Effects of perinatal risk factors on common neonatal respiratory morbidities beyond 36 weeks of gestation

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ABSTRACT

The objectives: To assess the incidence of respiratory morbidity (RM) in all single live neonates born >36 weeks of gestation, and the effects of perinatal characteristics on these morbidities.

Methods: This is a prospective hospital based study covering a 12-month period. The study took place at the Department of Pediatrics, Jordan University Hospital, Amman, Jordan, between January and December 2009. The effects of different perinatal characteristics on RM including transient tachypnea of the newborn (TTN) and respiratory distress syndrome (RDS) were analyzed.

Results: A total of 2282 newborns were included. One thousand two hundred and seventy-six (55.9%) of the newborns were delivered by vaginal delivery and 1,006 (44%) by cesarean section (CS) (24.5% by emergency CS and 19.5% by elective CS). Respiratory morbidity was reported in 3.7%. The incidence of TTN was 2.9% and RDS was 0.7%. Elective CS was found to be a risk factor for RM development when the gestational age was <39 weeks. Maternal hypertension and diabetes mellitus, and the absence of labor were independent risk factors for RM. The emergency CS and large for gestational age babies were risk factors for TTN, while male gender and GA <37th weeks were risk factor for RDS.

Conclusion: The collaborative obstetric and neonatology responsibility helps to identify the risk factors for adverse respiratory outcome when considering the time and mode of delivery. The pregnant mother should be informed regarding this possibility if delivery by elective CS is performed before the 39th weeks of gestation.


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Factors associated with neonatal respiratory morbidity are poorly described in our region including Jordan. Liberal obstetrical practices and the changes in maternal characteristics increased the rate of deliveries by cesarean section (CS) in both developing and developed countries. Similarly, Jordan's CS delivery rate increased from 7.7% in 1991 to 16% in 2004. This rise has an effect on the neonatal outcome especially if CS delivery was performed before the 39 weeks of gestation. Several previous studies have shown a positive correlation between elective CS delivery and the risk of respiratory morbidity (RM) when compared to those born vaginally, especially when delivery occurs before the onset of labor. The mechanism of RM is postulated to be due to iatrogenic prematurity, absence of labor with delay in lung adaptation due to failure of activation of epithelial sodium channels mediated by physiologic hormonal media and surfactant deficiency. Controversy remains on the preventive role of late administration of corticosteroids during the antenatal period and a trial of labor before elective cesarean delivery in reducing neonatal RM. It has been reported that this practice was associated with the occurrence of a small increased risk of perinatal death, birth asphyxia, trauma, and meconium aspiration. The correlation between early elective CS and short-term neonatal morbidities led to the development of guidelines recommending elective CS delivery at term (39 weeks or later based on menstrual dates) or waiting for the onset of spontaneous labor. Neonates who were born to mothers with medical illnesses were at a higher risk of morbidities including respiratory morbidity especially if they were late preterm. Our study objective is to assess the incidence of RM in neonates born at or after 36 weeks of gestation, and to study the effects of maternal and neonatal characteristics and different modes of delivery on these respiratory morbidities aiming at preventing these morbidities among this group of neonates. The postulated protective effect of labor was also investigated.

Methods. This is a prospective study covering the 12-month period between January and December 2009 at Jordan University Hospital (JUH), Department of Pediatrics, Amman, Jordan. This is a general hospital that provides tertiary perinatal care. Inclusion criteria include all delivered single live term or near term (>36 week of gestation) newborns. Exclusions were those newborns who were less than 36 weeks of gestation, newborns with any known congenital malformations, syndromes, or meconium aspiration. The main studied outcomes were the 2 common diseases of the respiratory morbidity (RM) which include 1) transient tachypnea of the newborn (TTN) and 2) respiratory distress syndrome (RDS). Other respiratory morbidities including pulmonary hypertension and pneumothorax were not included in the final analysis due to the small number of neonates with these morbidities. Maternal data were collected by a questionnaire that is filled by a trained research assistant through direct face-to-face interview and abstraction of information from the medical records at the time of delivery under the supervision of the attending obstetrician. The maternal data included: age, parity, smoking, pre pregnancy body mass index (weight [kg] per height squared [m^2]), the presence of intra uterine growth retardation (IUGR), maternal illnesses (before and during pregnancy) and data about placental and cord problems. Data on the course of delivery included the presence and duration of labor, and intrapartum complications. Neonatal data were abstracted daily from the charts and reviewed with the attending neonatologist. Data included: birth weight, gender, baby condition at birth (Apgar scores, resuscitation parameters), hospitalization course if admitted and gestational age at birth. If a wrong gestational age was suspected on admission, Ballard assessment (scoring system known for neonatologists that assess the gestational age) in the first 24 hours was carried out. Deliveries were grouped into: vaginal and CS including elective CS and emergency CS. Mothers were divided into 2 groups according to their illness that may affect the neonatal outcome. Group I included medically free women who do not have any identified illnesses (no maternal illness) while Group II included mothers with maternal illnesses including hypertension (gestational or chronic), diabetes (gestational, or chronic), asthma, active cardiac illnesses, hematological, rheumatologic, and oncological diseases, and so forth.

Ethical approval was obtained from the Institutional ethical committee at Jordan University Hospital and the Deanship of Scientific Research at the University of Jordan. Academic Grant Number: 114/2008-2009.
Jordan. All participant mothers received full information about the study. Informed consent was obtained from each subject and subject’s guardian after receiving approval of the study protocol by the institutional human ethical committee. This study was conducted according to the principles of Helsinki Declaration.

Gestational age was determined according to the last menstrual period and confirmed by dating the fetal ultrasound. Elective CS was defined as a planned CS delivery regardless of the presence of labor. Emergency CS was defined as CS due to urgent obstetrical, medical, or fetal causes. The respiratory distress syndrome was defined as the presence of signs of respiratory distress that start within few hours after birth consistent with radiological features and respiratory support need for at least 24 hours. Transient tachypnea of the newborn was defined as the presence of tachypnea within hours after birth with typical radiological findings. Small for gestational age was defined as birth weight less than, or equal to the 10th percentile. Large for gestational age was defined as birth weight greater than, or equal to the 90th percentile.18

The Statistical Package for Social Sciences version 17 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Data were described using frequencies and percentages. The differences between proportions were tested using chi-square test. Multivariate analysis of factors associated with RM including TTN and RDS was conducted using binary logistic regression with forward selection method in separate models. Only variables that were statistically significant were reported and interpreted after adjusting for other variables including maternal illness, women pre-pregnancy BMI, labor, baby’s gender, and birth weight. Adjusted odds ratios and their 95% confidence intervals were reported. A p-value less than 0.05 was considered statistically significant.

Results. Newborns’ and mothers’ characteristics. A total of 2282 newborns were included in the study. More than half of the newborns (55.9%) were delivered by vaginal delivery and 44% by CS (24.5% emergency CS and 19.5% elective CS). Labor preceded elective CS in 2.9% (13/446) of the cases with a mean duration of 2.2 hours. Table 1 shows comparison of the neonatal and maternal characteristics among the 3 groups.

Respiratory morbidities according to newborns’ and mothers’ characteristics. Overall, 3.7% (95%
Confidence interval (CI): 2.4%-4.5%) of babies were born with RM. The incidence rate of TTN was 2.9% (95% CI: 2.2%-3.6%) and RDS was 0.7% (95% CI: 0.4%-1.0%). Table 2 shows the RM according to maternal and neonatal characteristics. Babies born to mothers with medical illnesses had higher incidence of RM (6.9% versus 3.2%, *p*=0.001) including both TTN (4.7% versus 2.6%, *p*=0.04), and RDS (2.2% versus 0.5%, *p*=0.001) without increased risk of mortality. Of the maternal illnesses, hypertension and diabetes mellitus were associated with higher rates of newborn RM, mainly TTN. None of the other maternal characteristics were correlated with a higher incidence of RM. The only neonatal characteristics that were associated with RM were the gender of the baby and gestational age. Male babies had higher rates of RDS (1.1% versus 0.4% for females, *p*=0.04) and those who were large for gestational age had higher rates of TTN (6.8% versus 2.9% for babies with normal weight, *p*=0.008). Of the whole cohort, there were 4 deaths, 2 had pulmonary hypertension, and the other 2 died of proved sepsis and adrenal hemorrhage.

**Respiratory morbidities according to mode of delivery and presence of labor.** Table 3 shows the incidence of RM according to mode of delivery and presence of labor. The incidence rate of RM for neonates born by elective CS (8.7%) was significantly higher than neonates born by vaginal delivery (2%) and those born by emergency CS (3.6%), *p*<0.005. In comparison with newborns delivered vaginally, those delivered by emergency CS had higher incidence of TTN (3% versus 1.5%) but not RDS (0.5 versus 0.3%), while those born by elective CS had higher incidence of both TTN (6.7% versus 1.5%) and RDS (2% versus 0.3%). However, when the incidence of RM was stratified by gestational age (Table 4), the risk of RM varied significantly according to the mode of delivery for babies born at 38 weeks (2.4% for vaginal delivery, 0% for emergency CS, and 6.8% for elective CS, *p*=0.007) and 39 weeks (1.0%...
for vaginal delivery, 1.7% emergency CS, and 5.6% for elective CS, \( p=0.047 \). The presence of labor was associated with decreased risk of respiratory morbidity, including both TTN and RDS.

Table 4 shows the incidence of respiratory illness according to mode of delivery stratified by gestational age.

**Multivariate analysis of factors associated with respiratory morbidity.** The only factors that were significantly correlated with any RM were gestational age and mode of delivery (Table 5).

### Table 3 - The respiratory morbidities according to mode of delivery and presence of labor.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Respiratory morbidity</th>
<th>TTN</th>
<th>RDS</th>
<th>P-value</th>
<th>P-value</th>
<th>P-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode of delivery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>26 (2.0)</td>
<td>19 (1.5)</td>
<td>4 (0.3)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Emergency CS</td>
<td>20 (3.6)</td>
<td>17 (3.0)</td>
<td>3 (0.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective CS</td>
<td>39 (8.7)</td>
<td>30 (6.7)</td>
<td>9 (2.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Presence of labor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No</td>
<td>37 (8.2)</td>
<td>28 (6.2)</td>
<td>9 (2.0)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48 (2.6)</td>
<td>38 (2.1)</td>
<td>7 (0.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Newborns delivered by vaginal delivery represented the control group.

CS - cesarean section, TTN - transient tachypnea of the newborn, RDS - respiratory distress syndrome

The risk of TTN disappeared at 39\(^{0}+6\) weeks of gestation while the risk of RDS disappeared after 37\(^{0}+6\) weeks of gestation. Children who were born at an earlier GA were more likely to have RM including both TTN and RDS compared to those born at \( \geq 40 \) weeks of gestation. The odds of having these outcomes were the highest for those who were born at 36\(^{0}+6\) weeks of gestation. Babies who were born via elective CS were more likely to have RM (OR=7.30) and TTN (OR=9.01) when compared to children born via vaginal delivery.

**Discussion.** The high rate of CS delivery (44%) encountered in this study is significantly higher than what has previously been reported in Jordan in 2004 (16%).\(^3\) This may not reflect the true rate of CS delivery in Jordan rather than an overestimated figure because the study was conducted in a tertiary referral center and included only term and near term babies. It is noticeable that most of our elective CS deliveries (79.7%) were performed at less than 39 weeks of gestation and almost half (47%) before completing 38 weeks. This clearly shows that the practice of performing elective CS at 39 weeks or more is not adhered to.

The risk of RM was 7 times more in elective CS when compared to vaginal delivery. This rate is higher than...
what has been reported by others,9,19 likely secondary to
the high rates of elective CS delivery before completing
390+6 weeks of gestation in our cohort. Babies born
by elective CS showed relatively higher rates of both
TTN (6.7%) and RDS (2%) compared to vaginal and
emergency CS. However, in concordance with what is
reported by Zanardo et al,7 the risk of TTN disappeared
after 39 0+6 weeks of gestation while the risk of RDS
significantly disappeared after 37 0+6 weeks (Table 5).
Babies delivered by emergency CS showed significantly
lower rates of RM including both TTN and RDS when
compared to elective CS. The possible explanation is the
stress experienced by these fetuses at the time of birth
resulting in physiological changes of the hormonal
media that permitted better lung adaptation.14 These
results add more evidence to the protective role of
labor against RM.11,20 Our trend of earlier delivery
affected the short-term respiratory outcome even after
adjustment of confounders and confirmed that the risk
of RM decreased with increasing gestation age up to
390+6 weeks, being highest at 360+6 weeks (OR 15.7).
This is consistent with previously reported findings.5,9,19
Our findings also stress the importance of perinatal
characteristics in predicting adverse respiratory outcome.
This study showed that the absence of maternal illness
is protective against TTN and RDS.6 In concordance
with Flinston et al,5 we found that the only maternal
illnesses that are associated with higher rates of RM
were hypertension and diabetes mellitus. The role of
maternal diabetes has shown to be an independent
variable in RDS.21 The present work showed that infants
of diabetic mothers are at higher risk for elective CS and
more prone to RM particularly TTN. This is very likely
to be attributed to the obstetrical practice of delivering
these babies before 39 week by elective CS.
As for neonatal characteristics, this study showed
that LGA babies had a higher rate of TTN, while male
gender was associated with increased rate of RDS,
which is consistent with other results.21-23 This study
emphasizes the role of careful planning for elective
CS by obstetricians to prevent the negative impact on
immediate neonatal outcomes.

**Study limitations.** 1) It is conducted in a single
tertiary care center where the practice of performing
elective CS may not reflect the practice in the country
at large. 2) The small number of total cases with RM.
However, since one of the purposes of this study is
to identify the risks for respiratory morbidities with
respect to the mode of delivery, we still believe that our
results provide important information that may guide
for delivery planning particularly when considering
elective CS delivery in high-risk situations.

In conclusion, TTN is 4 times most common than
RDS (2.9 versus 0.7). The responsible obstetrician
should collaborate with the responsible neonatologist to
identify the risk factors for adverse neonatal respiratory
outcome such as maternal illness, maternal age, parity,
gestational age, absence of labor, gender and weight
of the baby when considering the time and mode of
delivery. The pregnant mother should be informed
on the possible respiratory morbidities if delivery by
elective CS is performed before 390+6 weeks of gestation.

### Table 5 - Multivariate analysis of factors associated with respiratory morbidities.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Respiratory morbidity</th>
<th>Transient tachypnea of the newborn</th>
<th>Respiratory distress syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% confidence interval*</td>
<td>P-value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gestational age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>360+6</td>
<td>15.70</td>
<td>6.35 - 38.84</td>
<td>0.000</td>
</tr>
<tr>
<td>370+6</td>
<td>5.15</td>
<td>2.15 - 12.36</td>
<td>0.000</td>
</tr>
<tr>
<td>380+6</td>
<td>2.59</td>
<td>1.04 - 6.46</td>
<td>0.042</td>
</tr>
<tr>
<td>390+6</td>
<td>1.56</td>
<td>0.57 - 4.22</td>
<td>0.386</td>
</tr>
<tr>
<td>≥400+6</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Mode of delivery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Emergency CS</td>
<td>1.40</td>
<td>0.76 - 2.58</td>
<td>0.286</td>
</tr>
<tr>
<td>Elective CS</td>
<td>7.30</td>
<td>1.75 - 30.51</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*Data are adjusted for maternal illness, women pre-pregnancy BMI, labor, and baby's gender and birth weight,1 gestation age more than 40 week group
was considered as the control group. Vaginal delivery group was considered as the control group. CS - cesarean section, TTN - transient tachypnea of the
newborn, RDS - respiratory distress syndrome, OR - odds ratio
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References


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