

# Hospitalisation for bronchiolitis in infants is more common after elective caesarean delivery

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## ABSTRACT

**Background** The authors previously reported an increased risk of hospitalisation for acute lower respiratory infection up to age 2 years in children delivered by elective caesarean section. In view of increasing rates of elective caesarean delivery, this association warranted further investigation.

**Objective** To examine associations between the number of hospital admissions for bronchiolitis and pneumonia and elective caesarean delivery.

**Design** Retrospective population-based data linkage cohort study of 212 068 non-Aboriginal singleton births of 37–42 weeks gestation.

**Methods** Negative binomial regression was used to examine associations between mode of delivery and hospitalisations for both bronchiolitis and pneumonia in children aged <12 months and 12–23 months. Models were adjusted for obstetric and known risk factors.

**Results** 16% of children were delivered by elective caesarean section (n=33 421). In adjusted analysis, compared with spontaneous vaginal delivery, these children had increased risk of admissions for bronchiolitis at age <12 months (incidence rate ratio (IRR) 1.11; 95% CI 1.01 to 1.23) and 12–23 months (IRR 1.20; 95% CI 0.94 to 1.53) independent of other fetal and maternal factors. There was no association between elective caesarean delivery and number of pneumonia admissions aged <12 months (IRR 1.03; 95% CI 0.80 to 1.33) and 12–23 months (IRR 1.09; 95% CI 0.88 to 1.34).

**Conclusion** Delivery by elective caesarean was independently associated with infant admissions for bronchiolitis but not pneumonia. Elective caesareans or delivery without labour may result in impaired immunity in the newborn leading to increased risk of early viral lower respiratory infections.

## INTRODUCTION

The rates of elective caesarean delivery are increasing in the Western world. In Sweden the proportion of children delivered by elective caesarean section increased from 5.1% in 1992 to 19.3% in 2005<sup>1</sup> and in Canada from 13.4% to 17.5% between 1988 and 2000.<sup>2</sup> In Western Australia (WA), the proportion of elective caesarean deliveries increased from 6.4% in 1984–1988 to 13.2% in 1999–2003; this increase was thought to be due to maternal request.<sup>3</sup>

There have been numerous reports associating elective caesarean delivery with poor outcomes, including birth trauma in infants,<sup>4</sup> respiratory morbidity of the newborn,<sup>5</sup> respiratory distress syndrome,<sup>6</sup> admissions to advanced care nursery and transient tachypnoea of the newborn.<sup>7</sup> Furthermore, compared with normal vaginal

## What is already known on this topic

- ▶ Elective caesarean rates are increasing worldwide.
- ▶ Caesarean sections have been associated with an increased risk of asthma in children.
- ▶ We previously reported an increased risk of hospitalisation for acute lower respiratory infections before age 2 years in non-Aboriginal children delivered by elective caesarean section.

## What this study adds

- ▶ Elective caesarean delivery is associated with an increased risk of repeated admissions for bronchiolitis independent of maternal factors and pregnancy complications.
- ▶ We did not find an association between elective caesarean delivery and repeated pneumonia hospitalisations.

delivery, children delivered by caesarean section have a 20–60% increased risk of asthma in childhood<sup>8–9</sup> and a threefold increased risk in adulthood,<sup>10</sup> although it is not known if these associations were found with elective or emergency caesarean deliveries. In our previous analysis using population-based record linked data, we noted an increased risk of hospitalisation for acute lower respiratory infection (ALRI) under 24 months of age in non-Aboriginal children who were delivered by elective caesarean section (OR 1.34; 95% CI 1.22 to 1.48).<sup>11</sup> Such an association was not found in the Aboriginal population.

Early viral illness, in particular bronchiolitis caused by respiratory syncytial virus, has been shown to be associated with increased risk of asthma in children,<sup>12–13</sup> and the risk of persistent wheeze in children increases with increasing number and severity of viral infection episodes.<sup>14</sup> If elective caesarean delivery heightens the risk of ALRI, specifically bronchiolitis, it may explain the relationship noted between caesarean delivery and subsequent asthma.

Previously, we investigated risk factors of children hospitalised at least once for ALRI. In the current analysis we used number of hospitalisations as a continuous measure of severity. We examined the relationship with elective caesarean delivery, independent of obstetric factors, by investigating

the associations with hospitalisation frequency for both bronchiolitis and pneumonia in children aged <12 months and at age 12–23 months.

## METHODS

### Data source

Data were extracted using the Western Australian Data Linkage System (WADLS), a record linkage system that brings together data from numerous population-based administrative health datasets.<sup>16</sup> We identified a population cohort of singleton live births between 1996 and 2005 from the Midwives' Notification System detailing pregnancy, labour and birth details, the Birth and Death Register and the Hospital Morbidity Database System providing details of all hospitalisations throughout WA. Details of extraction and data cleaning are provided elsewhere.<sup>11 17</sup> We identified hospitalisations for both bronchiolitis and pneumonia under 24 months of age using one principal and 20 additional International Classification of Diseases (ICD) diagnosis codes. ICD-10 code J21 was used to identify bronchiolitis admissions and ICD-10 codes J12–J18, B59, B05.2, B37.1 and B01.2 were used to identify pneumonia admissions. Admissions for bronchiolitis or pneumonia within 14 days of a previous admission were classified as a single episode. If an admission had ICD-10 codes for both bronchiolitis and pneumonia, the admission was coded as pneumonia.

Mode of delivery was obtained from the Midwives' Notification System. As many births had multiple modes of delivery recorded, an algorithm was developed that ranked the different delivery methods in the following order: emergency caesarean, elective caesarean, instrumental (combining vacuum and forceps) and spontaneous vaginal so that a delivery was classified as an elective caesarean if that was one of the modes recorded regardless of other information on the midwives' form unless an emergency caesarean was noted. According to guidelines for completion of the midwife form,<sup>18</sup> an elective caesarean is defined as a planned procedure prior to the onset of labour and before spontaneous rupture of membranes and without any procedure used to induce labour. These guidelines also state that if a woman is scheduled for an elective caesarean and either goes into spontaneous labour or has a spontaneous rupture of membranes and the caesarean section is performed prior to the intended elective caesarean section, then the delivery is recorded as an emergency caesarean.<sup>18</sup> Therefore, according to the guidelines, elective caesareans recorded on the Midwives' Notification Form should reflect true elective caesareans and can be considered as delivery in the absence of labour. The study was approved by the Princess Margaret Hospital for Children Ethics Committee. Access to data from WADLS was approved by the Confidentiality of Health Information Committee and the WA Data Linkage Branch.

## Statistical analysis

Factors were included in the analysis based on their significant association with ALRI hospitalisation from logistic regression analyses conducted previously.<sup>11</sup> In addition to these factors, we controlled for obstetric factors that might both predispose a woman to deliver a child through elective caesarean section and increase risk of ALRI in her offspring. The analysis therefore included: maternal age, number of previous pregnancies, pre-eclampsia, gestational diabetes, breech presentation, maternal smoking during pregnancy, maternal asthma, infant gender, season of birth, gestational age in weeks, birth year and proportion of optimal birth weight (POBW), a measure which takes into account gestational duration, fetal sex, maternal age, maternal height and parity.<sup>19</sup> Socio-economic status was measured using the Socio-Economic Index for Areas for relative disadvantage, derived from low income, low educational attainment, high unemployment and jobs in unskilled occupations.<sup>20</sup>

Analysis was restricted to births of 37–42 weeks gestation. Due to the lack of association between mode of delivery and ALRI hospitalisation in Aboriginal children,<sup>11</sup> analyses were restricted to non-Aboriginal births. The outcome was number of hospitalisations (count data and therefore generated by a Poisson-like process) and to account for overdispersion in the outcome which allows for certain groups in the population having a higher chance of being admitted to hospital, we chose negative binomial regression with *nbreg* in Stata to assess the relationship between mode of delivery and number of hospitalisations. Four separate models were generated for bronchiolitis and pneumonia, each in children aged <12 months and at age 12–23 months. Smoking during pregnancy was not collected in 1996 so our models were restricted to 1997–2005. We report incidence rate ratios (IRRs) and 95% CIs from the fully adjusted models for each of the four outcomes. For the number of bronchiolitis and pneumonia hospitalisations at age 12–23 months, we included the number of bronchiolitis or pneumonia hospitalisations under 12 months of age in the model as a continuous covariate. We used the likelihood ratio test to determine whether the negative binomial model was a better fit than a Poisson model. Non-linearity of some covariates such as year of birth was considered with initial models using fractional polynomials. However, the model with linear terms as we present here was the best fit to the data. Data cleaning was conducted in SPSS 15.0 and analysis in Stata 10.0.

## RESULTS

Our population cohort consisted of 212 068 singleton live non-Aboriginal births of 37–42 weeks gestation between 1996 and 2005. Mode of delivery was available for all births. Overall, 15.8% of deliveries were by elective caesarean section (n=33 421; table 1) but increased from 11.7% in 1996 to 20.6% in 2005. Over 90% (n=30 353) of elective

**Table 1** Delivery method of singleton non-Aboriginal infants of 37–42 weeks gestation and the proportion admitted to hospital at least once for bronchiolitis and pneumonia

Delivery method	Births		Bronchiolitis <12 months		Bronchiolitis 12–23 months		Pneumonia <12 months		Pneumonia 12–23 months	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Spontaneous vaginal	127,045	(59.9)	3465	(2.7)	570	(0.5)	621	(0.5)	842	(0.7)
Instrumental	29,555	(13.9)	547	(1.9)	105	(0.4)	79	(0.3)	157	(0.5)
Elective caesarean	33,421	(15.8)	1051	(3.1)	156	(0.5)	145	(0.4)	214	(0.6)
Emergency caesarean	22,047	(10.4)	494	(2.2)	91	(0.4)	81	(0.4)	163	(0.7)
Total	212,068	(100)	5557	(2.6)	922	(0.4)	926	(0.4)	1376	(0.7)

caesarean deliveries occurred between 37 and 39 weeks gestation. Of the 212 068 pregnancies, 51% were male, 4.8% had pre-eclampsia, 2.9% had gestational diabetes, 3.4% recorded a breech presentation, 17.8% reported smoking during pregnancy and 8.4% reported maternal asthma during pregnancy.

A higher proportion of infants delivered by elective caesarean than by other delivery methods were admitted to hospital at least once for bronchiolitis between 1996 and 2005 (table 1). There were 6104 admissions for bronchiolitis in children aged <12 months (5102 children had one admission, 377 had two admissions, 65 had three admissions, 12 had four admissions

**Table 2** Associations between delivery method and maternal and infant factors and number of bronchiolitis hospitalisations in non-Aboriginal children aged <12 months and 12–23 months

Risk factor	<12 months		12–23 months	
	Adjusted IRR*	(95% CI)	Adjusted IRR*	(95% CI)
<b>Delivery method</b>				
Spontaneous vaginal	Reference		Reference	
Elective caesarean	1.11	(1.01 to 1.23)	1.20	(0.94 to 1.53)
Instrumental	0.96	(0.85 to 1.08)	0.91	(0.69 to 1.19)
Emergency caesarean	1.00	(0.89 to 1.13)	1.10	(0.83 to 1.45)
Pre-eclampsia	1.07	(0.91 to 1.25)	1.13	(0.79 to 1.61)
Gestational diabetes	1.05	(0.88 to 1.25)	0.75	(0.45 to 1.23)
Breech presentation	0.99	(0.82 to 1.20)	0.63	(0.37 to 1.08)
<b>Gestational age</b>				
37 weeks	1.78	(1.58 to 2.00)	1.27	(0.93 to 1.72)
38 weeks	1.49	(1.34 to 1.64)	1.20	(0.94 to 1.53)
39 weeks	1.23	(1.11 to 1.35)	1.28	(1.02 to 1.60)
40 weeks	Reference		Reference	
41 weeks	0.97	(0.85 to 1.10)	1.09	(0.82 to 1.44)
42 weeks	1.26	(0.85 to 1.85)	0.81	(0.29 to 2.27)
Maternal smoking during pregnancy	1.48	(1.37 to 1.60)	1.17	(0.96 to 1.43)
Maternal asthma	1.47	(1.34 to 1.61)	1.28	(1.01 to 1.61)
<b>Infant gender</b>				
Female	Reference		Reference	
Male	1.55	(1.45 to 1.66)	1.17	(0.99 to 1.37)
<b>Season of birth</b>				
Spring	Reference		Reference	
Summer	1.54	(1.39 to 1.71)	1.35	(1.05 to 1.74)
Autumn	2.37	(2.14 to 2.61)	1.71	(1.35 to 2.16)
Winter	1.78	(1.61 to 1.98)	1.80	(1.42 to 2.29)
<b>POBW</b>				
Low <85%	1.15	(1.04 to 1.28)	1.21	(0.94 to 1.55)
Normal 85–114%	Reference		Reference	
High ≥115%	0.93	(0.83 to 1.05)	1.01	(0.76 to 1.33)
<b>Number of previous pregnancies</b>				
0	Reference		Reference	
1	2.07	(1.87 to 2.30)	1.28	(1.02 to 1.61)
2	2.63	(2.35 to 2.95)	1.34	(1.04 to 1.74)
≥3	3.25	(2.90 to 3.65)	1.58	(1.21 to 2.05)
<b>Maternal age (years)</b>				
≥35 years	Reference		Reference	
30–34 years	1.21	(1.08 to 1.35)	1.15	(0.88 to 1.51)
25–29 years	1.60	(1.43 to 1.79)	1.36	(1.03 to 1.78)
20–24 years	2.01	(1.78 to 2.29)	1.67	(1.23 to 2.26)
<20 years	3.24	(2.72 to 3.86)	2.07	(1.36 to 3.14)
<b>Socio-economic index</b>				
91–100% (least disadvantaged)	Reference		Reference	
76–90%	1.23	(1.03 to 1.46)	1.38	(0.91 to 2.10)
26–75%	1.24	(1.07 to 1.45)	1.38	(0.94 to 2.02)
11–25%	1.45	(1.23 to 1.71)	1.43	(0.95 to 2.16)
0–10% (most disadvantaged)	1.53	(1.28 to 1.83)	1.75	(1.13 to 2.71)
Year of birth	0.97	(0.96 to 0.99)	0.89	(0.86 to 0.93)
Number of admissions aged <12 months	NA		4.43	(3.66 to 5.35)

Likelihood ratio test comparing these negative binomial models to Poisson models was significant ( $p < 0.001$ ). Sample size for each model=137 536.

\*Adjusted for all other factors in model.

IRR, incidence rate ratio; POBW, proportion optimal birth weight.

and one had five admissions) and 958 (889 children had one admission, 30 had two admissions and three had three admissions) at age 12–23 months. There were 948 admissions for pneumonia in children aged <12 months between 1996 and 2005 (904 children had one admission and 22 had two admissions) and 1425 (1334 children had one admission, 37 had two admissions, three had three admissions and two had four admissions) at age 12–23 months. In total, bronchiolitis was responsible for 21 336 hospital bed-days (18 882 days for admissions at age <12 months and 2454 days for admissions at age 12–23 months) and pneumonia was responsible for 10 168 hospital bed-days (4809 days at age <12 months and 5359 days at age 12–23 months).

In univariate analysis, those delivered by elective caesarean section were 17% (95% CI 9% to 25%) more likely to have multiple hospitalisations for bronchiolitis under 12 months of age compared to those who had a spontaneous vaginal delivery. In models adjusted for all other covariates, the IRR was slightly lower (IRR 1.11; 95% CI 1.01 to 1.23; table 2). For bronchiolitis admissions in the 12–23-month age group, the IRR in the fully adjusted model increased to 1.20, although this was not statistically significant. The number of hospitalisations for bronchiolitis under 12 months of age was associated with the number of subsequent admissions for bronchiolitis at age 12–23 months (IRR 4.43; 95% CI 3.66 to 5.35). When the number of admissions under 12 months of age was removed from the model, the effect of elective caesarean delivery did not change (IRR 1.21; 95% CI 0.95 to 1.55). There was no significant association between an emergency caesarean delivery and number of admissions for bronchiolitis in either age group (table 2). Similar to our previous analysis using any admission for ALRI before age 2 years as the outcome,<sup>11</sup> other significant risk factors for admissions for bronchiolitis were gestational age <39 weeks, maternal smoking during pregnancy, maternal asthma, male gender, birth date outside of spring, low POBW, one or more previous pregnancies, maternal age <35 years and low socio-economic status. The number of bronchiolitis admissions declined with increasing birth year from 1996 to 2005.

There was no significant association between elective caesarean delivery and number of pneumonia hospitalisations in the models adjusted for all other covariates in either age group (see online supplementary table 1). However, children delivered by emergency caesarean were 32% more likely (IRR 1.32; 95% CI 1.06 to 1.63) to be admitted for pneumonia at age 12–23 months compared with those who had a spontaneous vaginal delivery. Maternal smoking during pregnancy, maternal asthma, male gender, low POBW, one or more previous pregnancies, maternal age <35 years and low socio-economic status were also identified as significant risk factors for the number of hospitalisations for pneumonia (online supplementary table 1). Similar to bronchiolitis, the number of hospitalisations for pneumonia in both age groups declined with increasing birth year from 1996 to 2005.

## DISCUSSION

We have found evidence of an independent association between elective caesarean delivery and repeated hospitalisations for bronchiolitis in infants, a finding which to our knowledge has not been previously reported. In this era of increasing rates of elective caesarean deliveries across the Western world,<sup>1–3</sup> this association between a potentially modifiable factor and significant infant morbidity is of public health importance.

There have been reported associations between caesarean delivery and subsequent asthma in childhood and

adulthood.<sup>8–10</sup> There are also numerous reports linking early viral infections and subsequent asthma in children.<sup>12 13 22</sup> The association we report here follows on from these previous findings and biologically plausible explanations are now needed. The essential difference between elective caesarean and other modes of delivery is the absence of labour.<sup>18</sup> The act of labour promotes the production of various cytokines and activates the infant's and mother's immune system.<sup>23 24</sup> Therefore the cytokine environment differs in a newborn delivered by elective caesarean section, as shown by the lower levels of interleukin (IL) 6 and IL-10 in their cord blood than in those who had a normal vaginal delivery.<sup>25</sup> The differing cytokine environment with elective caesarean delivery may lead to increased susceptibility to respiratory infections in infancy and could explain the lack of association between bronchiolitis and emergency caesarean section. The anti-inflammatory cytokine IL-10 may be particularly important in this regard as production of this cytokine in neonates has been linked with resistance to the development of bronchiolitis.<sup>26</sup> Moreover, elective caesarean delivery has been associated with increased risk for early allergic sensitisation,<sup>27</sup> and the expression of allergy-trophic Th2-polarised immunity in young children has in turn been associated with increased susceptibility to symptomatic viral illness requiring hospitalisation in infancy.<sup>28</sup>

We did not see an association between elective caesarean delivery and repeated pneumonia hospitalisations. While bronchiolitis is most often caused by respiratory syncytial virus, pneumonia is more severe and has a varied aetiology with an increased frequency of bacterial infection.<sup>29</sup> Therefore it is plausible to have different patterns of risk or mechanisms of susceptibility for the two respiratory conditions. Although there may be some diagnostic overlap between bronchiolitis and pneumonia, this would likely underestimate the size of the association between elective caesarean delivery and bronchiolitis. We did see an association with emergency caesarean delivery and number of hospitalisations for pneumonia which could reflect a different causal pathway with alternative immunological mechanisms.

We do not believe the association between bronchiolitis and elective caesarean delivery relates to the treatment-seeking behaviour of women, that is, those opting for an elective caesarean section would be more likely to seek healthcare treatment for their child. This would be plausible if we were investigating emergency department presentations or general practitioner visits. However a hospitalisation, which we have used here, should reflect disease severity as opposed to treatment-seeking behaviour. Furthermore our analysis only included non-Aboriginal children as the proportion of elective caesarean deliveries in the Aboriginal population are considerably lower at 7%<sup>11</sup> and therefore we found no significant association between method of delivery and hospitalisations for bronchiolitis or pneumonia.

We have used a population-based record linkage system which allows us to investigate associations at a population level with adequate numbers and power for meaningful statistical analyses. These linked longitudinal data will allow further studies to investigate causal pathways to hospitalisation for recurrent bronchiolitis and subsequent risk of asthma in order to understand the relationship between mode of delivery, bronchiolitis and asthma. Hospital diagnosis coding is homogeneous throughout WA, thereby reducing any bias in our study. Additionally, we have been able to distinguish between elective caesarean, emergency caesarean, instrumental and spontaneous vaginal deliveries, where other studies have not.<sup>4</sup>

Our study does have some limitations. We were unable to determine if elective caesarean delivery was purely by maternal request or whether the physician recommended an elective caesarean section for medical reasons. To account for this, we have restricted our analysis to singleton births, as multiple births are increasingly likely to be delivered by caesarean section.<sup>30</sup> We adjusted for pregnancy factors such as pre-eclampsia and breech presentation that may lead the physician to recommend an elective caesarean delivery,<sup>31 32</sup> and adjusted for various socio-economic factors such as maternal smoking and a socio-economic index that may influence the physician or the mother's decision to have an elective caesarean delivery. There was minimal change in the IRR between the unadjusted and adjusted analyses; therefore we believe there is little residual confounding in the relationship between elective caesarean delivery and bronchiolitis.

Caesarean delivery is a major abdominal surgical operation and can present a greater risk of maternal morbidity compared with spontaneous vaginal delivery.<sup>33</sup> Maternal request and a mother's right to choose her delivery method need to be respected, but also viewed in terms of the unnecessary use of healthcare funds.<sup>34</sup> Although we have documented other important modifiable factors associated with hospitalisation for ALRI in young children,<sup>11</sup> we have now highlighted an association between elective caesarean delivery and hospitalisation frequency for bronchiolitis which adds to the body of evidence surrounding the different immunological environment of elective caesarean delivery and the relationship between early viral illness and subsequent asthma. Physicians and expectant parents need to be made aware of this additional risk of elective caesarean sections and associated infant morbidity to aid in deciding the most appropriate mode of delivery. Qualitative studies are now needed to understand women's and physicians' views regarding elective caesarean delivery, and laboratory studies should be undertaken to test the hypothesis that elective caesarean delivery results in altered development of antiviral immunity in infants.

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**Competing interests** None.

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## Hospitalisation for bronchiolitis in infants is more common after elective caesarean delivery

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