Caesarean delivery and risk of atopy and allergic disease: meta-analyses

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CRD summary
This review concluded that caesarean section delivery is associated with a moderately increased risk of allergic rhinitis, asthma, hospitalisation for asthma, and possibly food allergy in the offspring, but is not associated with inhalant atopy or atopic dermatitis. The potential for publication bias, lack of validity assessment and significant heterogeneity between studies mean that these conclusions may not be reliable.

Authors' objectives
To assess whether delivery by caesarean section is associated with an increased risk of atopy and allergic disease in the offspring.

Searching
PubMed was searched from inception to May 2007. Search terms were reported. Reference lists of identified studies were screened for other potentially relevant studies. Only studies published in a peer-reviewed journal were eligible for inclusion.

Study selection
Epidemiological studies that assessed the potential association between obstetric complications and one of the following allergic outcomes were eligible for inclusion: food allergy/food atopy; inhalant atopy; eczema/ atopic dermatitis; allergic rhinitis; asthma or hospitalisation for asthma. Studies had to provide outcome data on measures of relative risk, or sufficient data to calculate measures of relative risk to be eligible for inclusion.

Included studies were conducted in USA, Europe, UK and Japan. The years of births ranged from 1966 to 2003.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Odds ratios (ORs) along with 95% confidence intervals (CIs) were extracted from the included studies.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Odds ratios (ORs) were pooled using fixed-effect and random-effects models. Statistical heterogeneity was assessed using the Q statistic. Subgroup analyses were conducted according to: adjustment of relative risks; a priori aim; study design; year of birth; population size; country of study; exclusion of persons born pre-term and/or with a low birth weight; proportion of caesarean sections; and age. Adjustment of relative risks included basic (maternal age, prematurity and sibship), parental allergy, smoking in pregnancy and socioeconomic factor. Publication bias was assessed using funnel plots.

Results of the review
Twenty-six studies were included in the review (n=1,308,387) comprised of 23 cohort studies and three case-control studies.

Delivery by caesarean section was associated with a statistically significant increased risk of food allergy/food atopy (OR 1.45, 95% CI: 1.12, 1.86, six studies), allergic rhinitis (OR 1.24, 95% CI: 1.08, 1.43, seven studies), asthma (OR
1.18, 95% CI: 1.05, 1.32, 13 studies) and hospitalisation for asthma (OR 1.21, 95% CI: 1.12, 1.31, seven studies), but not inhalant atopy or eczema/atopic dermatitis. There was significant statistical heterogeneity for the outcomes asthma and hospitalisation for asthma (all the results presented here are from random effects meta-analyses). The proportion of allergic cases attributable to delivery by caesarean section was 4% for food allergy/food atopy, 1.5% for allergic rhinitis, 1.5% for asthma and 1.1% for hospitalisation for asthma.

Publication bias may have been present for the outcome food allergy/food atopy, but for other outcomes the funnel plots appeared to be generally symmetrical.

Results of subgroup analyses were presented.

**Authors' conclusions**
Delivery by caesarean section is associated with a moderately increased risk of allergic rhinitis, asthma, hospitalisation for asthma, and possibly food allergy/food atopy in the offspring, but is not associated with inhalant atopy or eczema/atopic dermatitis. The increased use of caesarean section over the last few decades is unlikely to have contributed much to the allergy epidemic observed during the same time period.

**CRD commentary**
This review addressed a clear question. The potential for publication bias was increased, as only limited attempts were made to identify relevant studies and unpublished studies were not eligible for the review. Publication bias was assessed and found to be likely for only one outcome of interest. However, given the small number of studies included for some outcomes, the assessment may not have been valid for these outcomes. The authors did not appear to have assessed the validity of the included studies. Methods used for selecting studies for the review and data extraction were not reported, so the potential for reviewer bias and error cannot be assessed. Limited details of the included studies were presented. Appropriate methods were used to pool the results of included studies and to investigate statistical heterogeneity, which was found to be present for two of the six outcomes assessed. Whilst the authors’ conclusions reflect the evidence presented, the potential for publication bias, lack of validity assessment and significant heterogeneity between studies mean that these conclusions may not be reliable.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that larger, well designed studies are required to investigate the association between caesarean section delivery and food allergy.

**Funding**
Danish Medical Research Council (grant number 271-05-0700); Aase and Ejnar Danielsen's Foundation (grant number 104988); Dagmar Marshall's Foundation; General Manager Kurt Bonnelycke and Wife's Foundation.

**Bibliographic details**

**PubMedID**
18266879

**DOI**
10.1111/j.1365-2222.2008.02939.x

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Accession Number
12008106258

Date bibliographic record published
02/03/2009

Date abstract record published
27/05/2009

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.