

The Impact of Timing of Elective Cesarean Delivery at Term in Neonatal Respiratory Morbidity

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Abstract

The aim is to investigate the association between elective caesarean sections and neonatal respiratory morbidity and the importance of timing of elective caesarean sections

Methods: Cohort study with prospectively collected data of all elective Caesarean sections on mothers with a gestational age of 37+0 weeks and more, that were performed in our Hospital from 1 January 2011 to 1 January 2017. Multiple pregnancies, fetuses with congenital anomalies, intrauterine deaths, and emergency Caesarean sections were excluded. Primary outcome measures of neonatal respiratory morbidity included transient tachypnea of newborn, respiratory distress syndrome, persistent pulmonary hypertension of the newborn.

Results: 4290 infants were delivered by elective caesarean section at 37+0 and then after Compared with newborns from vaginal delivery, and emergency caesarean section an increased risk of respiratory morbidity was found for infants delivered by elective caesarean section at 37 +0 weeks' gestation to 37+6 weeks (odds ratio 5.7 95% confidence interval 4.3 to 8.9), 38+0 weeks' gestation to 38+6 weeks (2.8 , 2.1 to 4.2), and 39+0 weeks' gestation (2.1, 1.5 to 2.8). Also increasing the incidence of admission to the NICU with decreasing gestational age at term birth below the 39 weeks of gestation

Conclusions: Compared with newborn delivered vaginally or by emergency caesarean sections, those delivered by elective caesarean section around term have an increased risk of respiratory morbidity. The relative risk increased with decreasing gestational age.

Keywords: Elective caesarean section, neonatal respiratory morbidity, neonatal transient tachypnea, Respiratory distress syndrome, pulmonary hypertension

Introduction

Infants born before 39 weeks of gestation are at increased risk for neonatal adverse respiratory outcomes, and the risk increases progressively as gestational age at birth declines. [1, 2] As compared with infants born vaginally, those born by caesarean section are at increased risk for adverse respiratory

outcomes, especially when delivery occurs before the onset of labor.[1, 2, 5] This increased risk persists even in infants who are delivered by caesarean section at full term (i.e., at or beyond 37 completed weeks of gestation).

The rate of caesarean delivery in the United States rose from 20.7% in 1996 to 31.1% in 2006.[6] Deliveries by caesarean section continue to increase in both developed and developing countries. Rates as high as 50% have been reported in some regions of Latin America.[4]

Recently many other factors, such as reduced risk to the mother as a result of improved anesthetic procedures and surgical techniques, elective caesarean section because of breech presentation, or previous caesarean section may have contributed to changes in obstetric practice and patient choice. [2, 3, 4] Thus increased rates of elective caesarean section without any obvious or generally accepted medical or obstetric indication have been reported to contribute further to the increasing rate of elective caesarean sections. [7, 8] If no medical indication is present evidence based information about risks and benefits for mothers as well as newborns becomes all the more important for adequate counselling.

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Gestational age at the time of elective caesarean section may also be important for respiratory morbidity in neonates. [10, 11, 12, 13]

We evaluated the association between elective caesarean section and neonatal respiratory morbidity in a large cohort of women with low risk pregnancies. We also separately analyses the effect of gestational age at the time of elective caesarean section.

Material and Methods

Cohort study with prospectively collecting data from 1 January 2011 and 31 December 2016 at University Obstetric-Gynecologic Hospital "Queen Geraldine" for 41 095 live singletons delivery. We included in our analyses all live born singletons without congenital malformations of gestational ages 37 to 40 completed weeks (24836 pregnancies). A subgroup (23414 pregnancies) was constructed to analyze the outcome of low risk pregnancies only. We therefore excluded all pregnancies associated with intrauterine growth retardation (n 320), diabetes (gestational or overt; n=120) and pre-eclampsia or hypertension (n=982). We defined intrauterine growth retardation as birth weight less than 2500 g in infants born after 36 completed weeks of gestation.

Deliveries were categorized as vaginal, elective caesarean section, emergency caesarean section. We categorized caesarean sections after start of labor or rupture of the membranes as emergency caesarean sections. Labor was defined as regular uterine contractions with progression of cervical dilation.

We measured gestational age in completed weeks on the basis of last menstrual period. (LMP) or ultrasound of the first –trimester.

We considered information only related to newborn admissions to hospital immediately after delivery. The following neonatal outcomes adverse respiratory outcomes (respiratory distress or transient tachypnea of the newborn), admission to the neonatal intensive care unit (ICU), and day hospital care. The prespecified primary outcome was a composite that included any of the above outcomes. The infants were followed up until discharge from the hospital.

The diagnosis of respiratory distress required signs as cyanosis, tachypnea (RF > 60/min), intercostal and epigastric withdrawn, expiratory grunting, consistent radiologic features, and oxygen therapy with a fraction of inspired oxygen (FIO₂) of 0.40 or greater for at least 24 hours or until death. Transient tachypnea of the newborn (TTN) was defined by the presence of tachypnea within hours after birth and typical radiologic findings, and persistent pulmonary hypertension of the newborn as a serious respiratory morbidity requiring treatment for three or more days with continuous oxygen supplementation, nasal continuous positive airway pressure, or any period of mechanical ventilation.

We repeated analyses after exclusion of newborns with meconium aspiration syndrome (n=82), sepsis; 253),

or pneumonia (; n=45) because these conditions may cause respiratory symptoms unrelated to delayed transition from fetus to newborn but are associated with vaginal delivery.

We carried out bivariate analyses to compare the risk of respiratory morbidity in babies delivered by elective caesarean section with the risk after vaginal delivery and emergency section caesarean within each gestational week. We present the association between mode of delivery and respiratory morbidity as odds ratios with 95% confidence intervals. We used logistic regression analyses to evaluate potential confounding variables (parity, maternal age,). Adjusted odds ratios are also presented for respiratory morbidity but not for serious respiratory morbidity owing to the small number of observations.

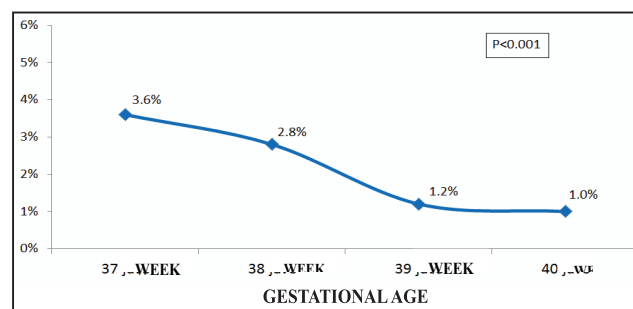
The statistical analysis has been made with Statistical Package for Social Sciences (SPSS), version 19.

Results

Between January 2011- December 2016 there were 23414 live singleton births at our hospital. Among them 17497 term newborn or 74.7% delivered vaginally, 4290 (18.3 %) term new born section.

Assessing the Impact of Time of Performing Elective Cesarean Section on the Frequency of Neonatal Transient Tachypnea

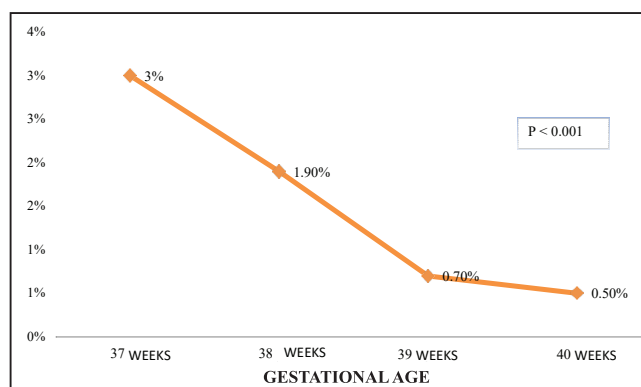
Graphic 1. Show the incidence of neonatal transient tachypnea by duration of pregnancy. The incidence of TTN decreases with increasing duration of pregnancy. The incidence of TTN is significantly higher in infants born to 37-week (3.6%) and 38-week pregnancies (2.8%) and decreases to a minimum in 40-week pregnancies (1%).



Graph.1. Incidence (%) of transitional tachypnea of neonate link with the gestational age 2011-2016

Assessing the Impact of Time of Performing Elective Cesarean Section on the Frequency of Respiratory Distress.

Graphic 2 show the incidence of respiratory distress by duration of pregnancy. The incidence of respiratory distress increasing duration of pregnancy. The incidence of D.R. is significantly higher in infants born to 37-week (3%) and 38-week (1.9%) pregnancies and decreases to a minimum in 40-week pregnancies (0.5%)



Graf. 2. Incidence (%) of Respiratory distress at neonates according to the gestational age, 2011-2016

Tab.1. Odds ratio of TTN of babies delivered from 2011-2016, after ECS, vaginal delivery and emergency section cesarean according to Completed Week of Gestation at Delivery.

The trends toward the increasing the incidence TTN with decreasing gestational age at term birth below the 39 weeks of gestation remained significant in analyses adjusted for potential confounders; the adjusted odds ratios 4.3 for ECS and 2.3 for vaginal delivery for 37 weeks of gestation, and for 38 weeks of gestation is respectively 2.4 for ESC and 1.9 for emergency section cesarean.

Tab 1. Odds Ratio of TTN According to Completed Week of Gestation at Delivery and way of birth -Odds Ratio from the Binary Logistic Regression

	Variable	Model 1 ‡			Model 2 ¶		
		OR §	95% CI *	Value of P †	OR	95% CI *	Value of P †
Vaginal delivery	Gestational age †			<0.001 (3)			<0.001 (3)
	37.0-37.06 weeks	2.6	1.7-4.0	<0.001	2.8	1.8-4.2	<0.001
	38.0-38.06 weeks	1.4	0.9-2.3	0.127	1.5	0.9-2.4	0.097
	39.0-39.06 weeks	1.0	0.7-1.5	0.822	1.1	0.7-1.5	0.797
	40.0-40.06 weeks	1.0	-	-	1.0	-	-
Emergency SC	Gestational age †			0.090 (3)			0.093 (3)
	37.0-37.06 weeks	1.2	0.3-5.4	0.828	1.3	0.3-6.1	0.735
	38.0-38.06 weeks	1.8	0.7-4.8	0.254	1.9	0.7-5.2	0.214
	39.0-39.06 weeks	0.4	0.2-1.1	0.081	0.4	0.2-1.2	0.113
	40.0-40.06 weeks	1.0	-	-	1.0	-	-
Elective SC	Gestational age †			<0.001 (3)			<0.001 (3)
	37.0-37.06 weeks	4.3	2.0-9.2	<0.001	4.3	2.0-9.3	<0.001
	38.0-38.06 weeks	2.4	1.1-5.0	0.022	2.4	1.1-5.0	0.022
	39.0-39.06 weeks	1.4	0.7-2.9	0.394	1.4	0.7-2.9	0.384
	40.0-40.06 weeks	1.0	-	-	1.0	-	-

§ Odds Ratio of transient tachypnea of the newborn (TTN) According to Completed Week of Gestation at Delivery – Binary logistic regression.

* confidence interval 95% (95% CI) per OR

† P value statistically significant from binary logistic regression and degrees of freedom (in parentheses).

‡ Model 1 unadjusted for any of factors

¶ Model 2: adjusted for mother age.

Tab2 Odds Ratio of Respiratory Distress (RD) after vaginal delivery, emergency S.C. and E.C.S. according to Completed Week of Gestation at Delivery for 2011-2016.

The trends toward the increasing the incidence of respiratory distress with decreasing gestational age at term

birth for 37 weeks of gestation at E.C.S remained significant in analyses adjusted for potential confounders; the adjusted odds ratios 39.8 at 37 weeks of gestation and 1.3 to 12.1 at 38 weeks of gestation, as compared with 1.0 at 40 weeks of gestation . (Model 2)

Tab 2. Odds Ratio of RD According to Completed Week of Gestation at Delivery and way of birth
-Odds Ratio from the Binary Logistic Regression

Type of Delivery	Variable	Model 1			Model 2 †		
		OR §	95% CI *	P value †	OR	95% CI *	P value †
Vaginal delivery	Gestational age †			0.019 (3)			0.017 (3)
	37.0-37.06week	1.5	0.8-2.7	0.197	1.5	0.8-2.8	0.176
	38.0-38.06week	2.1	1.3-3.5	0.003	2.2	1.3-3.6	0.003
	39.0-39.06week	1.1	0.7-1.7	0.599	1.1	0.7-1.7	0.588
	40.0-40.06week	1.0	-	-	1.0	-	-
Emergency Sectio Ceasarea	Gestational age †			-			-
	37.0-37.06week	NA	-	-	NA	-	-
	38.0-38.06week	NA	-	-	NA	-	-
	39.0-39.06week	NA	-	-	NA	-	-
	40.0-40.06week	1.0	-	-	1.0	-	-
Elective Sectio Ceasarea	Gestational age †			<0.001 (3)			<0.001 (3)
	37.0-37.06 week	39.4	5.4-286.7	<0.001	39.8	5.4-289.9	<0.001
	38.0-38.06 week	12.1	1.7-88.1	0.014	12.1	1.6-88.2	0.014
	39.0-39.06 week	2.4	0.3-18.5	0.414	2.4	0.3-18.6	0.411
	40.0-40.06 week	1.0	-	-	1.0	-	-

§ Odds Ratio of respiratory distress (RDS) for each week of gestational age at delivery – Binary logistic regression.

* confidence interval 95% (95% CI) per OR

† P value statistically significant from binary logistic regression and degrees of freedom (in parentheses).

‡ Model 1 unadjusted for any of factors

¶ Model 2: adjusted for mother age.

NA – Model Not Applied due to very few cases of interest

Tab 3. Odds ratios (95% confidence intervals) of neonatal respiratory morbidity after vaginal delivery, emergency s.c. and E.C.S. according to Completed Week of Gestation at Delivery for 2011-2016.

Compared with infants delivered by women intended to have a vaginal delivery, those delivered by elective caesarean section had an increased risk of respiratory

morbidity at any gestational age before 40 weeks. A nearly fourfold increased risk was found at 37 weeks' gestation (odds ratio 5.7, 95% confidence interval 4.3 to 8.9) and a threefold increase in risk at 38 weeks' gestation (2.8, 2.1 to 4.2), whereas the risk was doubled in infants delivered at 39 weeks' gestation (2.1, 1.5 to 2.8;)

Tab 3. Odds Ratio of Neonatal Respiratory Morbidity According to Completed Week of Gestation at Delivery and way of birth-Odds Ratio from the Binary Logistic Regression

GESTATIONAL AGE		Model 1 ‡			Model 2 ¶		
		OR §	95% CI *	P value †	OR	95% CI *	P value †
37 weeks	Type of delivery †			<0.001 (3)			<0.001 (3)
	Vaginal delivery	1.0	-	-	1.0	-	-
	Emergency SC	3.0	1.4-6.6	0.005	2.9	1.3-6.3	0.008
	Elective SC	6.2	4.3-8.9	<0.001	5.7		<0.001
38 weeks	Type of delivery			<0.001 (3)			<0.001 (3)
	Vaginal delivery	1.0	-	-	1.0	-	-
	Emergency SC	1.3	0.6-3.2	0.516	1.3	0.5-3.1	0.548
	Elective SC	2.9	2.1-4.2	<0.001	2.8	2.0-4.0	<0.001
39 weeks	Type of delivery			<0.001 (3)			<0.001 (3)
	Vaginal delivery	1.0	-	-	1.0	-	-
	Emergency SC	1.0	0.5-1.8	0.968	1.0	0.5-1.9	0.968
	Elective SC	2.1	1.5-2.8	<0.001	2.1	1.5-2.9	<0.001
40 weeks	Type of delivery			0.411 (3)			0.411 (3)
	Vaginal delivery	1.0	-	-	1.0	-	-
	Emergency SC	1.3	0.7-2.4	0.400	1.3	0.7-2.4	0.399
	Elective SC	1.5	0.7-2.9	0.269	1.5	0.7-2.9	0.269

§ Odds Ratio of respiratory morbidity for each week of gestational age at delivery – Binary logistic regression.

* confidence interval 95% (95% CI) per OR

† P value statistically significant from binary logistic regression and degrees of freedom (in parentheses).

‡ Model 1 unadjusted for any of factors

¶ Model 2: adjusted for mother age.

NA – Model Not Applied due to very few cases of interest

Tab 4. Odds Ratio of Admission to the NICU after vaginal delivery, emergency S.C. and E.S.C. According to Completed Week of Gestation at Delivery for 2011-2016.

The trends toward the increasing the incidence of admission to the NICU with decreasing gestational age at term birth below the 39 weeks of gestation remained

significant in analyses adjusted for potential confounders; the adjusted odds ratios 16.2 for ECS and 9 for Emergency cesarean section for 37 weeks of gestation, and for 38 weeks of gestation is respectively 5.3 for ESC ,1.6 for vaginal delivery. (Model 2).

Tab 4. Odds Ratio of Admission to the NICU According to Completed Week of Gestation at Delivery and way of birth -Odds Ratio from the Binary Logistic Regression

		Model 1			Model 2 †		
		OR §	95% CI *	P value †	OR	95% CI *	P value †
Vaginal delivery	Gestational age †			<0.001 (3)			<0.001 (3)
	37.0-37.06 week	2.0	1.4-3.0	<0.001	2.0	1.4-3.0	<0.001
	38.0-38.06week	1.6	1.1-2.4	0.018	1.6	1.1-2.4	0.022
	39.0-39.06week	1.1	0.8-1.4	0.760	1.1	0.8-1.4	0.768
	40.0-40.06week	1.0	-	-	1.0	-	-
Emergency Sectio Ceasarea	Gestational age †			0.002 (3)			0.002 (3)
	37.0-37.06 week	7.5	2.4-23.8	0.001	9.0	2.7-30.3	<0.001
	38.0-38.06 week	0.6	0.1-4.9	0.619	0.7	0.1-5.6	0.700
	39.0-39.06 week	1.7	0.6-4.5	0.296	1.9	0.7-5.3	0.212
	40.0-40.06 week	1.0	-	-	1.0	-	-
Elective Sectio Ceasarea	Gestational age †			<0.001 (3)			<0.001 (3)
	37.0-37.06week	16.2	5.8-44.6	<0.001	16.2	5.9-44.8	<0.001
	38.0-38.06week	5.3	1.9-14.6	0.001	5.3	1.9-14.7	0.001
	39.0-39.06week	1.7	0.6-4.9	0.315	1.7	0.6-4.9	0.313
	40.0-40.06week	1.0	-	-	1.0	-	-

§ Odds Ratio of Admission to NICU for each week of gestational age at delivery – Binary logistic regression.
 * confidence interval 95% (95% CI) per OR

† P value statistically significant from binary logistic regression and degrees of freedom (in parentheses).

‡ Model 1 unadjusted for any of factors

¶ Model 2: adjusted for mother age.

NA – Model Not Applied due to very few cases of interest

Discussion

Births after elective cesarean section before the 39th week of pregnancy are common and are associated with neonatal respiratory morbidity as well as other neonatal diseases.

Neonate born before the 39th week of gestation have a higher risk of developing neonatal respiratory diseases and this risk increases with the reduction of gestational age. [1, 2] Compared to neonates from vaginal delivery those from cesarean section presents a higher risk for respiratory problems especially when birth occurs before the onset of birth activity. [1, 2, 5 -11]

Our study included approximately 23414 unique births during the period 2011-2016, of which approximately 4290 babies or 18.3% were born with elective section cesarea. Among the latter the distribution by age of pregnancy is respectively 12.2% at week 37, 37.4% at week 38, 40.8% at week 39, and 9.6% performed at week 40 of pregnancy. To achieve the objectives established births were divided into three groups as mentioned above.

The *Morrison et al.* report on respiratory distress (DR) and transitory tachypnea of neonate (TTN) for over 33,000 births per term comparing birth and gestational age at birth [19]

Although the incidence of DR and TTN was lower at 2.2 per 1000 births and 5.7 per 1000 births, respectively, compared to our study where the incidence of DR and TTN was higher at 30 per 1000 births and 39 per 1000 births, respectively. respiratory morbidity was higher for neonates born with CS before initiation of labor (35.3 out of 1000) compared to vaginal births (5.4 out of 1000; OR: 6.8; 95% CI: 5.2-7.9) while in the study ours have OR3.7; 95% CI: 3.1-4.3, $p < 0.001$)

According to *Hansen et al.* a systematic review is undertaken to evaluate the association between birth by ECS and neonatal respiratory morbidity. [10]

A total of nine studies were included (one case-control, one prospective cohort, and seven retrospective cohort studies), but the results were not able to be combined in a meta-analysis due to differences in methodology. [3]

Overall, there was a 2-3-fold increased risk of occurrence of all respiratory morbidity nosology's (DR, TTN, persistent pulmonary hypertension, mechanical ventilation, pneumonia, and meconium aspiration) in SC deliveries in term. [10]

Similarly, a *WHO study* involving almost 100,000 births confirmed that delivery with elective cesarean section and intrapartum was associated with a doubling of the risk of transfer (for each indication) to neonatal REA for 7 days or more (adjusted for gestational variables and age) [2]

The risk of respiratory illness and transfer of neonate to REA varies from gestational age to term.

In a systematic review of Hansen, the magnitude of this risk decreased with advancing gestational age, although a small risk remained at births after week 39 of pregnancy. [11]

In a prospective cohort study by *Hansen al.* the incidence of respiratory morbidity (DR, TTN, HP) and severe respiratory morbidity (oxygen therapy for more than

2 days, pressure or mechanical ventilation) is approximately 10% at week 37 of pregnancy while in our study it reached 18%. At week 40 of pregnancy this incidence at 1.5% is not significant and is similar to that of vaginal births. The same is observed in our study where incidence of respiratory disease at week 40 is 1.9% approximate to that of vaginal births of 1.5%. [11]

Vaginal born neonates constitute the standard reference group. Neonates born with CS had a significantly higher risk of developing respiratory disease at 37 weeks approximately 3.9 times higher, at 38 weeks approximately 3.0 times higher, and at 39 weeks approximately 1.9 times higher gestational age. [11] The same was observed in our study that the risk of developing respiratory illness increased at 37 weeks approximately 5.7 times, at 38 weeks increased by 2.8 times, and at 39 weeks increased 2.1 times gestational age. It should remind that the Hansen and Al study included the 41st week of pregnancy as the reference group while the 40th week of pregnancy is the reference group in our study.

Conclusion

The risk of neonatal respiratory morbidity after elective caesarean section in singletons born at University Obstetric Gynecologic Hospital "Queen Geraldine", between 1 January 2011 and 31 December 2016 was twice to four times that after intended vaginal delivery within each gestational week from 37 to 39 weeks. When the risk of respiratory morbidity after elective caesarean section in each gestational week was compared with the risk after intended vaginal delivery at 40 weeks' gestation, the relative risk decreased from seven times higher at 37 weeks to three times higher at 38 weeks, whereas the relative risk at 40 weeks was no longer statistically significance. Based on the fact that respiratory morbidity in babies born with ESC is significantly associated with gestational age when the intervention is performed, we recommend careful planning for SC after 39 gestational age bringing about a decrease in gestational age, hospital costs as well as avoiding the need to separate neonates from parents.

This information should be considered and suggested to women seeking to undergo an elective S.C.

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