

Risk of respiratory morbidity in term infants delivered by elective caesarean section: cohort study

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ABSTRACT

Objective To investigate the association between elective caesarean sections and neonatal respiratory morbidity and the importance of timing of elective caesarean sections.

Design Cohort study with prospectively collected data from the Aarhus birth cohort, Denmark.

Setting Obstetric department and neonatal department of a university hospital in Denmark.

Participants All liveborn babies without malformations, with gestational ages between 37 and 41 weeks, and delivered between 1 January 1998 and 31 December 2006 (34 458 pregnancies).

Main outcome measures Respiratory morbidity (transitory tachypnoea of the newborn, respiratory distress syndrome, persistent pulmonary hypertension of the newborn) and serious respiratory morbidity (oxygen therapy for more than two days, nasal continuous positive airway pressure, or need for mechanical ventilation).

Results 2687 infants were delivered by elective caesarean section. Compared with newborns intended for vaginal delivery, an increased risk of respiratory morbidity was found for infants delivered by elective caesarean section at 37 weeks' gestation (odds ratio 3.9, 95% confidence interval 2.4 to 6.5), 38 weeks' gestation (3.0, 2.1 to 4.3), and 39 weeks' gestation (1.9, 1.2 to 3.0). The increased risks of serious respiratory morbidity showed the same pattern but with higher odds ratios: a fivefold increase was found at 37 weeks (5.0, 1.6 to 16.0). These results remained essentially unchanged after exclusion of pregnancies complicated by diabetes, pre-eclampsia, and intrauterine growth retardation, or by breech presentation.

Conclusion Compared with newborns delivered vaginally or by emergency caesarean sections, those delivered by elective caesarean section around term have an increased risk of overall and serious respiratory morbidity. The relative risk increased with decreasing gestational age.

INTRODUCTION

Elective caesarean section has been associated with an increased risk of respiratory morbidity in neonates,¹ although the causality and magnitude of the association are difficult to evaluate because of methodological shortcomings and differences between studies.

It is plausible that hormonal and physiological changes associated with labour are necessary for lung maturation in neonates and that these do not occur with elective caesarean sections.²⁻⁷ Gestational age at the time of elective caesarean section may also be important for respiratory morbidity.^{8,9}

We evaluated the association between elective caesarean section and neonatal respiratory morbidity in women with high and low risk pregnancies. We also analysed the effect of gestational age at the time of elective caesarean section.

METHODS

Since September 1989 women scheduled for delivery at Aarhus University Hospital, Denmark have been invited to participate in the Aarhus birth cohort study.¹⁰ Women attending routine antenatal care were asked to complete a questionnaire in the second trimester on medical and obstetric history, smoking, alcohol intake, marital status, educational level, and occupational status. Information on delivery and newborns was collected by midwives. Data on neonatal morbidity were obtained from discharge forms and neonatologists.

Between January 1998 and December 2006 our department delivered 41 095 live singletons. We analysed all liveborn singletons without congenital malformations of gestational ages 37 to 41 weeks, delivered between 1 January 1998 and 31 December 2006 (34 458 pregnancies). A subgroup of low risk pregnancies was also analysed (32 580 pregnancies).

We categorised caesarean sections as emergencies after start of labour or rupture of the membranes. For our final analyses we categorised deliveries in to elective caesarean section or intended vaginal delivery.

We considered information only related to newborn admissions immediately after delivery. Neonatal respiratory morbidity was coded using the international classification of diseases, 10th revision: any respiratory distress, transient tachypnoea of the newborn, and persistent pulmonary hypertension of the newborn (see bmj.com). We defined serious respiratory morbidity as that 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, sepsis, or pneumonia because these may cause respiratory symptoms unrelated to delayed transition from fetus to newborn but are associated with intended vaginal delivery.

We carried out bivariate analyses to compare the risk of respiratory morbidity in babies delivered by elective caesarean section with that after intended vaginal delivery within each gestational week. We then compared the risk of respiratory morbidity after elective caesarean section in each gestational week

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with the risk after intended vaginal delivery at 40 weeks as the reference.

We present the association between delivery type 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 confounders (for example, maternal smoking during pregnancy). Adjusted odds ratios are presented for respiratory morbidity but not for serious morbidity owing to small numbers.

RESULTS

Overall, 2687 liveborn singletons (7.8%) were delivered by elective caesarean section at Aarhus University Hospital between 1 January 1998 and 31 December 2006, leaving 31 771 women (92.2%) with intended vaginal delivery of which 2877 delivered by emergency caesarean section (see [bmj.com](#)). Overall, 1.8% (n=604) of infants had respiratory morbidity and 0.2% (n=64) had serious respiratory morbidity: 1.7% (n=556) and 0.2% (n=57) in the low risk population.

Compared with infants delivered vaginally 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 3.9, 95% confidence interval 2.4 to 6.5) and a threefold increased risk at 38 weeks (3.0, 2.1 to 4.3), whereas the risk was doubled in infants delivered at 39 weeks (1.9, 1.2 to 3.0; see [bmj.com](#)).

Adjustment for potential confounders failed to change considerably the risk estimates (see [bmj.com](#)). Bivariate analyses were repeated for low risk pregnancies, resulting in slightly higher risk estimates (see [bmj.com](#)).

Exclusion of newborns with meconium aspiration syndrome, sepsis, or pneumonia resulted in an increased risk in infants delivered by elective caesarean section regardless of gestational age, and the results tended towards slightly higher risk estimates (see [bmj.com](#)).

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 (see [bmj.com](#)). A significantly increased risk was found for infants delivered by elective caesarean section at 37 and 38 weeks' gestation (see [bmj.com](#)). Delivery by elective caesarean section at 39 weeks still showed an increased risk of respiratory morbidity compared with intended vaginal delivery at 40 weeks, despite not being statistically significant.

The risk of serious respiratory morbidity was increased in babies delivered by elective caesarean section from 37 to 39 weeks' gestation compared with babies delivered during the same weeks after intended vaginal delivery (see [bmj.com](#)). The relative risk increased with decreasing gestational age but the risk estimates were higher than those for respiratory morbidity, with a fivefold increase for infants delivered

at 37 weeks, a fourfold increase for infants delivered at 38 weeks, and a more than twofold increase for infants delivered at 39 weeks, although the increased risk at 39 weeks was not statistically significant.

Restricting analyses to low risk pregnancies showed slightly smaller relative risk estimates at 37 weeks' gestation but essentially unchanged estimates at 38 and 39 weeks (see [bmj.com](#)).

Exclusion of babies with meconium aspiration syndrome, sepsis, or pneumonia resulted in higher relative risk estimates for babies delivered at 37 and 38 weeks' gestation (see [bmj.com](#)).

When the risk of serious respiratory morbidity after elective caesarean section at different gestational ages was compared with the risk after intended vaginal delivery at 40 weeks, a high increased risk of serious respiratory morbidity was found for newborns delivered by elective caesarean section at 37 weeks (13.6, 5.1 to 36; see [bmj.com](#)). The risk remained increased at 38 and 39 weeks' gestation. The increased risk at 39 weeks was not, however, statistically significant.

DISCUSSION

The risk of neonatal respiratory morbidity after elective caesarean section in singletons born at Aarhus University Hospital, Denmark, between 1 January 1998 and 31 December 2006 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, the relative risk decreased from seven times higher at 37 weeks to three times higher at 38 weeks, whereas the relative risk at 39 weeks was no longer statistically significant.

Even among term deliveries we found a major modification of the association between elective caesarean section and respiratory morbidity by gestational age, with the earlier elective caesarean sections associated more with respiratory morbidity than the later ones. This was found even when comparing with babies intended for vaginal delivery during the same gestational week.

A large cohort study compared elective caesarean section at different gestational ages with vaginal deliveries after 40 weeks, without accounting for intended vaginal deliveries that resulted in emergency caesarean sections.⁸ This could have overestimated the effect of elective caesarean section owing to exclusion of sick newborns and is in keeping with the authors' higher estimated risks for respiratory morbidity in the comparison group (5.2 per 1000 infants) compared with our estimates (up to 16 per 1000 infants). We analysed our data in an adapted intention to treat manner (including emergency caesarean sections in the comparison group), which gave odds ratios lower than the ones in the large cohort study.⁸

We collected data prospectively. Information on delivery type was validated by midwives and

information on respiratory morbidity was provided by neonatologists. By analysing respiratory morbidity as one unit, instead of analysing separate subgroups of respiratory morbidity, we sought to avoid any imprecision caused by variation in the use of codes for respiratory morbidity. We also repeated the analyses by looking at intervention categories (for example, ventilatory support) rather than diagnostic categories. These analyses corroborated our initial findings. To test potential effects of confounding by indication we repeated all analyses for the group of low risk pregnancies but found no influence on the estimated risk of respiratory morbidity.

Several relatively rare conditions might influence the risk of neonatal respiratory morbidity. We therefore repeated our analyses after exclusion of infants born to women given steroids or selective serotonin reuptake inhibitors during pregnancy. Our risk estimates did not change.

In a proper intention to treat analysis women who were originally scheduled for elective caesarean section but had emergency caesarean sections (intended vaginal delivery in our analyses) should have been categorised as elective caesarean sections. We repeated our analyses after recategorising these women and found no significant change in the risk estimates (data not shown).

Even when elective caesarean section was carried out at 39 weeks' gestation an increased risk of respiratory morbidity remained evident. Lack of hormones associated with labour could explain this association. During spontaneous labour the decrease in fetal lung liquid secretion, the increase in its absorption, and the release of surfactant may be mediated by raised catecholamine levels in the fetus in response to rupture of membranes and labour.²⁻⁵ When caesarean sections are carried out before labour this catecholamine surge is absent.

Our results support the notion that the risk of overall and serious respiratory morbidity is increased in newborns delivered by elective caesarean section. Our results also suggest that a significant reduction in neonatal respiratory morbidity may occur if elective caesarean section is postponed to 39 weeks' gestation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Elective caesarean section has been associated with increased risk of neonatal respiratory morbidity

This has been attributed to "iatrogenic prematurity" or lack of physiological changes related to labour

WHAT THIS STUDY ADDS

Babies delivered by elective caesarean section at 37 to 39 weeks' gestation are at twofold to fourfold increased risk of respiratory morbidity compared with babies delivered by intended vaginal delivery

A reduction in neonatal respiratory morbidity may be obtained if elective caesarean section is postponed until 39 completed weeks of gestation

Carrying out elective caesarean sections at greater gestational ages may, however, result in higher rates of intrapartum caesarean sections because some women would go into spontaneous labour. Compared with elective caesarean sections, intrapartum caesarean sections may carry an increased risk of complications such as uterine rupture in women with previous caesarean section.¹¹ In contrast the influence of labour or rupture of membranes before caesarean section may be beneficial to newborns.^{12 13}

Conclusion

This study suggests that elective caesarean section compared with intended vaginal delivery leads to a twofold to fourfold increased risk of overall neonatal respiratory morbidity and even higher relative risks of serious respiratory morbidity in term newborns. Our results also suggest that a significant reduction in neonatal respiratory morbidity may be obtained if elective caesarean section is postponed to 39 weeks' gestation.

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