# Influence of Mode of Delivery at Term on the Neonatal Respiratory Morbidity

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**Abstract:** <u>Aim</u>: To investigate the association between elective caesarean sections and neonatal respiratory morbidity and the importance of timing of elective caesarean sections. <u>Methods</u>: 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 newborn. <u>Results</u>: 4290 infants were delivered by elective caesarean section at 37+0 and then after Compared with newborns from vaginal delivery, and emergency cesarean section to 37+6 weeks (odds ratio 4.5 95% confidence interval 3.3 to 6.3), 38+0 weeks' gestation to 38+6 weeks (2.7, 1.9 to 3.6), and 39+0 weeks' gestation (2.1, 1.6 to 3.0). <u>Conclusions</u>: Infants born by elective caesarean delivery at term are at increased risk for developing respiratory disorders compared with those born by vaginal delivery. A significant reduction in neonatal RDS would be obtained if elective caesarean delivery were performed after 39+0 gestational weeks of pregnancy.

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

#### 1. 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.<sup>1,2</sup> As compared with infants born vaginally, those born by cesarean section are at increased risk for adverse respiratory outcomes, especially when delivery occurs before the onset of labor.<sup>1,2,5-</sup>This increased risk persists even in infants who are delivered by cesarean section at full term (i.e., at or beyond 37 completed weeks of gestation).

The rate of cesarean delivery in the United States rose from 20.7% in 1996 to 31.1% in 2006.<sup>6</sup> Caesarean section used to be carried out primarily because of obstetric complications or serious maternal illness. Lately many other factors, such as reduced risk to the mother as a result of improved anesthetic procedures and surgical techniques, may have contributed to changes in obstetric practice and patient choice.<sup>234</sup> 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.<sup>789</sup>

It is plausible that hormonal and physiological changes associated with labor are necessary for lung maturation in neonates and that these changes may not occur in infants delivered by elective caesarean sections.  $\frac{10 \ 111213}{10 \ 111213}$  Gestational age at the time of elective caesarean section may also be important for respiratory morbidity in neonates.  $\frac{10}{10}$ 

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.

### 2. 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

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following neonatal outcomes adverse respiratory outcomes (respiratory distress syndrome or transient tachypnea of the newborn), resuscitation, Apgar score at 1 and 5 minute ,, admission to the neonatal intensive care unit (ICU), and day hospital care . The infants were followed up until discharge from the hospital.

The diagnosis of respiratory distress syndrome required signs of respiratory distress syndrome (RDS), 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. To evaluate effect modification by gestational age we used stratified analyses. 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.

## 3. Results

Between January 2011 –December 2016 there were 23414 live singleton births at our hospital. Among them 17497 term newborn or 74.7% delivered vaginaly, 4290 (18.3%) term newborns delivered by elective caesarean section, and 1627 (6.9%) delivered by emergency cesarean section.

The number of infants with respiratory morbidity (RDS, TTN, PH) associated with elective caesarean delivery or vaginal delivery between the weeks at term is shown in Fig. 1.

The incidence of respiratory morbidity (RDS, TTN and HP) after elective caesarean delivery at term and after vaginal delivery was, respectively, 180 and 19 /1000 deliveries, and 47and 10/1000 deliveries. In comparison with vaginal births, infants delivered by elective caesarean section showed a significant progressive reduction in the incidence of neonatal Respiratory morbidity from week 37 + 0 to week 37 + 6 and thereafter.

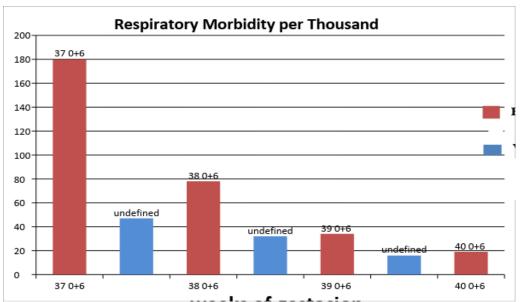


Figure 1: Incidence of respiratory morbidity per thousand live births shown by each week of gestation and mode of delivery

The number of infants with RM following elective caesarean delivery diminishes significantly with each week of gestation up to week

Link between gestacional ages and Transient tachypnea of the newborn

Tab. 1. Odds ratio of TTN of babies delivered from2011-2016, after ECS ,vaginal delivery and emergency

## sectio 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.

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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** 

Binary Logistic Regression							
		Model 1 <sup>‡</sup>			Model 2		
	Variable	OR §	95% CI *	Value of P †	OR	95% CI *	Value of P †
Vaginal delivery	Gestacional 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	Gestacional 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	Gestacional 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) për OR

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

‡ Model 1 unadjusted for any of factors

¶ Model 2: adjusted for mother age.

Tab 2 Odds Ratio of Respiratory Distress Sindrom( RDS) 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)

Delivery and way of birth -Odds Ratio from the Binary Logistic Regression								
		Modeli 1 <sup>‡</sup>			Modeli 2 ¶			
	Variabli	OR §	95% CI *	P value †	OR	95% CI *	P value †	
	Gestacional age †			0.019 (3)			0.017 (3)	
	37.0-37.06 week	1.5	0.8-2.7	0.197	1.5	0.8-2.8	0.176	
Vaginal delivery	38.0-38. 06 week	2.1	1.3-3.5	0.003	2.2	1.3-3.6	0.003	
	39.0-39. 06 week	1.1	0.7-1.7	0.599	1.1	0.7-1.7	0.588	
	40.0-40. 06 week	1.0	-	-	1.0	-	-	
	Gestational age †			-			-	
	37.0-37. 06 week	NA	-	-	NA	-	-	
Emergency sectio cesarea	38.0-38 .06 week	NA	-	-	NA	-	-	
	39.0-39. 06 week	NA	-	-	NA	-	-	
	40.0-40. 06 week	1.0	-	-	1.0	-	-	
Elective Secio cesarea	Gestacional 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	-	-	

Table 2: Odds Ratio of Respiratory Distres According to Completed Week of Gestation at Delivery and way of birth -- Odds Patio from the Binany Logistic Pegression

gestacional age at delivery - Binary logistic regresion.

confidence interval 95% (95% CI) për OR

degrees of fredom (in parentheses).

<sup>‡</sup> Modeli 1 unadjusted for any of factors

¶ Modeli 2: adjusted for mother age.

NA - Modeli Not Applied due to very few cases of interest

Tab 3. Odds ratios (95% confidence intervals) of neonatal respiratory morbidity after vaginal delivery

<sup>§</sup> Odds Ratio of respiratory distress (RDS ) for each weeknewgency 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 <sup>†</sup> P value statistically significant from binary logistic regression varginal 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 4.5, 95% confidence interval 3.3 to 6.3) and a threefold increase in risk at 38 weeks' gestation (2.7, 1.9 to 3.6), whereas the risk was doubled in infants delivered at 39 weeks' gestation (2.1, 1.6 to 3.0;)

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 Table 3: Odds Ratio of Respiratory Morbidity According to Completed Week of Gestation at delivery and way of birth
Odds Ratio from the Binary Logistic Regression

GESTACIONAL AGE	Nr. Delivery	Nr % of infant	Odds ratio <sup>§</sup>	95% Cl *	Value of P <sup>†</sup> (3)
Type of delivery					
37 0+6 week					
E. S.C.	525	97 (18)	4.5	3.3 to 6.3	p<0.0001
Vaginal delivery	1559	74(4.7)	Reference		
38 0+6 week					
E. S.C.	1603	126(7.8)	2.7	1.9 to 3.6	p<0.0001
Vaginal delivery	1869	58 (3.2)	Reference		
39 0+6 week					
E. S.C.	1750	60(3.4)	2.1	1.6 to 3.0	p<0.001
Vaginal delivery	7115	114(1.6)	Reference		
40 0+6 week					
E. S.C.	411	8(1.9)	1.2	0.6 to 2.6	P =0.50
Vaginal delivery	6954	106 (1.5)	Reference		

<sup>§</sup> Odds Ratio of Neonatal Respiratory Morbidity for each wReferences

gestacional age at delivery - Binary logistic regresion. confidence interval 95% (95% CI) për OR

<sup>†</sup> P value statistically significant from binary logistic regression and spiratory morbidity and mode of delivery at term: degrees of fredom (in parentheses).

¶ Modeli 2: adjusted for mother age.

No mortality was recorded among either vaginally or caesarean delivered neonates.

#### 4. Discussion

The risk of neonatal respiratory morbidity after elective caesarean section in singletons born at University Obstetric Gynecologic Hospital "Queen Geraldin", 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 significant.

The careful planning of elective caesarean deliveries after week 39+ 0 could mean substantial cost savings and avoid the need to separate babies from their parents, which causes considerable anxiety to the family. Although mortality from respiratory disease in our infants was zero, the affected babies suffered painful procedures with the related risks of complications and additional morbidity, negative effects on their physiological and biochemical responses to birth, the development of pulmonary air leaks and persistent fetal circulation, and continuing respiratory symptom after discharge  $\frac{14}{}$ .

Adopting a policy to perform elective caesarean delivery at 39 +0 week of pregnancy also involves considering the risk of intrapartum versus elective caesarean delivery, the likelihood of spontaneous labor starting and informed maternal wishes 15

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