

Caesarian section delivery and atopic dermatitis - meta-analysis of observational studies

Mihaela Panduru,
Nicolae M. Panduru,
Daniela A. Ion

Department
of Pathophysiology,
„Carol Davila” University
of Medicine and Pharmacy,
Bucharest (Romania)

Correspondence:
Dr. Nicolae M. Panduru
e-mail: nicolae.panduru@
umf.ro

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Abstract

Objective. Knowing that caesarean section presents an increasing incidence, it has been showed to be one of the factors delaying the maturation of the immune system. In this respect, the caesarean section delivery is supposed to be a possible risk factor for atopic dermatitis, but so far the major of studies have been only inconclusive. This study aims to conduct a meta-analysis of the available studies in the literature regarding the role of birth by caesarean section at risk of atopic dermatitis. **Methods.** A major searching was conducted in international databases to identify the studies that evaluated the role of birth by caesarean section in developing atopic dermatitis. **Results.** Only 67 studies were identified of which 8 articles met the inclusion criteria. **Conclusion.** This is the first meta-analysis of the available studies in the literature, which consists of 36337 subjects and shows the absence of significant association between caesarean section delivery and atopic dermatitis. **Keywords:** atopic dermatitis, allergic eczema, birth method, caesarean section

Introduction

The number of births by caesarean section has increased in recent years. The incidence of allergic diseases has simultaneously presented an upward trend. It has been suggested a possible association between the two diseases, being known that birth by caesarean section causes the delay of the colonization of intestinal microflora in new-born. This leads to the delayed development of the immune system thereby possible favouring the appearance of allergies. The lack of contact for the new-born child with the maternal vaginal and perineal flora also causes an alteration in the composition of the microflora characterized by the absence of *Bacteroides* spp, bifidobacteria and lactobacilli⁽¹⁾. In addition, there are studies that claim that caesarean section delivery increases the risk of bronchial asthma^(2,3) but in terms of the risk of atopic dermatitis studies were inconclusive.

This study bring into light a meta-analysis of the existing studies in the literature that analyses the risk of atopic dermatitis in subjects born by caesarean section.

Methods

From October 2011 till December 2011, we conducted a broad search in the following databases: Web of knowledge, Scopus and Pubmed for the following words “caesarean section or birth method and atopic or allergic dermatitis”. Study inclusion criteria were established before searching. There were analysed cohort, case-control and cross-sectional studies that followed the role of birth by caesarean section in developing atopic dermatitis. Studies in which the language was not English, which were abstract type, systematic review, meta-analysis, letter or conference presentation were excluded.

The research was conducted by two independent reviewers (PM and IDA) who investigated the titles and abstracts of the initial studies to determine whether they satisfy the selection criteria. The reference list of the selected articles was also analysed in order to find other conclusive items. The full text of the articles found was extracted.

Data extraction

The data collected included the characteristics of the studies (publication date, country, design), the characteristics of the patients (number of patients, follow-up, method of birth, the risk of atopic dermatitis) (Table 1).

Statistical analysis

We evaluated the risk of atopic dermatitis in new-borns by caesarean section compared to babies born vaginally. In order to calculate the size of the effect “fixed-effects” model was used, assuming the homogeneity of studies. Q test was used to assess heterogeneity. τ^2 test was used to assess the variability between studies. Heterogeneity was also checked using I^2 index. The value considered significantly statistical was $p < 0.05$. The data obtained were analysed using Mix software 2.0.1.4. Pro (BiostatXL)⁽²⁾.

Results

Only 67 articles were found that met the criteria described above, until December 2011. About 63 of these were from international databases, Web of knowledge (n=26), Scopus (n=20), and Pubmed (n=17) and 4 from the references of the articles. After analysing them, 8 studies were introduced in the meta-analysis (Figure 1)⁽³⁻¹⁰⁾. The characteristics of the studies included are shown in Table 1.

Table 1 Features of studies included in the meta-analysis

Id	Author	Journal	Year	Country	Design	Patients number	Follow-up (years)
1	Xu B	J Allergy Clin Immunol	2001	Finland	prospective cohort	1953	31
2	McKeever TM	J Allergy Clin Immunol	2002	England	prospective cohort	29238	2,9
3	Laubereau B	Arch Dis Child	2004	Germany	prospective cohort	865	1
4	Negele K	Pediatr Allergy Immunol	2004	Germany	prospective cohort	2500	2
5	Sugiyama M	Pediatrics	2007	Japan	prospective cohort	213	1
6	Kvenshagen	Arch Dis Child	2009	Norway	prospective cohort	609	2
7	Kumar R	J Allergy Clin Immunol	2009	USA	prospective cohort	680	6
8	Park YH	Allergy Asthma Immunol Res.	2010	Korea	retrospective	279	16

The association between caesarean section delivery and atopic dermatitis

The meta-analysis included 36337 subjects and suggested that caesarean section delivery is not a factor for the development of atopic dermatitis (OR =1, 01, CI 0,95-1,08, p=0,70) (Figure 2). Three of the studies we introduced in the meta-analysis were conducted both on full-term and premature infants^(3,8,9) and one study was carried out on children with allergic parents⁽⁵⁾.

Exploration of heterogeneity and publication bias

Following the statistical analysis of heterogeneity it results that the studies included in our meta-analysis are homogeneous, Q statistic (1.32; p=0.98), τ^2 (0; 95% CI = 0.00-0.00), and I2 (0%; 95% CI = 0.00-67.58). After the funnel plot type analysis, all the studies respected the expected distribution in the absence of potential publicist interference.

Discussion

The meta-analysis conducted is the first meta-analysis that studies the risk of advance diabetic in babies by caesarean section. The main aim of this meta-analysis was to show the lack of association between caesarean section delivery and atopic dermatitis in a population of over 35,000 subjects, which provides sufficient power to detect even small magnitudes of the size effect of a risk factor. The result of the meta-analysis is consistent with the studies in the literature. Furthermore, none of the

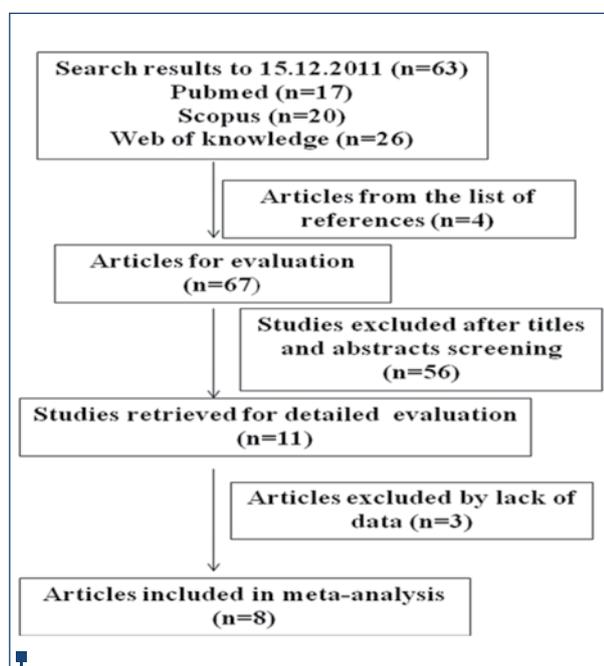


Figure 1. Diagram of evaluation of articles found in the literature

studies found highlighted the significant increase in the risk of atopic dermatitis after giving birth by caesarean section compared to a natural birth.

Natural birth submits the new-born to a major stress with increased levels of cortisol, interleukin-8

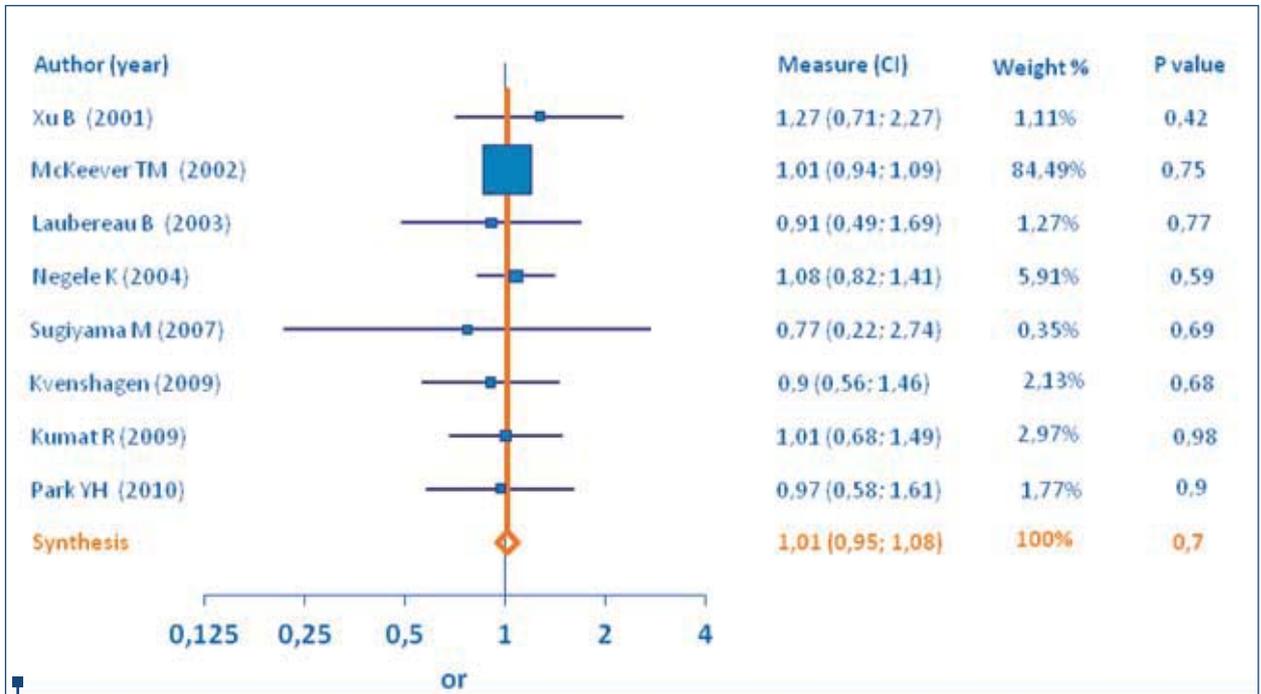


Figure 2. Meta-analysis of studies regarding the role of birth by caesarean section in developing atopic dermatitis

and E-selectin, the activation and redistribution of the immune system cells, preparing it for the skin and mucosal contact with the external microbial flora, which once achieved contributes to the maturation of the immune system⁽¹¹⁾. The vaginal passage of the fetus in the case of natural birth leads to temporary insemination (up to 6 months) of the digestive tract, skin and mucous membranes with the maternal bacterial flora, favouring early maturation of the immune system and thereby possibly protecting the newborn child against allergic diseases⁽¹²⁾. Despite this very attractive pathophysiological theories, no study included in the meta-analysis or final result of the meta-analysis seem to confirm this while the number of patients included in the meta-analysis would provide a power of over 90% to detect a difference of 0.01 OR. However, being a meta-analysis,

the results need to be confirmed in larger prospective studies.

The size of the population studied is one of the strengths of our meta-analysis. A possible limitation may be that the studies were not randomized and it was not possible to make adjustments for other potential risk factors in the statistical analysis. However, such studies about birth are extremely difficult to achieve. In addition, the p value of 0.70 and the number of patients included in the study are an argument that these limitations do not seem to have a decisive influence on the result.

Conclusions

Our study represents the first meta-analysis from our knowledge, which consists of 36,337 subjects and shows the lack of a significant association between caesarean section delivery and atopic dermatitis. ■

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