

Original article

Vacuum-assisted delivery is associated with late-onset asthma

Background: Perinatal factors during delivery might modulate fetal immunological development and thereby be associated with the development of allergic diseases and asthma later.

Methods: Perinatal data was recorded during pregnancy and at the time of delivery in regard to 5823 children who were born in Northern Finland in 1985–1986. Data from self-administered questionnaires were available at the ages of 7 and 15–16 years and skin prick tests for four main allergens were carried out at the age of 15–16 years. Only singletons delivered by the vaginal route were analyzed.

Results: There was a higher prevalence of doctor-diagnosed asthma at any time of life among children who were delivered by vacuum extraction (RR 1.80, 95% CI 1.27–2.56; $P < 0.001$) in comparison with spontaneously delivered children. In particular, this risk was increased as regards late-onset asthma (RR 2.41, 95% CI 1.52–3.81; $P < 0.001$). Perinatal effects had less impact on the development of other asthma, atopy or hay fever.

Conclusions: The delivery by vacuum extraction had significant impact on the development of late-onset asthma compared with spontaneously delivered children.

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The development of allergic diseases may be aggravated by environmental factors during intrauterine life and the perinatal period (1). The underlying biological mechanisms have remained unclear and the main interest has been the mode of delivery, merely whether it is operative or spontaneous (2–13). The results of these studies have been inconsistent; the mode of delivery being regarded as a risk factor of later-developing allergic diseases has varied between study populations and study periods (2–14).

Conflicting results are explained partly by the examined populations, which have covered a wide age range, from toddlers to middle-aged people, and sometimes only females have been studied (5–7, 11). Further, in the evaluation of vaginal delivery often all assisted (vacuum extraction, forceps delivery and vaginal breech delivery) and spontaneous vaginal deliveries have been included in the same group (7, 8, 11). Similarly, when evaluating cesarean deliveries, nonelective, elective and emergency operations have been included in the same group, and not analyzed separately (3–13). At the same time, modern obstetric practices have developed and the rates of cesarean operation have increased over time to more than 20% of all births in many Western countries.

There are different types of vaginal delivery as well as cesarean operations. Likewise, various factors play a role

in whether or not vaginal delivery ends up as cesarean delivery. These clinical factors that affect or are related to the mode of delivery have not attracted a great deal of interest in epidemiological evaluations. When trying to understand the possible reasons why the mode of delivery might play a role in the development of allergic diseases and asthma in later life it is not much value to group deliveries simple as being either vaginal or cesarean, or as either normal or complicated deliveries including all operative deliveries together. In addition, there is no much data of possible clinical intrapartum factors that may modulate and associate with the development of allergic diseases and asthma. Therefore, we evaluated associations between intrapartum clinical factors and the risk of allergic diseases among offspring who were delivered solely by the vaginal route in a longitudinal cohort study, examining study subjects twice, at seven and at 15–16 years.

Methods

The target population of the Northern Finland Birth Cohort 1985–1986 consisted of all births in the two northernmost provinces of Finland with a date of birth between 1 July 1985 and 30 June 1986 ($n = 9575$) (15). The original data included 9479 births (99% of all

births). Pre- and perinatal data collection started during pregnancy and was completed at delivery. When the children were seven years old a postal questionnaire (concerning the health of the child and sociodemographic background) was mailed to the parents of 9326 children. Data concerning the presence of children's asthmatic disease was available for 7812 (83.8%) children, of which 7620 (97.5%) were singletons. The overall caesarean delivery rate was 14.1%. The second follow-up concerning health and well-being of the adolescents was organized at the age of 15–16 years. It included postal questionnaires to the adolescents and their parents and clinical examinations including measurements of weight and height, and skin prick tests. All children with a known address were invited ($n = 9215$), of which 7344 (79.7%) returned the questionnaires and 6798 (73.8%) attended clinical examinations. Data collection at the age of 15–16 years started at the end of May 2001 and continued until spring 2002.

The results of the earlier follow-up (at the age of 7 years) concerning allergic outcomes and obstetric risk factors are described in detail in our earlier reports (2, 16, 17). In the present study, only children who were delivered by the vaginal route after singleton pregnancies and who attended clinical examinations including skin prick tests or who had answered allergic outcome questions concerning doctor-diagnosed asthma or hay fever at the age of 15–16 years were included ($n = 5823$). All examined subjects gave their written consent to take part in the study and the study protocol was approved by the Ethics Committee of the University of Oulu.

Midwives collected pre- and perinatal information during pregnancy or right after delivery during the perinatal period. Information on obstetric clinical factors, including the mode of delivery, the duration of labor (stages I and II), the use of oxytocin or prostaglandin for labor induction and for labor augmentation, maternal fever (higher than 37.5°C during delivery), the quality of amniotic fluid, the use of electronic fetal cardiography monitoring during labor and delivery and the type of labor analgesia during delivery was collected from delivery records in hospitals. Data on parental allergic diseases, current smoking and education were obtained using postal questionnaires when the children were 15–16 years of age. Parental allergic disease was defined as either the mother or father recorded as having asthma, hay fever or atopic eczema.

Doctor-diagnosed hay fever at any time of life was defined in the 15–16-year follow-up questionnaire as a positive answer to the question 'Have you ever had doctor-diagnosed hay fever?' Doctor-diagnosed asthma at any time of life was defined in the 15–16-year follow-up questionnaire as a positive answer to the question 'Have you ever had doctor-diagnosed asthma?' Early-onset persistent asthma was recorded on the basis of the following three definitions: (i) Data on the occurrence of asthma at the age of seven years obtained from the questionnaire with a positive answer to the question 'Does your child have long-term illness?' Asthma was one of the main concerns listed. (ii) Data on doctor-diagnosed asthma at any time of life. (iii) Current asthma defined by either self-reported asthma during the last 12 months or asthmatic symptoms during the last 12 months (current wheezing, wheezing during or after physical training and a typical cough, especially at night), or current asthmatic medication. Late-onset current asthma was defined as (i) not having asthma at the age of seven years but (ii) a positive answer to the question concerning doctor-diagnosed asthma ever, and (iii) current asthma defined as above. Transient asthma was recorded as having doctor-diagnosed asthma at some point but not having current asthmatic symptoms or asthmatic medication. In addition, self-reported asthma and hay fever during past 12 months were reported in the 15–16-year follow-up questionnaire as a positive

answer to the question 'Have you ever had asthma or have you ever had hay fever?'.

Sensitivity to the three most common allergens in Finland, i.e., cat, birch and timothy grass, as well as sensitivity to house dust mite (*Dermatophagoides pteronyssinus*) was assessed by skin prick tests as earlier reported (18). Histamine dihydrochloride (10 mg/ml) and diluent of the allergen extracts were used as positive and negative controls. Skin reactions to each allergen tested were recorded after 15 min on average; the size of each wheal was documented as the maximum of the longest diameter and the diameter perpendicular to its midpoint. Atopy was defined as one or more reactions greater than or equal to 3 mm. All included subjects had a positive reaction to histamine and negative reactions to the negative controls of all four allergens examined.

In logistic analyses, the adjusted possible risk factors as regards the presence of allergic diseases were child's sex (female/male) and current BMI (in quartiles; ≤ 18.8 , 18.9–20.2, 20.3–22 and ≥ 22 kg/m²), maternal age (≤ 24 , 25–27, 28–31 and ≥ 32 years) and parity at delivery (0, 1, 2–3, ≥ 4), maternal smoking during pregnancy [no/yes (including those who stopped in the first trimester)], paternal occupation at the time of birth (farmer/non-farmer), parental allergy, season of birth (March–May, June–August, September–November, December–February), gestational age at birth (≤ 36 , 37–39, 40, ≥ 41 weeks) and ponderal index. Ponderal index was calculated as weight/length³ at birth and the index values were grouped in quartiles. If in any case the proportion of missing values exceeded 10%, the remaining data were included in the analysis as a separate group.

Logistic regression analysis was used to investigate the relationships between the presence of allergic outcomes and the adjusted effects of various predictors of allergic diseases including the perinatal clinical variables. All variables were entered simultaneously into the logistic model and were treated as categorical variables. The statistical significance of relationships between the mode of delivery and neonatal and current clinical factors was investigated by using the chi-square test or the Kruskal–Wallis test. The cut-off level of significance was set at 0.05.

Results

At the age of 15–16 years, the overall prevalence of atopy was 36.5% (1860/5089), that of doctor-diagnosed asthma at any time of life was 10.4% (488/4684) and that of doctor-diagnosed hay fever was 18.6% (851/4574). The prevalences of self-reported asthma and allergic rhinitis in the past 12 months were 6.0% (327/5447) and 23.7% (1261/5313), consequently. Out of 5823 children, 5413 (92.9%) had been born spontaneously by the vaginal route, 330 (5.7%) had been born by vacuum extraction delivery and 80 (1.4%) had been born by another means of assisted vaginal delivery (mainly breech extractions).

Table 1 shows the associations between intrapartum clinical variables and doctor-diagnosed asthma at any time of life among offspring. After controlling for confounding factors, there was still a significantly higher prevalence of asthma among children who were delivered by vacuum extraction (RR 1.80, 95% CI 1.27–2.56; $P < 0.001$) compared with spontaneously delivered children. The data on earlier asthma at the age of seven

Table 1. Intrapart variables and risk of doctor-diagnosed asthma among offspring at the age of 15–16 years

Variable	Asthma <i>n</i> (%)	Unadjusted RR (95% CI)	Adjusted RR* (95% CI)
Type of delivery			
Spontaneous vaginal delivery	432/4349 (9.9)	1	1
Vacuum extraction	46/268 (17.2)	1.88 (1.35–2.62)	1.80 (1.27–2.56)
Other assisted vaginal delivery	10/67 (14.9)	1.59 (0.81–3.14)	1.58 (0.79–3.16)
<i>P</i> -value		<0.001	<0.002
Duration of labor (stages I and II)			
≤ 6 h	234/2280 (10.3)	1	1
6–12 h	177/1769 (10.0)	0.97 (0.79–1.19)	0.93 (0.74–1.15)
≥12 h	77/635 (12.1)	1.21 (0.92–1.59)	1.11 (0.82–1.51)
<i>P</i> -value		0.31	0.45
Duration of stage I of labor			
Tertile I (≤ 265 min)	160/1601 (10.0)	1	1
Tertile II (266–470 min)	158/1556 (10.2)	1.02 (0.81–1.28)	0.97 (0.77–1.24)
Tertile III (≥470 min)	170/1527 (11.1)	1.13 (0.90–1.42)	1.05 (0.82–1.36)
<i>P</i> -value		0.53	0.81
Duration of stage II of labor			
Tertile I (≤ 5 min)	149/1561 (9.5)	1	1
Tertile II (6–12 min)	170/1586 (10.7)	1.14 (0.90–1.44)	1.12 (0.88–1.43)
Tertile III (≥12 min)	169/1537 (11.0)	1.17 (0.93–1.48)	1.11 (0.84–1.46)
<i>P</i> -value		0.37	0.64
Any use of oxytocin (augmentation or induction) during delivery			
No	316/3194 (9.9)	1	1
Oxytocin	172/1490 (11.5)	1.19 (0.98–1.45)	1.15 (0.94–1.41)
<i>P</i> -value		0.09	0.18
Any use of prostaglandin (augmentation or induction) during delivery			
No	447/4325 (10.3)	1	1
Prostaglandin	41/359 (11.4)	1.12 (0.80–1.57)	1.09 (0.76–1.55)
<i>P</i> -value		0.52	0.64
Quality of amniotic fluid			
Normal	407/3883 (10.5)	1	1
Meconium or greenish	52/517 (10.1)	0.96 (0.70–1.30)	0.96 (0.70–1.29)
Bloody	19/191 (9.9)	0.94 (0.59–1.53)	0.93 (0.57–1.51)
Unknown	10/93 (10.8)	1.03 (0.53–2.00)	1.01 (0.52–1.98)
<i>P</i> -value		0.99	0.98
Maternal intrapart fever during delivery >37.5°C			
No	460/4416 (10.4)	1	1
Yes	28/268 (10.4)	1.00 (0.67–1.50)	0.96 (0.63–1.44)
<i>P</i> -value		0.99	0.83
Electronic fetal monitoring during labor			
Yes, normal	413/4036 (10.2)	1	1
Yes, abnormal	39/267 (14.6)	1.50 (1.05–2.14)	1.38 (0.96–1.98)
No monitoring or data missing	36/381 (9.4)	0.92 (0.64–1.31)	0.93 (0.65–1.34)
<i>P</i> -value		0.07	0.19
Pain control during delivery			
No medication	224/2128 (10.5)	1	1
Epidural block (edb)	39/442 (8.8)	0.82 (0.58–1.18)	0.73 (0.50–1.07)
Paracervical (pcb)/pudendal (pud) block	99/900 (11.0)	1.05 (0.82–1.35)	1.00 (0.77–1.30)
Edb and pcb/pud	3/24 (12.5)	1.22 (0.36–4.10)	1.12 (0.32–3.86)
Inhaled nitrous oxide	42/415 (10.1)	0.96 (0.68–1.36)	0.87 (0.61–1.25)
Other medication	81/775 (10.5)	0.99 (0.76–1.30)	0.93 (0.70–1.23)
<i>P</i> -value		0.89	0.67

*Relative risks (RR) derived from logistic regression with 95% confidence intervals (CIs) in parenthesis. Values are adjusted for child's sex, current BMI, maternal age and parity at delivery, maternal smoking during pregnancy, paternal occupation at the time of birth, parental allergy, season of birth, gestational age and ponderal index at birth. *P*-value for unadjusted analysis obtained from the Pearson's chi-square test or Fisher's exact test. For adjusted analysis, *P*-value for trend obtained from the trend test (Wald) in logistic regression models.

years, doctor-diagnosed asthma at any time of life and current asthma symptoms and medication was limited to 4386 children, of which 3934 (89.7%) were healthy, 117

(2.7%) had early-onset persistent asthma, 236 (5.4%) had late-onset current asthma and 100 (2.3%) had transient asthma. Table 2 shows the association between selected

Table 2. Intrapartal variables and risk of early-onset persistent, late-onset current and transient asthma among offspring at the age of 15–16 years

Variable	Early-onset persistent asthma		Late-onset current asthma		Transient asthma	
	<i>n</i> (%)	Adjusted RR* (95% CI)	<i>n</i> (%)	Adjusted RR* (95% CI)	<i>n</i> (%)	Adjusted RR* (95% CI)
Type of delivery						
Spontaneous vaginal delivery	106/3772 (2.8)	1	206/3872 (5.3)	1	89/3755 (2.4)	1
Vacuum extraction	7/218 (3.2)	0.99 (0.44–2.22)	26/237 (11.0)	2.41 (1.52–3.81)	10/221 (4.5)	1.65 (0.81–3.34)
Other assisted vaginal delivery	4/60 (6.7)	2.45 (0.84–7.13)	4/60 (6.7)	1.34 (0.48–3.79)	1/57 (1.8)	0.72 (0.10–5.36)
<i>P</i> -value		0.26		0.001		0.36
Duration of stage II of labor						
Tertile I (≤ 5 min)	42/1364 (3.1)	1	65/1387 (4.7)	1	32/1354 (2.4)	1
Tertile II (6–12 min)	40/1367 (2.9)	0.92 (0.58–1.47)	85/1412 (6.0)	1.38 (0.78–1.94)	31/1358 (2.3)	0.86 (0.51–1.45)
Tertile III (≥ 12 min)	35/1319 (2.7)	0.70 (0.40–1.21)	86/1370 (6.3)	1.55 (1.06–2.29)	37/1321 (2.8)	0.89 (0.50–1.60)
<i>P</i> -value		0.41		0.07		0.84
Use of prostaglandin (augmentation or induction) during delivery						
No	102/3733 (2.7)	1	219/3850 (5.7)	1	92/3723 (2.5)	1
Prostaglandin	15/317 (4.7)	1.79 (0.99–3.25)	17/319 (5.3)	0.90 (0.53–1.52)	8/310 (2.6)	0.91 (0.44–2.05)
<i>P</i> -value		0.06		0.68		0.91
Electronic fetal monitoring during labor						
Yes, normal	96/3501 (2.7)	1	197/3602 (5.5)	1	89/3494 (2.5)	1
Yes, abnormal	8/219 (3.7)	1.14 (0.54–2.43)	23/234 (9.8)	1.80 (1.13–2.86)	7/218 (3.2)	1.12 (0.50–2.48)
No monitoring	13/330 (3.9)	1.58 (0.86–2.90)	16/333 (4.8)	0.88 (0.52–1.48)	4/321 (1.2)	0.51 (0.18–1.40)
<i>P</i> -value		0.33		0.04		0.40

*Relative risks (RR) derived from logistic regression with 95% confidence intervals (CIs) in parenthesis. Values are adjusted for child's sex, current BMI, maternal age and parity at delivery, maternal smoking during pregnancy, paternal occupation at the time of birth, parental allergy, season of birth, gestational age and ponderal index at birth. For adjusted analysis, *P*-value for trend obtained from the trend test (Wald) in logistic regression models.

significantly and almost significantly ($P < 0.10$) associated intrapartal variables and three different types of asthma. After controlling for confounding factors, there was significantly higher prevalence of late-onset asthma among children who were delivered by vacuum extraction (RR 2.41, 95% CI 1.52–3.81; $P < 0.001$) compared with spontaneously delivered children. In addition, there was a higher prevalence of late-onset asthma in those children who had abnormal intrauterine cardiotocographic tracings during birth compared with those with normal tracings (RR 1.80, 95% CI 1.13–2.86; $P < 0.014$) and in those children whose mothers had a duration of the second stage of delivery equal to or longer than 12 min compared with when it was equal to or less than 5 min (RR 1.55, 95% CI 1.06–2.29; $P < 0.026$). These three variables were strongly correlated and including all variables at the same time in logistic analysis slightly decreased their significance [RRs (95% CI) for vacuum delivery, abnormal cardiotocographic tracings and a longer duration of the second stage of delivery 2.08 (1.28–3.37), 1.52 (0.94–2.47) and 1.40 (0.95–2.09), respectively]. There tended to be more cases of early-onset persistent asthma among offspring whose mothers had been given prostaglandin during or before delivery, compared with the others (RR 1.79, 95% CI 0.99–3.25; $P = 0.06$).

Tables 3 and 4 show the associations between intrapartal clinical variables, and atopy and doctor-diagnosed hay fever among offspring. There was a significantly lower prevalence of atopy among children whose mothers

had had assisted vaginal deliveries other than vacuum extraction compared with offspring who were delivered spontaneously (RR 0.55, 95% CI 0.32–0.97; $P < 0.038$) (Table 3).

No significant associations were detected between intrapartal clinical variables and the prevalence of hay fever among offspring (Table 4).

Children who were born by vacuum extraction were more often male and born to primiparous mothers, their fathers were less often farmers and they had higher birth weights and greater head circumferences but lower ponderal indices compared with the two other groups (Table 5). In general, both groups of children who were delivered by the assisted vaginal route had lower Apgar scores at delivery, and needed more treatment in neonatal intensive care units (NICUs) compared with children who were delivered spontaneously (Table 5). Including the head circumference (with and without the ponderal index) and Apgar scores at birth, and treatment in NICUs in the logistic analysis gave fairly similar results (RRs 2.27–2.38) and did not change the significant association between delivery by vacuum extraction and the increased risk of late-onset doctor-diagnosed asthma. However, including current smoking, Apgar scores at birth (at 5 min), and treatment in NICUs in the logistic analysis changed the significant association between other assisted delivery and the decreased risk of atopy (RR 0.68; 95% CI 0.35–1.30; $P = 0.24$) to nonsignificant (mainly the effect of Apgar scores and current smoking).

Table 3. Intrapartal variables and risk of atopy among offspring at the age of 15–16 years

Variable	Atopy <i>n</i> (%)	Unadjusted RR (95% CI)	Adjusted RR* (95% CI)
Type of delivery			
Spontaneous vaginal delivery	1725/4731 (36.5)	1	1
Vacuum extraction	118/288 (41.0)	1.21 (0.95–1.54)	0.99 (0.77–1.29)
Other assisted vaginal delivery	17/70 (24.3)	0.56 (0.32–0.97)	0.55 (0.32–0.97)
<i>P</i> -value		0.03	0.12
Duration of labor (stages I and II)			
≤ 6 h	866/2476 (35.0)	1	1
6–12 h	736/1929 (38.2)	1.15 (1.01–1.30)	1.04 (0.91–1.19)
≥12 h	258/684 (37.7)	1.13 (0.95–1.34)	0.98 (0.80–1.18)
<i>P</i> -value		0.08	0.71
Duration of stage I of labor			
Tertile I (≤ 265 min)	572/1720 (33.3)	1	1
Tertile II (266–470 min)	649/1685 (38.5)	1.26 (1.09–1.45)	1.17 (1.01–1.36)
Tertile III (≥470 min)	639/1684 (37.9)	1.23 (1.07–1.41)	1.08 (0.92–1.26)
<i>P</i> -value		0.002	0.10
Duration of stage II of labor			
Tertile I (≤ 5 min)	578/1708 (33.8)	1	1
Tertile II (6–12 min)	619/1714 (36.1)	1.11 (0.96–1.27)	1.01 (0.87–1.18)
Tertile III (≥12 min)	663/1667 (39.8)	1.29 (1.12–1.49)	1.07 (0.88–1.27)
<i>P</i> -value		0.002	0.68
Use of oxytocin (augmentation or induction) during delivery			
No	1240/3494 (35.5)	1	1
Oxytocin	620/1595 (38.9)	1.16 (1.02–1.31)	1.11 (0.97–1.26)
<i>P</i> -value		0.020	0.12
Use of prostaglandin (augmentation or induction) during delivery			
No	1719/4672 (36.8)	1	1
Prostaglandin	141/417 (33.8)	0.88 (0.71–1.08)	0.84 (0.67–1.05)
<i>P</i> -value		0.23	0.13
Quality of amniotic fluid			
Normal	1534/4238 (36.2)	1	1
Meconium or greenish	209/549 (38.1)	1.08 (0.90–1.30)	1.07 (0.89–1.30)
Bloody	76/199 (38.2)	1.09 (0.81–1.46)	1.03 (0.77–1.40)
Unknown	41/103 (39.8)	1.17 (0.78–1.74)	1.20 (0.80–1.80)
<i>P</i> -value		0.69	0.74
Maternal intrapartal fever during delivery >37.5°C			
No	1757/4818 (36.5)	1	1
Yes	103/271 (38.0)	1.07 (0.83–1.38)	0.97 (0.75–1.26)
<i>P</i> -value		0.61	0.82
Electronic fetal monitoring during labor			
Yes, normal	1592/4382 (36.3)	1	1
Yes, abnormal	121/305 (39.7)	1.15 (0.91–1.46)	1.02 (0.80–1.30)
No monitoring or no data	147/405 (36.6)	1.01 (0.82–1.25)	1.05 (0.85–1.31)
<i>P</i> -value		0.50	0.89
Pain control during delivery			
No medication	812/2318 (35.0)	1	1
Epidural block (edb)	186/464 (40.1)	1.24 (1.01–1.52)	1.07 (0.85–1.34)
Paracervical (pcb)/pudendal (pud) block	386/989 (39.0)	1.19 (1.02–1.38)	1.10 (0.93–1.29)
Edb + pcb/pud	9/29 (31.0)	0.84 (0.38–1.84)	0.66 (0.30–1.49)
Inhaled nitrous oxide	165/455 (36.3)	1.06 (0.86–1.30)	0.97 (0.78–1.20)
Other medication	302/834 (36.2)	1.05 (0.89–1.24)	0.97 (0.82–1.16)
<i>P</i> -value		0.16	0.64

*Relative risks (RR) derived from logistic regression with 95% confidence intervals (CIs) in parenthesis. Values are adjusted for child's sex, current BMI, maternal age and parity at delivery, maternal smoking during pregnancy, paternal occupation at the time of birth, parental allergy, season of birth, gestational age and ponderal index at birth. *P*-value for unadjusted analysis obtained from the Pearson's chi-square test. For adjusted analysis, *P*-value for trend obtained from the trend test (Wald) in logistic regression models.

Discussion

In the present study, the risk of doctor-diagnosed asthma was increased among offspring if birth had ended up

being by way of vacuum extraction vaginal delivery. This was not explained by maternal demographic variables such as age or parity, or longer duration of delivery, fetal size, lower neonatal Apgar scores or neonatal need for

Table 4. Intrapartal variables and the risk of hay fever among offspring at the age of 15–16 years

Variable	Hay fever <i>n</i> (%)	Unadjusted RR (95% CI)	Adjusted RR* (95% CI)
Type of delivery			
Spontaneous vaginal delivery	789/4250 (18.6)	1	1
Vacuum extraction	53/258 (20.5)	1.13 (0.83–1.55)	0.93 (0.68–1.29)
Other assisted vaginal delivery	9/66 (13.6)	0.69 (0.34–1.41)	0.28 (0.67–1.38)
<i>P</i> -value		0.43	0.52
Duration of labor (stages I and II)			
<6 h	395/2216 (17.8)	1	1
6–12 h	337/1737 (19.4)	1.11 (0.95–1.30)	0.96 (0.81–1.15)
>12 h	119/621 (19.2)	1.09 (0.87–1.37)	0.85 (0.66–1.10)
<i>P</i> -value		0.42	0.46
Duration of stage I of labor			
Tertile I (<265 min)	272/1561 (17.4)	1	1
Tertile II (266–470 min)	279/1512 (18.5)	1.07 (0.89–1.29)	0.98 (0.80–1.17)
Tertile III (>470 min)	300/1501 (20.0)	1.18 (0.99–1.42)	0.97 (0.79–1.19)
<i>P</i> -value		0.19	0.95
Duration of stage II of labor			
Tertile I (<5 min)	239/1518 (15.7)	1	1
Tertile II (6–12 min)	297/1549 (19.2)	1.27 (1.05–1.53)	1.16 (0.95–1.41)
Tertile III (>12 min)	315/1507 (20.9)	1.41 (1.17–1.70)	1.15 (0.90–1.43)
<i>P</i> -value		0.001	0.30
Use of oxytocin (augmentation or induction) during delivery			
No	574/3117 (18.4)	1	1
Oxytocin	277/1457 (19.0)	1.04 (0.89–1.22)	0.99 (0.84–1.16)
<i>P</i> -value		0.63	0.86
Use of prostaglandin (augmentation or induction) during delivery			
No	786/4223 (18.6)	1	1
Prostaglandin	65/351 (18.5)	0.99 (0.75–1.32)	0.98 (0.73–1.32)
<i>P</i> -value		0.97	0.89
Quality of amniotic fluid			
Normal	689/3797 (18.1)	1	1
Meconium or greenish	103/499 (20.6)	1.17 (0.93–1.48)	1.17 (0.92–1.48)
Bloody	41/185 (22.2)	1.28 (0.90–1.84)	1.26 (0.88–1.82)
Unknown	18/93 (19.4)	1.09 (0.64–1.82)	1.01 (0.64–1.85)
<i>P</i> -value		0.33	0.39
Maternal intrapartal fever during delivery >37.5°C			
No	799/4313 (18.5)	1	1
Yes	52/261 (19.9)	1.09 (0.80–1.50)	0.96 (0.70–1.33)
<i>P</i> -value		0.57	0.81
Electronic fetal monitoring during labor			
Yes, normal	729/3942 (18.5)	1	1
Yes, abnormal	59/260 (22.7)	1.29 (0.96–1.75)	1.13 (0.83–1.55)
No monitoring or no data	63/372 (16.9)	0.90 (0.68–1.19)	0.95 (0.71–1.27)
<i>P</i> -value		0.17	0.67
Pain control during delivery			
No medication	376/2065 (18.2)	1	1
Epidural block (edb)	81/433 (18.7)	1.03 (0.79–1.35)	0.80 (0.60–1.07)
Paracervical (pcb)/pudendal (pud) block	173/887 (19.5)	1.09 (0.89–1.33)	0.96 (0.78–1.19)
Edb and pcb/pud	6/25 (24.0)	1.42 (0.56–3.58)	1.02 (0.39–2.64)
Inhaled nitrous oxide	82/407 (20.1)	1.13 (0.87–1.48)	0.99 (0.75–1.30)
Other medication	133/757 (17.6)	0.96 (0.77–1.19)	0.84 (0.67–1.30)
<i>P</i> -value		0.80	0.57

*Relative risks (RR) derived from logistic regression with 95% confidence intervals (CI) in parenthesis. Values are adjusted for child's sex, current BMI, maternal age and parity at delivery, maternal smoking during pregnancy, paternal occupation at the time of birth, parental allergy, season of birth, gestational age and ponderal index at birth. *P*-value for unadjusted analysis obtained from the Pearson's chi-square test. For adjusted analysis, *P*-value for trend obtained from the trend test (Wald) in logistic regression models.

intensive treatment after birth. Vaginal birth-related variables had little effect as regards the development of hay fever and atopy.

As far as we know there have been only four earlier studies where the different modes of vaginal delivery have been evaluated as regards the incidence of allergic

Table 5. Fetal, early neonatal and current clinical characteristics of the offspring in relation to the mode of vaginal delivery

	Spontaneous vaginal delivery <i>n</i> = 5413	Vacuum extraction <i>n</i> = 330	Other assisted delivery <i>n</i> = 80	<i>P</i>
Primiparous mothers	1554/5413 (28.7%)	237/330 (71.8%)	30/80 (37.5%)	0.0001
Paternal occupation at birth (farmers)	356/5413 (6.6%)	8/330 (2.4%)	6/80 (7.5%)	0.014
Parental allergic disease	3115/5413 (57.5%)	178/330 (53.9%)	48/80 (60.0%)	0.390
Birth weight, grams	3600 (492)	3703 (494)	3357 (489)	0.001
Head circumference at birth, cm	35.1 (1.4)	35.5 (1.6)	35.2 (1.4)	0.001
Ponderal index at birth	2.76 (0.22)	2.71 (0.23)	2.73 (0.25)	0.001
Male sex	2620/5413 (48.4%)	195/330 (59.1%)	35/80 (43.8%)	0.001
Preterm < 37 gestational weeks	161/5413 (3.0%)	5/330 (1.5%)	7/80 (8.8%)	0.003
Apgar 1 min	8.9 (0.8)	8.2 (1.5)	7.9 (1.4)	0.001
<7	71/5404 (1.3%)	32/330 (9.7%)	10/79 (12.7%)	0.001
Apgar 5 min	9.3 (0.7)	8.9 (0.9)	8.8 (0.8)	0.001
<7	23/4428 (0.5%)	4/248 (1.6%)	1/57 (1.8%)	0.001
Treatment in neonatal intensive care unit	510/5413 (9.4%)	64/330 (19.4%)	17/80 (21.3%)	0.001
Normal taking home after birth	4867/5413 (89.9%)	276/330 (83.6%)	66/80 (82.5%)	0.0001
Current smoking	1044/3448 (30.3%)	54/193 (28.0%)	25/67 (37.3%)	0.358
Current BMI	20.8 (3.0)	21.1 (3.6)	20.2 (2.3)	0.152

Values are mean (SD) or *n* (%) and were not acquired from all subjects. *P*-values derived from chi-square or the Kruskal–Wallis test.

disorders among offspring (5, 6, 9, 19). Bager and associates showed no increased risk of the development of allergic rhinitis or current asthma in 20- to 28-year-old pregnant women among those delivered by vacuum extraction (6). However, they showed an increased tendency to have asthma at some time of life among those women who were born by cesarean section (6). In a large British birth cohort, McKeever et al. showed that being born by forceps or vacuum extraction was associated with a small increase in the risk of developing eczema, but not asthma (5). In their study, the total incidence of asthma was exceptionally high (21%), and the population studied included mainly toddlers, since the median age of the study population at the time was 1.6 years (5). Bernsen et al. showed in a retrospective study based on 6-year-old Dutch children that delivery by vacuum extraction was associated with a significantly increased risk of allergy, but not asthma (9). Vonk et al. evaluated young adults in their study and showed that those with atopy were more often delivered by vacuum or forceps extraction compared with the others (19). We reported earlier that in the present birth cohort there was a nonsignificant tendency towards an increased risk of asthma at the age of seven years if the child was delivered by vacuum extraction (RR 1.32, 95% CI 0.80–2.19) (2). This association became even stronger as these cohort members aged, with some developing late-onset asthma. The discrepancies among earlier studies might be due to different study populations and criteria in diagnosing allergic outcomes and asthma, and differences in obstetric practices between countries. We showed that the significance of vacuum delivery was exceptionally high as regards the development of asthma, and none of the confounding factors could explain this effect. A strength of our work is that we have been the first to evaluate perinatal factors in association with allergic diseases in a

longitudinal cohort study, examining the same population twice, at 7 and at 15–16 years, with confirmation of our results.

What could be plausible reasons behind the increased tendency towards asthma in those children who were born by vacuum delivery? Indications for vacuum or forceps delivery are most commonly prolonged labor, maternal exhaustion and emergencies at the second stage of delivery. Children born by vacuum or forceps extraction are more often exposed to intraparturial distress and other negative factors, such as blood loss, infection or aspiration of meconium-stained amniotic fluid. The presence of meconium-stained or bloody amniotic fluid, or maternal intraparturial fever, indicating possible infection was not associated with an increased risk of asthma. It has been suggested that prolonged maternal stress during pregnancy would be associated with sustained excessive cortisol secretion, affecting the developing immune system and thereby increasing susceptibility to allergic diseases (20). In a recent animal study, Pincus-Knackstedt et al. showed that prenatal stress rendered murine offspring more susceptible to airway hyperreaction in response to allergens (21). To be born by vacuum delivery is stressful to the neonate and is associated with increased morbidity such as scalp injury, cephalhematoma, skull fractures and shoulder dystocia (22). The levels of umbilical cord blood cortisol have been increased in those neonates who have undergone instrumental delivery (23–25). Long-term effects of instrumental deliveries on the health status of the newborn have not been greatly studied, and we do not know if there have been any studies in which the effects of instrumental delivery on the development of neonatal immunomodulation have been evaluated. However, in a large birth cohort of 53 000 people, the mean intelligence scores at 17 years were significantly higher among offspring who were delivered

by vacuum and forceps compared with the spontaneously-delivered group, but after adjustment this difference was lost (26). It remains questionable how this stress experience during birth could have such a strong impact on the development of asthma, and especially development of asthma later during childhood. Further research is obviously needed to clarify this association between the mode of delivery and the development of asthma later on.

Abnormal results in fetal monitoring during delivery and a prolonged duration of the second stage were also associated with the development of late-onset asthma. Partly, these associations may be explained by the conjoint effect of the use of vacuum delivery, abnormal cardiotocographic data and a longer second stage of delivery. It would be interesting to evaluate the association between possible fetal asphyxia by means of umbilical blood gas values, and asthma, but in our material, the numbers of neonates who had their umbilical blood analyzed were too low to carry out statistical analysis. Nonetheless, neonatal Apgar scores were not associated with the development of asthmatic diseases in a Finnish study on twins by Räsänen et al. (27). Naturally, abnormal fetal cardiotocographic results during delivery might

mirror fetal intrapartum temporary or permanent distress, but fetal cardiotocographic monitoring is of low specificity and there is always subjective interpretation, varying between individuals.

This study was limited to subjects who were delivered solely by the vaginal route in order to control better and evaluate different types and stages of vaginal delivery as well as different clinical situations. Our study showed that there was an increased risk of late-onset asthma in those children who were delivered by vacuum extraction, which is possibly explained by intrapartum stress. According to our results, labor-related factors played minor roles in the development of early-onset and transient asthma. We hope that our results will encourage further investigation of maternal and fetal interactions during pregnancy and delivery and their long-lasting effects on the development of chronic diseases among offspring.

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