outcomes of 272 infants delivered by elective cesarean section as scheduled (at 38.8 ± 0.8 weeks gestation) and 44 infants who had to be delivered earlier than planned (at 37.9 ± 1.1 weeks).

Results: We found no morbidity directly related to delivery by cesarean section before the scheduled date. There were no significant differences in the need for resuscitation after delivery. Although more of the infants who were delivered early were admitted to intensive care and overall stayed longer in the hospital (5.8 ± 7.3 vs. 3.9 ± 0.8 days, P < 0.02), their more severe respiratory illness and subsequent longer hospitalization was the result of their younger gestational age. Transient tachypnea of the newborn was associated with younger gestational age at delivery in both groups.

Conclusions: We suggest continuing with the current recommendation to postpone elective cesarean singleton deliveries beyond 38–39 weeks of gestation whenever possible.

KEY WORDS: elective cesarean section, timing, gestational age, neonates, neonatal morbidity, transient tachypnea of the newborn (TTN)

The percentage of newborns delivered by cesarean section has risen substantially in recent years, reaching 19–20% in Israel [1], more than 30% in the United States [2], and as high as 40% in Latin America [3]. The cesarean rate has increased rapidly even among women considered to be at low risk – i.e., women with a full-term singleton infant in vertex presentation [4]. Much of the overall increase is due to a substantial rise in primary cesarean section rates, with the main contributing factors being maternal request, the effect of malpractice litigation, convenience for the clinician, and repeat CS with no attempt at vaginal birth after a previous cesarean [3,5]. Medical indications for planned elective cesareans have also broadened over the years and have influenced medical practice. For example, the recommendation for CS whenever there is breech presentation in a singleton term baby [6] has led to loss of experience in conducting vaginal breech deliveries [7]. In Israel, there were about 32,000 cesarean sections in 2010, of which about 53% were primary and 47% were repeat cesareans after a previous CS [1]. About 1.7% were performed electively upon maternal request, with no other medical indication [1].

In terms of neonatal outcome, the timing of an elective CS is critical. Previous studies have led to a nearly unanimous recommendation to schedule planned elective cesarean deliveries at or after 39 full weeks of gestation, and not before 38 weeks [8-10]. This recommendation is based chiefly on the higher rates of neonatal respiratory morbidity found at gestational age under 38–39 weeks [10-16]. However, scheduling an elective CS at 39 weeks or beyond may carry the risk of other maternal or fetal consequences as compared to earlier delivery at 38 weeks [8]. When gestational age is over 38 but under 39 weeks, 10–14% of women go into spontaneous labor, meaning that a considerable number of those women scheduled for an elective CS will deliver earlier in an unscheduled frequently emergent CS, with the potential for significant implications for the mother or newborn that may be related to the emergency delivery [8,17-19]. Scheduling elective cesarean sections earlier may also occasionally prevent intrauterine fetal demise, which has been shown to increase with increasing gestational age [8,17,19].

Clearly, prospective randomized trials comparing the consequences of scheduling elective CS before and after 39 or 38 weeks are problematic, particularly for ethical reasons. We therefore addressed this question by retrospectively comparing neonatal outcomes of infants born by early CS before the...
scheduled date to those of infants born by elective CS at the originally planned gestational age.

**PATIENTS AND METHODS**

This 18 month retrospective study was conducted at the Bnai Zion Medical Center, Haifa, Israel. We reviewed the medical records of all mothers with a singleton pregnancy who were scheduled for elective cesarean delivery during the study period (1 September 2007 – 1 March 2009), and the medical records of their newborn infants. The study was approved by the institutional review board.

Maternal data included timing of the CS, whether it was performed electively as scheduled or earlier than planned, and the reason for the earlier delivery. Based on these data, the infants were divided into two groups: those born by elective cesarean delivery at the scheduled date, and those delivered by early CS before the scheduled date.

Neonatal outcomes were compared between the scheduled and early delivery groups. Neonatal data included the following: GA at birth and planned GA, if different; birth weight, small or large for gestational age – i.e., less than the 10th percentile or more than the 90th percentile, respectively, according to the Israeli intrauterine growth charts [20]; gender; need for resuscitation after delivery and 5 minute Apgar score; admission to the neonatal intensive care unit; length of stay in hospital after delivery; and respiratory morbidity and treatment (observation, supplemental oxygen, or ventilatory support). The typical respiratory morbidity in term and late-preterm newborns is transient tachypnea of the newborn. TTN tends to occur more often after CS, and particularly after elective CS (i.e., in the absence of labor) [14]. Diagnosis of TTN was based on a combination of clinical signs, chest X-ray findings and clinical course. TTN was diagnosed in term or near-term babies (GA ≥ 35 weeks) if:

- symptoms began within the first hours after delivery
- there were signs of respiratory distress (i.e., tachypnea, retractions, grunting, nasal flaring, or mild cyanosis) with good response to oxygen supplementation
- chest X-ray was consistent with “wet lungs,” with signs of congestion and perihilar streaking
- the symptoms and radiographic findings were transient and self-limited, disappearing within the first week of life (usually within 3–4 days)
- based on the clinical course and the physical and radiographic findings, other pathologies (e.g., pneumonia or respiratory distress syndrome) were excluded [14].

Other neonatal morbidities were also recorded, including birth trauma, birth asphyxia and hypoxic ischemic encephalopathy, intracranial hemorrhage, meconium aspiration, air leaks (pneumothorax), hypoglycemia, polycythemia, sepsis, neonatal jaundice (based on pre-discharge bilirubin levels, which are screened routinely and plotted on an hour-specific normogram) [21], and necrotizing enterocolitis (stage 2 or more, based on Bell’s staging criteria).

Respiratory morbidity was defined as the primary neonatal outcome for investigation, while all other outcomes were defined as secondary outcomes. Calculations of the estimated sample size required were based on the average annual number of deliveries in our hospital, the average rate of cesarean deliveries (23%) and scheduled elective CS (approximately a quarter of all CS), the average frequency of early CS before the scheduled date (approximately 15% of all scheduled CS), and the average rate of respiratory morbidity after elective CS (3.5–4.0%) [11,14].

The study was designed to try to detect a 2.5-fold increase in respiratory morbidity in the early delivery group compared to the scheduled delivery group (using a power of 80% and alpha of 0.05). Since this study was retrospective, these calculations of sample size helped us define the period and the number of infants to be studied.

**STATISTICAL ANALYSIS**

This included descriptive statistics, Student’s t-test for normally distributed continuous variables, and the appropriate non-parametric tests when the normality test failed. The chi-square test was used to assess differences with respect to dichotomous outcomes (SigmaStat version 2.03, Chicago, IL, USA). Statistical difference was set at the 5% level of probability. Unless indicated otherwise, the data are expressed as mean ± SD values. When non-parametric tests were applied, medians are presented. Since we wished to simultaneously assess the effect of multiple factors on the outcome, we conducted a multivariate analysis using a general linear model (Minitab version 12.23, State College, PA).

**RESULTS**

During the 18 month study period, 316 women with singleton pregnancies were registered for elective cesarean delivery at the Bnai Zion Medical Center. Of these, 272 delivered their babies by elective cesarean section on the scheduled date, while 44 underwent early cesarean delivery before the scheduled date. In most cases (81.8%), the CS was moved forward due to premature uterine contractions and/or rupture of membranes. The others were related to non-reassuring fetal monitoring or Doppler (4.5%), suspected fetal intrauterine growth restriction (2.3%), signs of maternal pre-eclampsia (4.5%), maternal thrombophlebitis (2.3%), vaginal bleeding (2.3%), or maternal request (2.3%).

Mean gestational age for the scheduled cesarean deliveries

\[GA = \text{gestational age}\]

\[TTN = \text{transient tachypnea of the newborn}\]
was 38.84 ± 0.84 weeks (median 38.7, range 36.1–41.8 weeks), with no significant difference in mean GA at the scheduled delivery time between the scheduled delivery and early delivery groups [Table 1]. As expected, newborns in the early delivery group were eventually delivered at a significantly younger gestational age than originally planned (37.9 ± 1.1 (median 37.7) vs. 38.8 ± 0.8 (38.6) weeks, P < 0.001), and also compared to the scheduled delivery group [Table 1]. Mean birth weight of the infants in the early delivery group was significantly lower compared to the scheduled delivery group, though rates of SGA and LGA did not differ significantly [Table 1]. There were no significant differences between the two groups in the need for resuscitation or recovery of the newborns after delivery, as expressed by their 5 minute Apgar scores [Table 1].

More newborns in the early delivery group were admitted to the NICU, and overall, infants in this group stayed in the hospital significantly longer after delivery than the scheduled delivery babies [Table 1]. Multivariate analysis using general linear modeling showed that this difference was related to their younger gestational age and not to the delivery by early cesarean section.

TTN was diagnosed in 12 of the scheduled delivery and 5 of the early delivery group. Although the rates of TTN did not differ statistically, the infants in the early delivery group were sicker, as expressed by their greater need for ventilatory support (nasal continuous positive airway pressure or endotracheal positive pressure ventilation) beyond oxygen supplementation, and their longer hospitalization [Table 2]. Again, multivariate analysis using general linear modeling showed that this difference in the severity of respiratory illness can be attributed to the fact that early delivery infants with TTN were significantly younger than their scheduled delivery counterparts, and not to the delivery by early cesarean section.

The relationship between gestational age and TTN is important for all CS deliveries, and especially so for elective cesareans, as scheduling cesarean delivery before a certain gestational age may affect respiratory morbidity. In both groups in our study, infants with TTN were delivered earlier. The mean gestational age at birth of babies with TTN in the scheduled delivery group was 38.2 ± 0.9 weeks (median 38.5, range 36.1–39.5), compared to 38.9 ± 0.8 (median 38.7, range 36.7–41.8) in those who had no respiratory problems after delivery (P < 0.04). In the early delivery group, these figures were 36.5 ± 0.9 in those with TTN, compared to 38.0 ± 0.9 in those without (P < 0.002). Only 2 of the 12 babies with TTN in the scheduled delivery group were born after 39 weeks (one at 39.1 and the other at 39.5 weeks).

There were no significant differences between the groups in rates of hypoglycemia or polycythemia [Table 2]. Infants in the early delivery group had statistically higher bilirubin levels [Table 2], though this was not of clinical importance in view of the current practice guidelines for the treatment of neonatal hyperbilirubinemia [21]. Again, general linear modeling showed that the younger gestational age of the

### Table 1. Characteristics of newborn infants delivered by elective cesarean section as planned compared to those delivered by early cesarean section before the scheduled date

<table>
<thead>
<tr>
<th></th>
<th>Scheduled delivery (n=272)</th>
<th>Early delivery (n=64)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA for scheduled CS (wk)</td>
<td>38.84 ± 0.85 (38.70)</td>
<td>38.79 ± 0.80 (38.60)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Actual GA at CS delivery (wk)</td>
<td>38.84 ± 0.85 (38.70)</td>
<td>37.86 ± 1.05 (37.70)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3357 ± 489 (3325)</td>
<td>3082 ± 507 (3218)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>SGA</td>
<td>3 (1.10%)</td>
<td>2 (4.54%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>LGA</td>
<td>20 (7.39%)</td>
<td>0</td>
<td>N.S.</td>
</tr>
<tr>
<td>Male:Female</td>
<td>1:06:1.00</td>
<td>0.83:1.00</td>
<td>N.S.</td>
</tr>
<tr>
<td>5 minute Apgar score</td>
<td>9.84 ± 0.41 (10.00)</td>
<td>9.75 ± 0.58 (10.00)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Required resuscitation</td>
<td>0</td>
<td>1 (2.27%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Admitted to NICU</td>
<td>5 (1.84%)</td>
<td>7 (15.91%)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>3.88 ± 0.82 (4.00)</td>
<td>5.77 ± 1.30 (4.00)</td>
<td>&lt; 0.02*</td>
</tr>
</tbody>
</table>

*Failed normality test: Mann-Whitney rank sum test on medians, t-test on means, Chi-square analysis

CS = cesarean section, GA = gestational age, SGA = small for gestational age, LGA = large for gestational age (indicator of macrosomia), NICU = neonatal intensive care unit, LOS = length of stay (length of hospitalization after delivery), NS = not significant

### Table 2. Morbidities of newborn infants delivered by elective cesarean section as planned compared to those delivered by early cesarean section before the scheduled date

<table>
<thead>
<tr>
<th></th>
<th>Scheduled delivery (n=272)</th>
<th>Early delivery (n=64)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory (TTN)</td>
<td>12 (4.41%)</td>
<td>5 (11.36%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Need for ventilatory support</td>
<td>5 (1.84%)</td>
<td>5 (11.36%)</td>
<td>&lt; 0.005*</td>
</tr>
<tr>
<td>GA of infants with TTN (wk)</td>
<td>38.18 ± 0.31 (38.45)</td>
<td>36.48 ± 0.89 (36.2)</td>
<td>&lt; 0.004*</td>
</tr>
<tr>
<td>LOS of infants with TTN (days)</td>
<td>3.92 ± 0.90 (4.00)</td>
<td>7.50 ± 19.14 (7.00)</td>
<td>&lt; 0.02*</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>2 (0.73%)</td>
<td>1 (2.27%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Polycythemia</td>
<td>1 (0.37%)</td>
<td>1 (2.27%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Neonatal jaundice: bilirubin level at discharge (mg/dl)</td>
<td>6.23 ± 3.08 (6.60)</td>
<td>7.49 ± 3.53 (8.00)</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>NEC</td>
<td>0</td>
<td>1 (2.27%)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

*Failed normality test: Mann-Whitney rank sum test on medians, t-test on means, Chi-square analysis

TTN = transient tachypnea of the newborn (retained fetal lung fluid), NEC = necrotizing enterocolitis, NS = not significant
scheduled delivery newborns was the only significant variable leading to higher bilirubin levels.

There were no cases of fetal demise or neonatal mortality, and no birth trauma, meconium aspiration, pneumothorax, neonatal sepsis, intracranial hemorrhage, perinatal asphyxia, or hypoxic ischemic encephalopathy in either the scheduled delivery or early delivery group. One baby in the early delivery group had necrotizing enterocolitis [Table 2]. He was born at 37.4 weeks with a birth weight of 1900 g (SGA).

**DISCUSSION**

This study questioned whether the current practice of trying to schedule elective cesarean sections at 39 weeks or later, and not before 38 weeks, is appropriate in view of risks to the newborn should the pregnancy have to be ended by cesarean section before the scheduled date. Our results suggest that there is no justification for changing the current practice.

Our results further suggest that the additional neonatal morbidity was not directly related to delivery by early cesarean section before the scheduled date. Statistically, the rates of neonatal morbidities in infants delivered by early CS before the scheduled date were not significantly different to those delivered by elective CS on the scheduled day. Yet, their respiratory morbidity was significantly more severe, as expressed by their increased need for ventilation support, higher rates of admission to the NICU, and longer stays in the hospital (findings which raise the possibility that the respiratory illness of these babies was in fact not TTN, but, rather, respiratory distress syndrome of premature infants, as indeed was eventually diagnosed in one case). Our analyses suggest that these differences are due to the early delivery group’s younger gestational age and not to the fact that they were born by early cesarean delivery. As expected, the babies delivered by early CS were born at a significantly lower GA, sometimes even in the range of late prematurity, and weighed less at birth, compared to their counterparts delivered by elective CS at the planned gestational age.

Late preterm infants, and even those born at 37 weeks gestation, are known to have more significant morbidity, especially respiratory morbidity [22,23]. Indeed, based on our understanding of the physiological effects of labor on fetal lung fluid clearance [24,25], it is possible that delivery by elective CS at this younger gestational age, in the absence of labor, could even have worsened the respiratory outcomes of many infants in our early delivery group (especially as it was uterine contractions or rupture of membranes that dictated early cesarean delivery in most of these newborns) [13]. This is an important point supporting the delay of elective CS, since infants whose mothers go into labor earlier may benefit from the physiological preparation for delivery.

This point suggests an additional conclusion: namely, that we are still not doing our best to delay elective cesarean deliveries beyond 39 weeks whenever possible. This can be seen in the mean gestational age at which deliveries were scheduled for both groups [Table 1]. The consequences of failure to postpone most of our elective cesarean deliveries is apparent in the non-negligible rate of TTN – 4.41% – among newborns born by elective CS at the scheduled date [Table 2], and in the fact that the infants with TTN were significantly younger in gestational age than those delivered by elective cesareans but with no evidence of respiratory morbidity. Moreover, 10 of the 12 babies with TTN in this group (83%) were electively delivered before 39 weeks of gestation, raising the uncomfortable question: could this respiratory morbidity have been prevented altogether had they been delivered later on?

Our study has several limitations. Chief among these is its retrospective nature, which necessitated determining from medical records the factors that dictated early cesarean delivery. However, since in most cases early delivery was prompted by either uterine contractions or rupture of membranes, we believe it is reasonable to claim that most of these babies underwent cesarean delivery in labor. Second, it may be argued that none of our early cesarean sections were due to serious emergencies like cord prolapse or severe fetal distress, so we could not really address the risk of early emergency cesarean sections in these neonates. However, since the true rate of real emergency cesarean sections is low, it is possible that many of the neonatal morbidities associated with such deliveries are in fact related to GA and other factors, and not to the early unscheduled CS itself. Finally, our study included no cases of intrauterine fetal demise, neonatal mortality, neonatal asphyxia and hypoxic ischemic encephalopathy, or birth trauma – all important consequences that could be related to the postponement of cesarean delivery. Our study was underpowered to detect these relatively infrequent neonatal morbidities, chiefly because their incidence is very low [8].

In conclusion, in terms of neonatal outcome, we reinstate the recommendation to postpone elective cesarean singleton deliveries as beyond 39 weeks of gestation whenever possible. Those newborns who are delivered earlier in an unscheduled cesarean section, usually because of labor, do not experience significant additional morbidity. The more severe respiratory illness and longer hospitalizations observed in this group seem to be a consequence of their younger gestational age and not their early cesarean delivery.

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Altitude adaptation in Tibetans caused by introgression of Denisovan-like DNA

As modern humans migrated out of Africa, they encountered many new environmental conditions, including greater temperature extremes, different pathogens and higher altitudes. These diverse environments are likely to have acted as agents of natural selection and to have led to local adaptations. One of the most celebrated examples in humans is the adaptation of Tibetans to the hypoxic environment of the high altitude Tibetan plateau. A hypoxia pathway gene, EPAS1, was previously identified as having the most extreme signature of positive selection in Tibetans, and was shown to be associated with differences in hemoglobin concentration at high altitude. Re-sequencing the region around EPAS1 in 40 Tibetan and 40 Han individuals, Huerta-Sánchez et al. found that this gene has a highly unusual haplotype structure that can only be convincingly explained by introgression of DNA from Denisovan or Denisovan-related individuals into humans. Scanning a larger set of worldwide populations, the authors find that the selected haplotype is only found in Denisovans and in Tibetans, and at very low frequency among modern humans. scanning a larger set of worldwide populations, the authors find that the selected haplotype is only found in Denisovans and in Tibetans, and at very low frequency among modern humans. These findings illustrate that admixture with other hominin species has provided genetic variation that helped humans to adapt to new environments.

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