Caesarian section delivery and the risk of atopic dermatitis - a cross-sectional study

Mihaela Panduru[1], Carmen M. Salavastru[2], Nicolae M. Panduru[3], Sorin G. Tiplica[2]

1. Dermatology Department Medlife Hyperclinic, Bucharest (Romania)
2. Dermatology 2nd Clinic - Colentina Clinical Hospital, Bucharest (Romania)
3. Department of Pathophysiology, "Carol Davila" University of Medicine and Pharmacy of Bucharest (Romania)

Correspondence:
Carmen M. Salavastru, MD
e-mail: galati1968@yahoo.com

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*All authors have equally contributed to this work.

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Abstract

The main objective of our study was to investigate the relation between caesarean-section (C-section) delivery and atopic dermatitis (AD) occurrence, in a group of Romanian children. During January to June 2012, a cross-sectional study was carried out, in schools and kindergartens from southern counties of Romania. The study uses data collected from questionnaires. We enrolled Romanian subjects aged 2 months till 18 years old. The main outcome of the study was AD occurrence in children born by C-section. The association between C-section delivery and AD occurrence was evaluated using different types of logistic regressions. We sent 2000 questionnaires and after the exclusion of questionnaires with missing data, finally remained 1011 questionnaires to be analyzed. Our study showed that C-section delivery is not a risk factor for AD occurrence (OR=1.22; p=0.38) nor increasing the risk of AD.

Keywords: *atopic dermatitis, allergic eczema, birth method, caesarean section, abdominal delivery*

Introduction

Nowadays caesarean section (C-section) rates are higher and still continue to rise[1,2,3]. There is a hypothesis according to which C-section delivery would lead to allergic diseases. This procedure may conduce to the development of atopic dermatitis (AD) due to the lack of contact between the newborn and the maternal vaginal flora, flora that plays a role in the colonization of the sterile digestive tract of the newborn. The lack of contact with the maternal vaginal flora causes a delay in the maturation of the immune system favouring the persistence of a Th2-type status, which seems to lead to the development of allergic diseases[4]. Starting from this assumption, the main objective of our study was to analyse the risk of developing AD in a number of newborn babies by C-section from Romania.

Methods

Design of study

Between January and June 2012, a cross-sectional study was performed based on the research conducted by ISAAC and it consisted of sending questionnaires to schools and kindergartens, parents filling them and analysing the data in order to evaluate a possible association between C-section delivery and AD.

Participants

The study was carried out in schools and kindergartens located in the southern counties of Romania (Arges, Vâlcea, Olt, Constanța and Bucharest cities). The schools and kindergartens were randomly selected, based on the school listings according to County Scholar Inspectorate, whereas all children from each school or kindergarten were asked to participate. The enrolment was voluntarily and has been performed according to Helsinki Declaration. For all subjects included in the study, parents signed an informed consent.

Inclusion criteria in the survey were the followings: 1) subjects over 2 months old; and 2) subjects aged less than 18 years old. The exclusion criteria were: 1) subjects of other nationality than Romanian; and 2) Romanian subjects living outside the country. No change of the protocol was performed after the start of the enrollment.

Questionnaires

The questionnaires comprised two parts: a part which contained the 'core' questions of the ISAAC questionnaire translated into Romanian (Table 1) and a part of analysis of the factors involved in AD development among them C-section birth. In order to avoid repeated enrollment study, subjects received a coupons with a unique number, which they were asked to give back with the completed questionnaire.

Diagnosis of atopic dermatitis

The cases diagnosed as having AD have been defined according to the ISAAC protocol, as having positive answers to the following 3 questions within ISAAC questionnaire translated into Romanian: 1) Have your child ever had an itchy rash which was coming and going for at least 6 months?; 2) Have your child had this itchy rash at any time in the past 12 months? and 3) Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?

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Table 1 'Core' questions within ISAAC questionnaire

1) Have your child ever had an itchy rash which was coming and going for at least 6 months?
2) Have your child had this itchy rash at any time in the past 12 months?
3) Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?
4) At what age did this itchy rash first occur?
5) Has this rash cleared completely at any time during the past 12 months?
6) In the past 12 months, how often, on average, have you been kept awake at night by this itchy rash?
7) Has the child ever been diagnosed with atopic eczema?

Statistical analysis

The normally distributed variables were presented as average ± standard deviation, and the non-normally distributed ones were presented as median (Interquartile Range). The categorical data were presented as percentage and compared using the $\chi 2$ test. The comparison of the averages between normally distributed variables was performed using the t-test for independent samples. The comparison of the averages between non-normally distributed variables was performed using

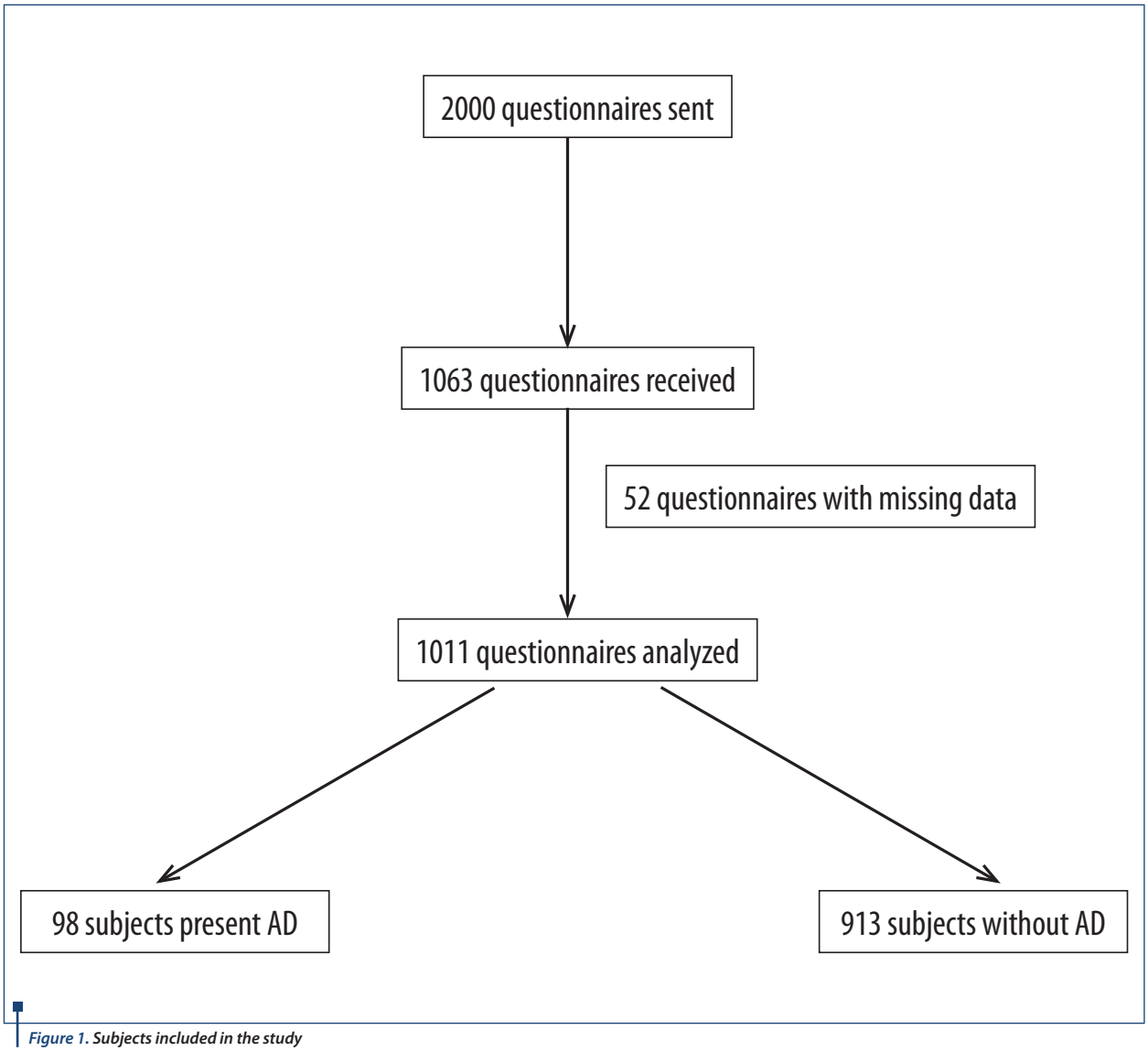

Figure 1. Subjects included in the study

Table 2 Studied population characteristics. Categorical data are presented as numbers or percentage, and continuous data are presented as mean±SD

	Healthy controls	Atopic dermatitis	P
Number of patients	911	97	
Women (%)	46.9	46.0	0.94
Men (%)	53.1	54.0	0.68
Antibiotherapy during pregnancy (%)	10.0	16.8	0.07
1st trimester (%)	4.2	5.3	0.64
2nd trimester (%)	3.9	5.3	0.53
3rd trimester (%)	1.8	6.4	0.009
Maternal allergy (%)	18.5	41.4	<0.0001
Paternal allergy (%)	15.5	55.6	<0.0001
Birth weight			
0-2500 g (%)	0	0	-
2500-4000 g (%)	87.7	79.6	0.03
>4000 g (%)	12.3	20.4	0.03
Gestational age			
<37 weeks (%)	11.7	10.4	0.82
37- 40 weeks (%)	80.3	71.9	0.06
>40 weeks (%)	8.0	17.7	0.002
Caesarean section (%)	30.2	35. 7	<0.31
Exclusive breastfeeding for 6 months (%)	57.4	57.3	0.93
Infections in the first year of life (%)	57.7	48.9	0.11
Smoking in the first year of life (%)	21.5	31.3	0.03
Body mass index (kg/m^2)	21.6 ± 3.2	22.0 ± 3.5	0.35
Studies of the mother (years)	13.8 ± 3.2	14.3 ± 3.1	0.20
Age of mother at childbirth			
<20 years old (%)	0.2	0	0.42
20-35 years old (%)	83.1	73.5	0.02
35-40 years old (%)	5.0	7.1	0.51
>40 years old (%)	11.7	19.4	0.04

'Kruskal–Wallis one-way analysis of variance' test. For the testing of the association we used the simple binary logistic regression and the multi-parametric logistic regression. In order to assess the association between C-section birth and AD we performed an analysis in three steps. In the first step of the analysis we built the model of risk factors (other than birth by C-section), significantly associated with the occurrence of AD. In order to build this model, we initially performed a simple binary logistic regression of factors for which there was a significant difference between the group with and without AD. The factors that were associated with AD at this univariate analysis were then introduced into a multi-parametric logistic regression, with a stepwise-type selection of covariates to select the final adjustment model. Then, in the second step we performed the simple binary logistic regression, with the dependent variable AD and independent variable birth by C-section. In the last step of the analysis we performed the multi-parametric logistic regression where we adjusted the independent variable 'birth by C-section' to the covariate model obtained in the previous step to see if the C-section is an independent risk factor for AD. The values considered significant were <0.05. The analysis was performed using MedCalc software 12.1.3.0 version.

Table 3 Adjustment model for C-section birth in multi-parametric logistic regression containing the risk factors significantly associated with atopic dermatitis

Adjustment Model	OR	95% CI	P value
Paternal history of allergy	1.43	1.03 - 2.00	0.03
Gestational age	2.13	1.18 - 3.86	0.01

Table 4 The distribution of babies born by C-section in the two study groups according to the presence of atopic dermatitis

		Atopic dermatitis		Total	
		No	Yes	Number	%
Normal birth		637	63	700	69.2
C-section birth		276	35	311	30.8
Total	Number	913	98	1011	
	%	90.3	9.7	100	

Table 5 The simple logistic regression analysis of C-section birth as a risk factor for atopic dermatitis

Unadjusted analysis	OR	95% CI	P value
Birth by C-section	1.28	0.83 - 1.98	0.26

Table 6 The multi-parametric logistic regression analysis of birth by C-section as a risk factor for atopic dermatitis

Adjusted analysis	OR	95% CI	P value
Birth by C-section	1.22	0.77 - 1.91	0.38
Paternal history of allergy	1.66	1.34 - 2.06	<0.0001
Gestational age	1.71	1.05 - 2.78	0.03

Results

We sent 2000 questionnaires in 5 cities located in the South (Arges, Vâlcea, Olt, Constanța and Bucharest). The questionnaires were randomly distributed in schools and kindergartens. Out of these we received back 1063 questionnaires, and after the exclusion of those questionnaires with missing data, we included in the final analysis 1011 questionnaires (Figure 1).

We noticed significant differences between the two groups in respect to allergy occurrence in parents. Out of AD patients, 41.4% presented a maternal history of allergic diseases as compared to 18.5% of the healthy

group (p<0.0001). Also, 55.6% of the patients with AD derived from fathers with history of allergies as compared with 15.5% in the group of healthy patients (p<0.0001). Significant differences between the two groups were also noticed in respect of birth weight (p=0.03 for weight over 4000 g) and gestational age (p=0.002 for gestational age higher than 40 weeks). The rate of patients with weight over 4000 g and a gestational age above 40 weeks was significantly higher in the group with AD. Furthermore, the rate of subjects who were exposed in the first year of life to cigarette smoke was higher in the group with AD 31.3%, as compared to 21.5% in the healthy group (p=0.03). For all other studied factors there was no difference between study groups. Table 2 shows the complete description of subjects' characteristics.

According to the algorithm described above, in order to achieve the adjustment model the following variables were introduced in the multi-parametric logistic regression with a stepwise-type selection of covariates: maternal allergic history, paternal allergic history, gestational age, birth weight, maternal age at birth, mother's period of study, exposure to cigarette smoke during pregnancy, the quarter of antibiotic administration during pregnancy, contact with furry animals, contact with dogs, contacts with cats, exclusive breastfeeding duration. Following this multivariate analysis, the final adjustment model consisted of the paternal history of allergy and gestational age (Table 3).

After analysing the distribution depending on the presence or absence of AD in babies born by C-section, it was noticed that 25.7% (n=35) of patients with AD were born by C-section compared with 29.2% (n=276) of children without AD. After comparing the two groups using $\chi 2$ test there was no significant difference between the two groups (p=0.31) (Table 4).

To assess the association of birth by C-section with AD we initially performed the simple binary logistic regression which showed that C-section birth is not associated with the occurrence of AD (OR=1.26; p=0.26) (Table 5).

In the last stage of the analysis we performed the analysis by the multi-parametric logistic regression, having as independent variable the C-section delivery adjusted for the model described above. Following this assessment it was confirmed that C-section birth is not a risk factor for AD (OR=1.22; p=0.38) (Table 6).

Discussion

The study that we conducted comprised 311 subjects born by C-section of which 35 had AD (11.25%). The result obtained showed a lack of association between C-section delivery and AD. Other studies in the literature presented similar conclusions, but no study was performed up to now in Romanian population regarding this subjects[5,6]. One of these studies was performed on a much larger number of subjects than the group that we analysed (29 238 subjects) and failed to reveal an association between C-section delivery and AD[7]. The meta-analysis of observational studies[8] also demonstrated a lack of association between AD and birth by C-section. There are studies that demonstrated that birth by C-section favours the occurrence of asthma and allergic rhinitis but not of AD[9].

Although C-section delivery does not affect the development of AD, studies demonstrated that the method of birth influences the composition of the intestinal flora, which plays a role in the development of the immune system. Due to the fact that there is no contact with the flora of the vaginal area during birth by C-section, this causes a delay in the development of the neonatal immune system[4]. It is also assumed that vaginal birth favours the secretion of cytokines involved in neonatal immunity, thus the newborn babies are protected from the development of allergic diseases[10]. Despite these mechanisms, none of the existing studies in literature or the study on the population in Romania has revealed an association between C-section and the emergence of AD.

One possible limitation of our study is that data were obtained from the questionnaires. However, since our questionnaires were built upon the model of ISAAC and the diagnostic section of the questionnaires was identical, we assume that this may not be that important to influence our result.

The strengths of our study are represented by the good internal validity demonstrated by the statistical analysis, but also by the good external validity of the study based on the random selection of patients at inclusion, a sufficient number of subjects for answering to the proposed question of the study.

Conclusions

Our study did not show the increased risk of AD in the group of subjects born by C-section in Romania. ■

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