

Neonatal respiratory morbidity risk and mode of delivery at term: influence of timing of elective caesarean delivery

V Zanardo, AK Simbi, M Franzoi, G Soldà, A Salvadori and D Trevisanuto

Department of Paediatrics, Padua University School of Medicine, Padua, Italy

Zanardo V, Simbi AK, Franzoi M, Soldà G, Salvadori A, Trevisanuto D. Neonatal respiratory morbidity risk and mode of delivery at term: influence of timing of elective caesarean delivery. *Acta Pædiatr* 2004; 93: 643–647. Stockholm. ISSN 0803-5253

Aim: To establish whether the timing of delivery between 37 + 0 and 41 + 6 wk gestation influences neonatal respiratory outcome in elective caesarean delivery, following uncomplicated pregnancy, thus providing information that can be used to aid planning of elective delivery at term. **Methods:** All pregnant women who were delivered by elective caesarean delivery at term during a 3-y period were identified from a perinatal database and compared retrospectively with pregnant women matched for week of gestation, who were vaginally delivered. Maternal characteristics, neonatal outcome, incidence of respiratory distress syndrome (RDS) and transient tachypnea of the newborn (TTN) were analysed. During this time, 1284 elective caesarean section deliveries occurred at or after 37 + 0 wk of gestation. **Results:** Neonatal respiratory morbidity risk (odds ratio, OR), including RDS and TTN, was significantly higher in the infant group delivered by elective caesarean delivery compared with vaginal delivery (OR 2.6; 95% CI: 1.35–5.9; $p < 0.01$). While TTN risk in caesarean delivery was not increased (OR 1.19; 95% CI: 0.58–2.4; $p > 0.05$), the RDS risk was significantly increased (OR 5.85; 95% CI: 2.27–32.4; $p < 0.01$). This RDS risk is greatly increased in weeks 37 + 0 to 38 + 6 (OR 12.9; 95% CI: 3.57–35.53; $p < 0.01$). After 39 + 0 wk, there was no significant difference in RDS risk.

Conclusions: 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.

Key words: *Elective caesarean delivery, timing, respiratory distress syndrome, transient tachypnea*

Vincenzo Zanardo, Department of Paediatrics, Padua University School of Medicine, Via Giustiniani 3, 35128 Padua, Italy (Tel. +49 720027, fax. +49 720027, e-mail. vincenzo.zanardo@libero.it)

Over the past 20 y, there has been an increase in the rates of elective caesarean delivery at term in the western world, largely due to the management of previous caesarean section and breech presentation (1). Current clinical practice varies without close scrutiny, but the operation is most frequently performed in weeks 38 + 0 to 38 + 6 of pregnancy, possibly because neonatal respiratory morbidity at term is thought to be low. It has nonetheless been clearly demonstrated in the literature that caesarean delivery increases the risk of transient tachypnea of the newborn (TTN) and respiratory distress syndrome (RDS) compared to vaginal births, even when it is performed electively at term (2).

Since the main determinants of the risk of RDS or TTN are gestational age and mode of delivery (3, 4), the influence of the timing of elective caesarean delivery is receiving increasing attention (5–7). There is evidence that performing elective caesarean delivery at 39 or

40 wk, rather than at 37 or 38 wk, dramatically reduces both overall respiratory morbidity and severe respiratory failure with its associated mortality risk (1, 8). These reports have been biased, however, by being limited to infants admitted to neonatal intensive care units, or by methodological problems, e.g. small sample size and the lack of a control group, or the selection of subpopulations of women who were offered a scheduled surgical delivery. There is therefore no information from control subjects on current clinical operative practice to enable informed decisions as to the ideal timing of elective caesarean delivery for each week of gestation at term, and this high-risk group remains less well characterized. As a consequence, the criteria used to establish whether medical care is needed at caesarean delivery following otherwise uncomplicated pregnancies need to be re-evaluated.

We undertook this study to determine the incidence of RDS and TTN in infants electively delivered by

caesarean section at term, to correlate their incidence with the vaginal or caesarean mode of delivery, and to examine the risk during each week of gestation between 37 + 0 and 41 + 6 wk.

Material and methods

Data were obtained from a database comprising maternal and neonatal information drawn from the medical charts of all patients admitted to the University of Padua (level III centre) nurseries from January 1998 to December 2000. The database was based on chart reviews and developed by trained personnel; diagnostic information was reviewed monthly for accuracy by maternal-foetal medicine and neonatology staff.

Questions and outcome variables, as well as analytical methods and exclusion criteria, were determined prospectively. To identify an obstetric population with no prenatally-identified risk factors, the maternal-foetal database was searched for women whose pregnancy was at term between 37 + 0 and 41 + 6 wk gestation (estimated by last menstrual period or, if uncertain, by sonogram) (9), and uncomplicated by conditions capable of increasing the risks to the neonate, e.g. acute or chronic maternal diseases (hypertension, renal failure, cardiac disorders, infectious diseases, etc), disorders of pregnancy (pregnancy-induced hypertension, hydramnios, oligohydramnios, gestational diabetes, etc.), foetal abnormalities (malformations), foetal distress or potential foetal asphyxia insult, or foetal growth retardation. All cases of surgical delivery upon explicit maternal request were recorded. Vaginally delivered women with conditions potentially affecting the likelihood of an adverse neonatal outcome (breech presentation, twinning) were also excluded from the low-risk population. Complications during or after delivery were not considered in determining the inclusion criteria; only factors that could be identified prenatally were considered in order to reflect the information available to the obstetrician when planning delivery.

For initial analysis, the obstetric population was classified into two groups: (1) women with vaginal deliveries and (2) women with caesarean deliveries. The caesarean delivery group was then narrowed down to include only women who had elective caesarean delivery in the absence of labour under conventional spinal anaesthesia with 2 ml of 0.5% bupivacaine in the form of bolus doses. Labour was diagnosed as regular uterine contractions combined with effacement of the cervix and dilatation of 3 cm or more. Patients in labour prior to caesarean section were excluded. Women who had elective caesarean delivery at term were then compared with women matched for week of gestation and vaginally delivered nearest to the caesarean delivery.

Information on the infants included birthweight, Apgar score, delivery room treatment, postnatal assess-

ment of gestational age, neonatal morbidity and mortality, type of respiratory support required, diagnostic tests, therapeutic measures, and hospital stay. Only the initial neonatal hospital stay was considered. Newborns with major malformations were excluded. The diagnosis of neonatal respiratory morbidity was established on the basis of characteristic clinical signs, i.e. tachypnea, retractions, nasal flaring, grunting and cyanosis, and the classic radiographic findings of TTN or the reticulogranular pattern of RDS (11, 12). All cases required supplemental oxygen therapy, but in TTN, lung clearance and clinical improvement (with the suspension of oxygen supplementation) always occurred within 24–48 h. All neonatal diagnoses were made at the time of the baby's discharge by an experienced neonatologist. Resuscitation in the delivery room was done according to the International Guidelines for Neonatal Resuscitation (13). The study was approved by the Institutional Review Board of the hospital.

The incidence of respiratory morbidity, odds ratios (OR) and 95% confidence intervals (CI) were calculated for the two groups using the Confidence Interval Analysis: Microcomputer Program (14). Testing for comparisons across multiple proportions was done using the χ^2 test for trend. A *p*-value of less than 0.05 was regarded as significant.

Results

Between January 1998 and December 2000 there were 10 177 live births at the Maternity Department of Padua University. Among the 2361 (23%) term newborns delivered by caesarean section, 1284 (13%) were delivered electively before labour (765 before 38 + 6 wk). The 1077 (11%) newborns delivered by emergency caesarean section answered to a maternal indication for expedient delivery and/or a clear foetal indication for delivery.

Indications for elective caesarean delivery at term were: prior caesarean section (51%), breech presentation (27%), twins (8%), suspected cephalopelvic disproportion (5%), nulliparous aged >35 y (2%) and fear of labour (1%). In 6% of elective caesarean deliveries, the indications for delivery were miscellaneous and included other malpresentations, uncomplicated placenta praevia, retinopathy and myopathies.

The number of infants with respiratory morbidity (RDS and TTN) associated with elective caesarean delivery or vaginal delivery between the weeks at term is shown in Fig. 1. The incidence of respiratory morbidity (RDS and TTN) after elective caesarean delivery at term and after vaginal delivery was, respectively, 22 and 4/1000 deliveries, and 9 and 8.5/1000 deliveries. In comparison with vaginal births, infants delivered by elective caesarean section showed a significant progressive reduction in the incidence of

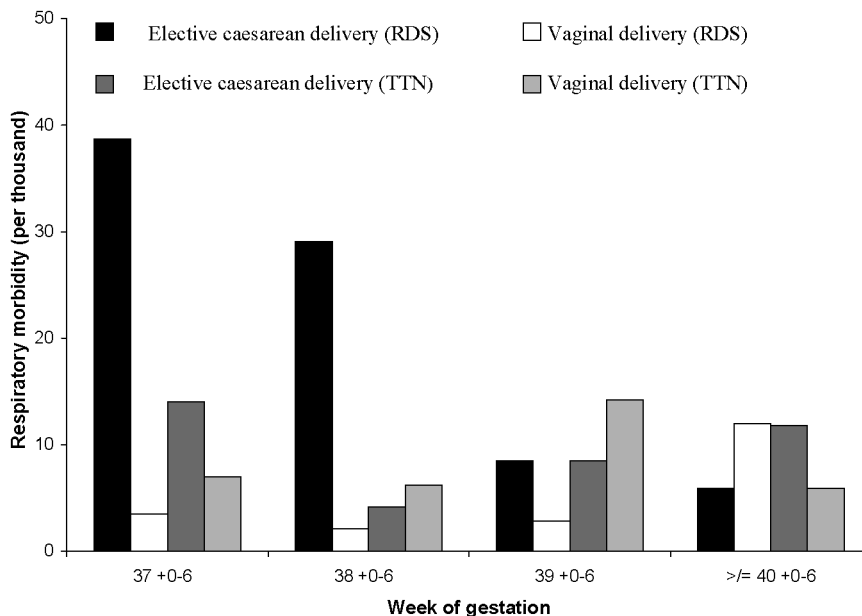


Fig. 1. Incidence of respiratory morbidity per thousand live births shown by each week of gestation and mode of delivery. The number of infants with RDS following elective caesarean delivery diminishes significantly with each week of gestation up to week $\geq 40 + 0-6$ of pregnancy (p per trend < 0.05).

neonatal RDS from week 37 + 0 to week 37 + 6 and thereafter (11 RDS newborns at 37 + 0-6 wk, 14 at 38 + 0-6 wk, 3 at 39 + 0-6 wk and 1 at $\geq 40 + 0-6$ wk, respectively), which fell from 38.7/1000 to 5.9/1000 for infants born at or after 40 + 0-6 wk (p for trend < 0.05). No significant differences were found in the incidence

of TTN (4 TTN newborns at 37 + 0-6 wk, 2 at 38 + 0-6 wk, 4 at 39 + 0-6 wk and 2 at $\geq 40 + 0-6$ wk, respectively). Infants born vaginally showed no difference in respiratory morbidity on testing across week 37 + 0 to 37 + 6 and thereafter (Table 1).

The neonatal respiratory morbidity risk (odds ratios,

Table 1. Maternal-infant pairs birth data and infant delivery room care.

	Elective caesarean delivery 1.284	Control vaginal delivery 1.284	Odds ratio (95% CI)	p^a
Elective caesarean delivery rate (n, %)				
$\leq 38 + 6$ (wk)	765 (62%)			
Maternal data				
Age (y)	30.9 \pm 2.3	29.7 \pm 2.5		
Nulliparae (%)	42 %	51 %		
Birth data				
Gestational age (wk)	38.8 \pm 1.2	38.8 \pm 1.6		
Weight (kg)	3.16 \pm 0.5	3.18 \pm 0.6		
Gender, male (%)	55 %	53 %		
Delivery room care (n, %)				
Apgar ≤ 5 at 1 min	21 (1.6%)	13 (1.0%)		
Resuscitation (phase II) (n, %)	71 (5.5%)	44 (3.4%)		$< .01$
NICU admission	17 (1.3%)	8 (0.6%)		$< .01$
RDS (n)	29	5	2.6 (1.35-5.9)	$< .01$
37 + 0-38 + 6 (wk)	25	2	12.9 (3.57-35.53)	$< .01$
>39 + 0- $\leq 41 + 6$ (wk)	4	3	1.15 (0.17-5.3)	
TTN (n)	12	11	1.19 (0.58-2.4)	
37 + 0-38 + 6 (wk)	7	5	1.61 (0.60-5.05)	
>39 + 0- $\leq 41 + 6$ (wk)	5	6	0.65 (0.35-5.15)	
Pneumonia (n)	1	1		
Length of hospital stay (d)	6 \pm 0.9	4 + 1.1		

Values expressed as number (%), mean \pm SD, odds ratio (95% CI).

^a Overall difference between the groups.

OR) for RDS and TTN was significantly higher in the elective caesarean group than in the vaginal delivery group (OR 2.6; 95% CI: 1.35–5.9; $p < 0.01$). While the TTN risk in the caesarean group remained unchanged (OR 1.19; 95% CI: 0.58–2.4; $p > 0.05$), the RDS risk rose significantly (OR 5.85; 95% CI: 2.27–32.4; $p < 0.01$), peaking in weeks 37 + 0 to 38 + 6 (OR 12.9; 95% CI: 3.57–35.53; $p < 0.01$). Whereas beyond 39 + 0 wk there was no longer any significant difference in RDS risk (OR 1.15; 95% CI: 0.17–5.3; $p > 0.05$) (Table 1).

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

Discussion

These findings show that elective caesarean delivery for term infants carries a significantly greater risk of neonatal respiratory morbidity than vaginal delivery. The demonstration of an association between elective caesarean delivery and increased risk of respiratory morbidity (in both premature and term infants) is not new (2, 3), but this cohort study revealed that it is the incidence of RDS, not TTN, that rises significantly with respect to vaginal delivery (22/1000 vs 4/1000 and 9/1000 vs 8.5/1000, respectively). This means one RDS case every 44 elective caesarean deliveries at term, extending the Parilla and Hook estimate of one case every 241 deliveries and one every 248 repeat caesarean sections (1, 2). Annibale reported higher rates of intermediated or intensive nursery care (6.3% vs 1.3%) in infants undergoing elective caesarean delivery after uncomplicated pregnancies (15).

In our 3-y study, the elective caesarean sections at term accounted for 13% of 10 177 deliveries. This was a time when caesarean section rates were high and stable, obstetric monitoring was common, obstetric experience with caesarean section and anaesthetic technique was extensive, attention was paid to estimating gestational age, and the practice of elective caesarean delivery at $\geq 39 + 0$ wk was not followed. The availability in our study of precise dating, conventional spinal anaesthesia for all elective caesarean deliveries, accurate prospective documentation on respiratory disease and large numbers of subjects per week of gestation (including more than 60% before 39 + 0 wk) enabled a detailed analysis, although the occurrence of TTN and RDS in the affected newborn was numerically limited. We demonstrated that RDS risk following elective caesarean delivery diminishes significantly for each week of gestation between 37 + 0 and $\geq 40 + 0-6$ wk, with a significant p per trend fall. Our results thus enabled us to calculate the current incidence of respiratory disease at term in uncomplicated pregnancies after vaginal or caesarean birth. Our figures are consistent with a previously published report from Morrison et al. (6). Calculations of the incidence of RDS after elective

caesarean delivery during weeks 37 + 0–6 to $\geq 40 + 0-6$ suggest that 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 foetal circulation, and continuing respiratory symptoms after discharge (16).

One limitation of available studies, including ours, is the lack of information on various mechanisms, such as retained pulmonary fluid (11), iatrogenic prematurity (2) and lack of catecholamine surge during labour (17), to explain the increase in neonatal respiratory problems after caesarean delivery (8). This study was retrospective, so we cannot say whether delaying caesarean delivery would have led to a higher perinatal mortality. The factors governing the choice of the week of gestation for caesarean delivery were entirely indiscriminate, with no apparent differences between the women who had caesarean deliveries in different weeks of gestation. Most elective caesarean deliveries were planned on the strength of a given clinician's opinion, a patient's request and the availability of an operating room, but there are major implications in the timing of elective caesarean delivery at term, since the incidence of respiratory morbidity could be halved for each additional week of pregnancy (5). Gestational age at delivery is thus a key to understanding the neonatal respiratory morbidity risk and related sequelae. Given the artificial neonatal problems resulting from the high rate of elective caesarean deliveries before 39 + 0 wk, it is important to discuss the neonatal respiratory risks prompting admission to the NICU when offering a woman delivery options, given the obstetrician's ethical and medico-legal obligation to obtain her informed consent (5, 15, 23). It is worth emphasizing that this study only considered pregnancies with no serial US or laboratory evidence of foetal compromise. The incidence of respiratory morbidity was found to be high for infants born by elective caesarean delivery, but this tells us nothing about the cause. The effects of other factors on the outcome of caesarean delivery, including physiological adaptation to pregnancy immediately prior to natural labour, differences between natural and induced labour, unexpected size-date discrepancies, and recently reported effects of ethnicity on foetal maturation, remain to be considered (15, 18, 19).

Adopting a policy to perform elective caesarean delivery at $\geq 39 + 0$ wk of pregnancy also involves considering the risk of intrapartum versus elective caesarean delivery, the likelihood of spontaneous labour starting and informed maternal wishes (20). Based on a small number of infants aged from 36 wk onwards with

respiratory morbidity, it has been suggested that awaiting the onset of labour may be appropriate before elective repeat caesarean deliveries (21). To prevent iatrogenic prematurity and its sequelae, the ACOG currently recommends basing elective repeat caesarean delivery at $\geq 39 + 0$ wk on an accurate assessment of foetal maturity to minimize respiratory complications (22). There is no evidence that this practice would have any adverse outcome on the mother (23).

In conclusion, in an obstetric population with no prenatally-identified risk factors, elective caesarean delivery at term remains associated with a higher risk of respiratory morbidity to the neonate compared to vaginal delivery. Our data on a cohort of 1274 elective caesarean deliveries at term and 41 newborns with TTN ($n = 12$) or RDS ($n = 29$) indicate that neonatal respiratory outcome definitely benefits from a better selection of mothers and from waiting until week $39 + 0$ before performing elective caesarean delivery. Information should be provided to all pregnant women and their attendants concerning the risk to the baby of delivery prior to $39 + 0$ wk.

Acknowledgements.—The authors would like to thank Prof. HL Halliday (The Queen's University of Belfast) for his help in the revision of the paper.

References

- Hook B, Kiwi R, Amini SB, Fanaroff A, Hack M. Neonatal morbidity after elective repeat cesarean section and trial of labor. *Pediatrics* 1997; 100: 348–53
- Parilla BV, Dooley SL, Jansen RD, Socol ML. Iatrogenic respiratory distress syndrome following elective repeat cesarean delivery. *Obstet Gynecol* 1993; 81: 392–5
- Levine EM, Ghai V, Barton JJ, Strom CM. Mode of delivery and risk of respiratory diseases in newborns. *Obstet Gynecol* 2001; 97: 439–42
- Wax JR, Hersen V, Carignan E, Mather J, Ingardia CJ. Contribution of elective delivery to severe respiratory distress at term. *Am J Perinatol* 2002; 19: 81–6
- Halliday HL. Elective delivery at term: implications for the neonate. *Acta Paediatr* 1999; 88: 1180–3
- Morrison J, Rennie JM, Milton PJ. Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective cesarean section. *Br J Obstet Gynaecol* 1995; 102: 101–6
- Madar J, Richmond S, Hey E. Surfactant-deficient respiratory distress after elective delivery at term. *Acta Paediatr* 1999; 88: 1244–8
- Keszler M, Carbone MT, Cox C, Schumacher RE. Severe respiratory failure after elective repeat cesarean delivery: a potentially preventable condition leading to extracorporeal membrane oxygenation. *Pediatrics* 1992; 89: 670–2
- Boylan P. Intrapartum fetal monitoring. *Clin Obstet Gynecol* 1987; 1: 73–95
- Manning FA. *Maternal and fetal medicine: principles and practice*. Philadelphia: WB Saunders; 1989
- Avery ME, Gatewood OB, Brumley G. Transient tachypnea of newborn. Possible delayed resorption of fluid at birth. *Am J Dis Child* 1966; 111: 380–5
- Stark A.R, Cloherty JP. *Manual of neonatal care*. 4th ed. Philadelphia–New York: Lippincott-Raven; 1998
- Bloom RS, Cropley C. *Textbook of neonatal resuscitation*. Elk Grove Village, III: Steering Committee, Chameides E, editors. 1990
- Gardner MJ, Gardner SB, Winter PD. Confidence interval analysis: microcomputer program. London: British Medical Journal; 1989
- Annibale DJ, Hulsey TC, Wagner CL, Southgate M. Comparative neonatal morbidity of abdominal and vaginal deliveries after uncomplicated pregnancies. *Arch Pediatr Adolesc Med* 1995; 149: 862–7
- Tudelhope DI, Smyth MH. Is transient tachypnea of the newborn always a benign disease? Report of 6 babies requiring mechanical ventilation. *Austr Pediatr* 1979; 15: 160–4
- Greenough A, Lagercrantz H. Cathecolamine abnormalities in transient tachypnea of the premature newborn. *J Perinat Med* 1992; 20: 223–6
- Hulsey TC, Alexander GR, Robillard PY, Annibale DJ, Keenan A. Hyaline membrane disease. *Am J Obstet Gynecol* 1993; 168: 572–6
- Steinborn A, Sohn C, Heger S, Niederhut A, Hilo R, Kaufmann M. Labour-associated expression of intercellular adhesion molecule-1 (ICAM-1) in placental endothelial cells indicates participation of immunological processes in parturition. *Placenta* 1999; 20: 567–73
- Rosen MG, Dickinson JC. Vaginal birth after cesarean. A meta-analysis of indications for success. *Obstet Gynecol* 1990; 76: 865–9
- Cohen M, Carson BS. Respiratory morbidity benefit of awaiting onset labor after elective cesarean section. *Obstet Gynecol* 1995; 65: 818–24
- American College of Obstetricians and Gynecologists Committee on Obstetrics. *Maternal and fetal medicine. Fetal maturity assessment prior to elective repeat cesarean delivery*. Washington: The College; 1991
- Mould TAJ, Chong S, Spencer AJD, Gallivan S. Women's involvement with the decision preceding their cesarean section and their degree of satisfaction. *Br J Obstet Gynaecol* 1996; 103: 1074–7

Received Mar. 21, 2003; revisions received Oct. 23, 2003; accepted Jan. 10, 2004