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# Is large birth weight associated with asthma risk in early childhood?

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## ABSTRACT

**Objective** To determine the association between large birth weight and the risk of developing asthma in early childhood.

**Methods** All single live births (n=687 194) born in Ontario between 1 April 1995 and 31 March 2001 were followed until their sixth birthday. Their birth weight was categorised as low (<2.5 kg), normal (2.5–4.5 kg), large (4.6–6.5 kg) or extremely large (>6.5 kg). Poisson regression analysis was used.

**Results** Compared with normal-birth-weight infants, large-birth-weight infants (2.3% of total) had a slightly lower risk of developing asthma by age 6 after adjusting for confounders (adjusted RR 0.90, 95% CI 0.86 to 0.93). There was a trend towards increased risk of asthma among extremely large-birth-weight infants (RR 1.21, 95% CI 0.67 to 2.19).

**Conclusions** Contrary to previous reports, large birth weight was associated with a lower risk for asthma. Instead, a trend towards increased risk of asthma was observed among extremely large-birth-weight infants and interventions to reduce the incidence of extreme large birth weight may help reduce the risk of asthma.

## INTRODUCTION

Asthma is the most common chronic disease in children. In Ontario, its prevalence is 12.3% for children under age 5 and 10.0% for those aged 5–10 years.<sup>1</sup> The aetiological factors of childhood asthma are not well understood. Considerations have been given to fetomaternal health, which may programme the initial susceptibility to allergic sensitisation, or may contribute to the development of asthma independently of sensitisation.<sup>2</sup> Birth weight may be a sensitive indicator of impaired fetal growth during critical periods of immunological and pulmonary development.<sup>3</sup> Several epidemiological studies have examined the relationship between birth anthropometric measures and the development of asthma.<sup>3–11</sup> These studies suggested that lower birth weight was linked to subsequent development of asthma. However, findings on the impact of larger birth weight on the risk of asthma were inconclusive. The objective of the current study was to determine the association between large birth weight and risks of developing asthma in early childhood.

## METHODS

### Sources of data

This study used three Ontario health administrative databases, which contain records of all provincial hospitalisations, emergency department

(ED) visits and fee-for-service codes billed by all physicians in the province. Each baby's birth record was linked with the mother's delivery record. Variables used were birth weight, gender, postal code, maternal age, mode of delivery and diagnosis. Diseases were coded according to the International Classification of Diseases, 9th Revision (ICD-9) and 10th Revision (ICD-10). In Canada, 97.9% births occurred in hospitals or clinics.

### Study cohort

The study included all single live births born in Ontario between 1 April 1995 and 31 March 2001. They were followed until 31 March 2007 or until they developed an outcome of interest, died or reached their sixth birthday. Infants who developed complex chronic conditions (as defined by Feudtner *et al*<sup>12 13</sup>) within 1 year after birth and those born with a birth weight <1.5 kg or gestational age <37 weeks were excluded.

### Outcome measures

The primary outcome was the diagnosis of asthma. A diagnosis of asthma was determined if a child had at least one asthma hospitalisation and/or two asthma physician visits within a 2-year period.<sup>14</sup> This algorithm was developed and validated through two chart abstraction studies involving over 1000 children and adults,<sup>14 15</sup> and had 89% sensitivity and 72% specificity in children aged 0–17 years.<sup>14</sup> The ICD-9 code 493 was used to identify asthma claims between 1 April 1995 and 31 March 2002, while ICD-10 codes J45 and J46 were used for subsequent years. Asthma diagnosis date was defined as the earlier date of either the hospitalisation or the physician visit that made the diagnosis. Secondary outcomes were asthma hospitalisation and ED visits during follow-up.

### Study variables

Baby's birth weight was categorised as low (<2.5 kg), normal (2.5–4.5 kg), large (> 4.5–6.5 kg) or extremely large (>6.5 kg). Maternal history of asthma was determined if the mother had at least one hospitalisation and/or two physician visits for asthma within a 2-year period. Maternal history of diabetes was determined using the Ontario Diabetes Database (excluding gestational diabetes).<sup>16</sup> Gestational diabetes was determined if the mother had not been diagnosed as having diabetes before pregnancy and had at least one hospitalisation or physician visit within 120 days prior to

## Short report

or 180 days after the delivery date for diabetes or gestational diabetes.<sup>17</sup> Rurality and socio-economic status (measured by neighbourhood income quintile) were obtained by linking the study cohort to Canadian Census 1996 using patients' postal code.<sup>18 19</sup>

## Analyses

The relationships between independent factors and the incidence of asthma were assessed using the  $\chi^2$  test and the Student *t* test in univariate analysis. Poisson regression analysis was used to estimate the effect of birth weight on the risks of asthma, asthma hospitalisation and asthma ED visits while adjusting for other covariates. The SAS/STAT version 9.1 was used for all analyses.<sup>20</sup>

## Ethics

Ethics approval for this study was received from the Research Ethics Boards of The Hospital for Sick Children and the Institute for Clinical Evaluative Sciences.

## RESULTS

A total of 687 194 babies were included (table 1). By age 6, 138 889 (19.9%) received a diagnosis of asthma. Compared with normal-birth-weight infants, large-birth-weight infants had a slightly lower risk of developing asthma by age 6 after adjusting for confounders (adjusted RR 0.90, 95% CI 0.86 to

0.93, table 2). There was a trend towards increased risk of asthma among extremely large-birth-weight infants (RR 1.21, 95% CI 0.67 to 2.19).

## DISCUSSION

Contrary to findings of a recent meta-analysis,<sup>21</sup> our population-based longitudinal birth cohort study found that children with a large birth weight (4.6–6.5 kg) had a slightly lower risk for asthma and related hospitalisations and ED visits in early childhood compared with normal-birth-weight children. However, there was a trend towards a high risk of asthma in children with an extremely large birth weight.

In comparison with the only other Canadian study which followed children until age 10,<sup>22</sup> our cohort was only followed until age 6 and would thus include a large population of transient and non-atopic wheezers who are different from children who develop atopic IgE-associated asthma in later childhood.<sup>23 24</sup> Furthermore, our study population likely included a large proportion with milder disease as compared with children whose asthma was captured only by ED visits for asthma.<sup>22</sup> No other study subdivided the large-birth-weight group into two categories as we did. It is possible that the association seen between large birth weight and asthma was overestimated for those with a birth weight between 4.6 and 6.5 kg.

There are several possible explanations for our findings. First, the risk of delivering a large-birthweight baby increases in multiparous women.<sup>25</sup> Therefore, children with a large

**Table 1** Characteristics of study population

|                                          | Birth-weight groups (%) |                     |                    |                           |
|------------------------------------------|-------------------------|---------------------|--------------------|---------------------------|
|                                          | Low (<2.5 kg)           | Normal (2.5–4.5 kg) | Large (4.6–6.5 kg) | Extremely large (>6.5 kg) |
| No (%)                                   | 10922 (1.6)             | 660480 (97.7)       | 15746 (2.3)        | 46 (0.01)                 |
| Baby factors                             |                         |                     |                    |                           |
| Male                                     | 41.2                    | 50.9                | 67.6               | 52.2                      |
| Asthma at 6 years of age                 | 23.3                    | 19.9                | 18.4               | 23.9                      |
| Mother factors                           |                         |                     |                    |                           |
| Rural living                             | 10.3                    | 11.9                | 16.3               | 19.6                      |
| Neighbourhood income quintile            |                         |                     |                    |                           |
| Quintile 1 (lowest)                      | 29.5                    | 23.0                | 19.5               | 28.3                      |
| Quintile 2                               | 21.9                    | 20.2                | 19.4               | 10.9                      |
| Quintile 3                               | 19.2                    | 19.6                | 20.1               | 19.6                      |
| Quintile 4                               | 17.0                    | 20.2                | 21.8               | 21.7                      |
| Quintile 5 (highest)                     | 12.1                    | 16.7                | 18.3               | 19.6                      |
| Ratio of quintile 1/quintile 5           | 2.4                     | 1.4                 | 1.1                | 1.4                       |
| Maternal history of asthma               | 9.6                     | 8.1                 | 7.9                | 6.5                       |
| Gestational diabetes                     | 3.2                     | 2.8                 | 5.4                | 8.7                       |
| Maternal age at delivery (mean $\pm$ SD) | 28.6 $\pm$ 5.9          | 29.1 $\pm$ 5.4      | 29.9 $\pm$ 5.2     | 29.3 $\pm$ 5.7            |
| Caesarean delivery                       | 25.4                    | 18.0                | 32.5               | 19.6                      |

All comparisons are statistically significant,  $p < 0.0001$ .

**Table 2** Adjusted RRs of incidence of asthma, asthma hospitalisation and asthma emergency department visits

|                                 | Asthma              |                     | Asthma hospitalisation |                     | Asthma ED visit     |                     |
|---------------------------------|---------------------|---------------------|------------------------|---------------------|---------------------|---------------------|
|                                 | 2 years             | 6 years             | 2 years                | 6 years             | 2 years             | 6 years             |
|                                 | RR (95% CI)         | RR (95% CI)         | RR (95% CI)            | RR (95% CI)         | RR (95% CI)         | RR (95% CI)         |
| Birth-weight groups             |                     |                     |                        |                     |                     |                     |
| Normal (2.5–4.5 kg) (reference) | 1.00                | 1.00                | 1.00                   | 1.00                | 1.00                | 1.00                |
| Low (<2.5 kg)                   | 1.20 (1.14 to 1.26) | 1.18 (1.13 to 1.22) | 1.38 (1.29 to 1.47)    | 1.33 (1.27 to 1.39) | 1.47 (1.32 to 1.64) | 1.38 (1.28 to 1.49) |
| Large (4.6–6.5 kg)              | 0.93 (0.88 to 0.97) | 0.90 (0.86 to 0.93) | 0.87 (0.81 to 0.93)    | 0.90 (0.86 to 0.94) | 0.90 (0.81 to 1.01) | 0.87 (0.81 to 0.94) |
| Extremely large (>6.5 kg)       | 1.38 (0.66 to 2.88) | 1.22 (0.67 to 2.19) | 1.84 (0.77 to 4.43)    | 1.08 (0.52 to 2.27) | 1.94 (0.49 to 7.77) | 2.35 (0.98 to 5.65) |

All models are adjusted for babies' gender, rurality, socio-economic status (measured by neighbourhood income quintiles), maternal age at delivery, maternal history of asthma, gestational diabetes and babies delivered by c-section.

birth weight may be more likely to have siblings at home and therefore have a lower risk for asthma as per the hygiene hypothesis.<sup>26</sup> Second, a larger mean birth weight is more common among certain ethnic groups.<sup>27</sup> It is possible that there is over-representation by certain ethnic groups in our cohort who may also have a lower genetic susceptibility to developing asthma.

There are some limitations of this study. First, our study is limited to the use of birth weight and lack measurement of birth length. Second, the algorithm of asthma diagnosis may be less accurate in identifying young children with asthma due to the clinical diagnostic uncertainty in this age group. These limitations may explain the comparable asthma risks in children born with a normal and large weight.

Albeit a limited analysis due to the small number, our results showed a trend towards a higher risk of asthma in children with an extremely large birth weight. Neonates with a large birth weight tend to have a higher weight throughout childhood and into adulthood, putting them at risk for obesity-related health problems including asthma.<sup>2 4 8 28</sup> Our findings suggest that the association between large birth weight and asthma manifested only beyond a certain cut-off. Further research is required to verify and determine the threshold beyond which the risk of asthma could be generalised.

In conclusion, contrary to previous reports, our study suggested that large birth weight was associated with a lower risk for asthma. However, we observed a trend towards increased risk of asthma among extremely large-birth-weight infants, interventions to reduce the incidence of extreme large birth weight, may help reduce the risk of asthma.

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**Competing interests** None.

**Ethics approval** Ethics approval was provided by the Research Ethics Boards of Hospital for Sick Children in Toronto and Institute for Clinical Evaluative Sciences, Ontario.

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