

The influence of parental educational level on the development of atopic sensitization, wheezing and eczema during the first year of life

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Several studies have investigated the association between socioeconomic status and the occurrence of allergies. Nevertheless, the results remain contradictory. The aim of this study was to evaluate the associations between parental education and the occurrence of atopic sensitization, recurrent wheezing and eczema during the first year of life, differentiating between atopic and non-atopic disorders based on specific serum IgE. We conducted an aetiological study in 690 children, based on a prospective birth cohort project in which environmental and health information was gathered using questionnaires. At the age of 1 yr a blood sample was taken for quantification of specific IgE. Adjusted odds ratios and 95% confidence intervals were computed as measures of association between the outcomes and parental education. Parental educational level was positively associated with the occurrence of atopic sensitization (OR: 2.1; 95% CI: 1.0–4.4) and eczema (OR: 1.9; 95% CI: 1.1–3.4), but negatively with the occurrence of recurrent wheezing (OR: 0.4; 95% CI: 0.2–0.8) in the first year of life. Atopic recurrent wheezing was positively associated with the education of the parents, whereas non-atopic recurrent wheezing was negatively associated. When maternal and paternal education were considered separately, only maternal education had a significant influence. Our results suggest that aspects associated with a high maternal educational level may play an important role in the development of atopic disorders.

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During the last few decades, the prevalence of allergic diseases has increased worldwide. Two large international studies, using standardized methodology, have been conducted to assess the geographical variation in asthma and allergies. The European Community Respiratory Health Survey (ECRHS) measured the prevalence of asthma, atopic sensitization and lung function in adults from 22 countries (1). The International Study of Asthma and Allergies in Childhood

(ISAAC) assessed the prevalence and severity of symptoms of asthma, atopic rhinoconjunctivitis and atopic eczema in children aged 6–7 and 13–14 yr (2). Both studies consistently found a wide variation of asthma and allergies prevalences with generally higher prevalences in developed countries and increasing prevalences in many countries undergoing rapid socioeconomic development (3, 4). This suggests that the rise in prevalence of allergic diseases in affluent

countries could be as a result of changes in environmental and lifestyle factors associated with a higher socioeconomic status (SES).

Several recent studies investigated the role of SES on the occurrence of allergic diseases, such as allergic rhinitis, atopic dermatitis, hay fever, atopic sensitization and asthma. However, their results remain contradictory. Some studies found a positive association (5–7) between SES and allergic diseases, while other studies have found a negative association (8–10) or no relationship (11).

One of the reasons for conflicting results between studies could be the different measures used for SES. Although the term 'SES' is frequently used, there is no general consensus regarding how to define and measure this construct. Often, measures cited in the literature are determined by convenience or availability. However, SES is a complex and multidimensional concept that includes both resource-based and prestige-based measures (12, 13). Consequently, it is impossible to investigate the influence of SES as a whole on a health outcome. In our opinion, it is more relevant to study only one aspect of SES at a time. It has been demonstrated that educational level of parents appears to act as an indicator of socioeconomic circumstances in early life of their children (14). As a result, we chose to study parental educational level (PEL) as an aspect of SES.

Another reason for contradictory results between studies could be differences in the definition of health outcomes. The importance of differentiation between atopic and non-atopic eczema and wheeze or asthma has already been emphasized (15, 16). Both forms have different risk factors and prognoses. However, none of the studies have taken the atopic status, based on objective-specific serum IgE measurements, into account when investigating the influence of SES on eczema, wheeze or asthma.

The objective of this study was to evaluate the relationship between PEL and the occurrence of atopic sensitization, eczema and recurrent wheezing (with further differentiation between atopic and non-atopic recurrent forms) during the first year of life. We also explored the role of PEL-related determinants, which might confound or explain these associations, using multiple logistic regression models.

Methods

Study design and population

This is an aetiological study, based on the Prospective Project on the Influence of Perinatal

Factors on the Occurrence of Asthma and Allergies (PIPO cohort). In 1997 the PIPO project, a prospective birth cohort, started in the province of Antwerp, Belgium. Between June 1997 and December 2001, 2006 women, who were around 20-wk pregnant, were recruited via four gynaecologists. Of all women who completed the screening questionnaire, 1072 agreed to participate (53%), leading to a total study population of 1128 children. All participating parents resided in the Antwerp urban or suburban region and had a sufficient knowledge of the Dutch language. Almost all children (99.3%) have Belgian nationality.

The Ethics Committee of the University of Antwerp granted approval for the assessments. Additionally, written consent was obtained from the parents before each assessment. Subjects were included in the current study if information on PEL, atopic status and the occurrence of recurrent wheezing and eczema was available.

Questionnaires and medical examination

Information on the family history of atopic diseases and environmental factors was obtained by questionnaires during home visits at 5 months of pregnancy and 3 months after birth. When the infants were 6- and 12-month old, postal questionnaires on environmental factors were filled in by the parents. Additionally, at the age of 1 yr, a questionnaire on morbidity during the first year of life was carried out by telephone. All questionnaires were based on ISAAC-questionnaires, which have also been validated in infants (17, 18). During the visit to the study centre in the University Hospital of Antwerp at the age of 1 yr, the children had a medical examination, and blood samples for allergy testing were taken.

Definitions

Atopic sensitization. A blood sample was taken for quantification of total and specific immunoglobulin-E (IgE) in the children and their parents. This was performed using a fluorescence enzyme immunoassay technique (CAP FEIA systems, Phadia, Brussels, Belgium). In the children, specific IgE against *Dermatophagoides pteronyssinus*, cat, dog, hen's egg and cow's milk were determined in serum. In the parents, specific IgE against seven common inhalant allergens (*D. pteronyssinus*, cat, dog, birch pollen, timothy grass pollen, mugwort pollen and *Cladosporium herbarum*) were quantified. Specific IgE levels equal or higher than 0.35 kU/l were considered as positive. Atopic sensitization was defined as

having at least one positive specific IgE. Atopic sensitization of the child was divided according to the origin of the allergens: i.e. sensitization to at least one inhalant allergen (house dust mite, cat or dog) or to at least one food allergen (hen's egg or cow's milk).

Skin and respiratory symptoms. Eczema in the children was ascertained on the basis of the answers to the following questions: 'Has your child ever had an itching skin disease in the last year?' and 'If yes, was this eczema?'. Children with at least three episodes of parent-reported wheeze during the first year of life were defined as having recurrent wheezing. Furthermore, eczema and recurrent wheeze were divided into their atopic and non-atopic forms, based on the presence or absence of IgE-antibodies at the age of 1 yr.

Parental educational level. We chose to study PEL as an aspect of SES, because PEL has a major influence on health-related behaviour and lifestyle (14). Maternal and paternal educational levels were categorized separately and combined. Maternal and paternal education was classified into 'elementary', 'secondary' and 'tertiary', based on the International Standard Classification of Education (ISCED 1997) (19). Because of the very small number of parents with an elementary education, we aggregated this group to parents with secondary education. As a result, two categories can be distinguished: low educational level (parents who only completed secondary school or lower) and high educational level (parents who had a Bachelors or Masters degree). Parental education (maternal and paternal education combined) was divided into two categories: high parental education (at least one parent with a high educational level) and low parental education (both parents with a low educational level).

Explanatory variables. Mediators that might explain or confound the potential associations between PEL and the outcomes, were considered according to evidence from previous studies (20, 21). For the assessment of the allergy status of the parents we used specific IgE measurements and a questionnaire based on the ECRHS screening questionnaire (22). In the pregnancy questionnaire, information was collected on the use of antibiotics, contact with pets, active and passive smoking during pregnancy and number of siblings. In the following questionnaires (at 3, 6 and 12 months) we obtained information on birth weight, maternal age at birth, breastfeed-

ing, day-care attendance, contact with pets, tobacco smoke exposure, recurrent cold (>2 episodes) and the use of antibiotics during the first year of life.

Statistical analyses

Because atopic sensitization, eczema and recurrent wheezing are status-type outcomes, prevalence odds ratios (ORs) and 95% confidence intervals (CIs) were computed as a measure of association between the outcome variables and educational level. Crude associations were assessed by contingency tables and evaluated by Pearson's chi-square tests or Fisher's exact test, when appropriate. After testing for normality with the Kolmogorov-Smirnov test (none of the distributions was normal), Mann-Whitney *U*-tests were used to evaluate the association with continuous variables (maternal age and birth weight). In addition, we explored the associations of PEL-related characteristics with the outcomes and to what extent high and low PEL-families differ with respect to outcome related determinants, which might explain the association between PEL and the outcomes. The covariates for the multiple logistic regression models were selected based on evidence from previous studies (20, 21) and their distribution within the study population. When maternal and paternal education were considered separately, interaction between these two characteristics was investigated. Two-sided *p*-values of less than 0.05 were considered statistically significant. Statistical analyses were performed using SPSS for Windows, Version 13.0 (SPSS Inc., Chicago, IL, USA).

Results

In total, 690 of the 1128 (61.2%) children had complete information on outcome and educational variables and were included in the study. Table 1 presents a description of the study population concerning outcome variables and educational levels of the parents. At the age of 1 yr, 13.3% of the children were atopic (3.5% sensitized to inhalant allergens and 10.7% sensitized to food allergens), 9.1% had recurrent wheezing and 25.1% had eczema. Eight out of 63 (12.7%) recurrent wheezers and 49/173 (28.3%) children with eczema were atopic. In total, 17.0% of the children had parents with both a low educational level, and 83.0% had at least one parent with a high educational level. Only 25.1% of the mothers and 33.4% of the fathers had a low educational level.

Table 1. Description of outcomes and parental education in the study population (N = 690)

Individual variables	n (%)
<i>Outcome variables</i>	
Atopic sensitization	92 (13.3)
Sensitized to inhalant allergens	24 (3.5)
House dust mite	15 (2.2)
Cat	10 (1.4)
Dog	5 (7.2)
Sensitized to food allergens	74 (10.7)
Hen's egg	59 (8.6)
Cow's milk	32 (4.6)
Recurrent wheezing (at least 3 episodes)	63 (9.1)
Recurrent wheezing with atopy	8 (1.2)
Recurrent wheezing without atopy	55 (7.9)
Eczema	173 (25.1)
Eczema with atopy	49 (7.1)
Eczema without atopy	124 (18.0)
<i>Educational level of the parents</i>	
Maternal educational level	
High	517 (74.9)
Low	173 (25.1)
Paternal educational level	
High	459 (66.6)
Low	230 (33.4)
Parental educational level	
High (at least one parent with a high education)	573 (83.0)
Low (two parents with a low education)	117 (17.0)

The distribution of the potential explanatory variables by different outcomes is shown in Table 2. Among the children with atopy, there was a higher proportion of boys and children with atopic fathers. Children with recurrent wheeze were more often male, more often exposed to environmental tobacco smoke (pre- and postnatal) and antibiotics during the first year of life, and had more often a recurrent cold. Children with eczema were more often exposed to prenatal antibiotics, were less often exposed to pets during the first year, and more often had a father with eczema.

Potential explanatory variables stratified by PEL are shown in Table 3. Children with low-educated parents had significantly younger mothers and were more exposed to pets and cigarette smoke during pregnancy and in the first year of life. On the other hand, the prevalence of day-care attendance and breastfeeding was higher among families with high PEL. Furthermore, children with highly educated parents tended to have a higher birth weight and more often a mother with asthma.

Table 4 presents the crude and adjusted associations between PEL and atopic sensitization of

Table 2. Distribution (frequency and percentage) of explanatory variables by outcome

Characteristic	Atopic sensitization		Recurrent wheeze		Eczema	
	No n/N (%)	Yes n/N (%)	No n/N (%)	Yes n/N (%)	No n/N (%)	Yes n/N (%)
Gender (male vs. female)	311/598 (52.0)	58/92 (63.0)**	329/627 (52.5)	40/63 (63.5)*	269/517 (52.0)	100/173 (57.8)
Breastfeeding	473/598 (79.1)	74/92 (80.4)	494/627 (78.8)	53/63 (84.1)	408/517 (78.9)	139/173 (80.3)
Exposure during pregnancy						
Pets	270/598 (45.2)	42/90 (46.7)	282/625 (45.1)	30/63 (47.6)	238/517 (46.0)	74/171 (43.3)
Cigarette smoke (active)	49/598 (8.2)	10/91 (11.0)	53/626 (8.5)	6/63 (9.5)	41/517 (7.9)	18/172 (10.5)
Cigarette smoke (passive)	138/589 (23.4)	15/90 (16.7)	134/618 (21.7)	19/61 (31.1)*	120/509 (23.6)	33/170 (19.4)
Antibiotics	108/584 (18.5)	20/90 (22.2)	114/612 (18.6)	14/62 (22.6)	86/505 (17.0)	42/169 (24.9)**
Exposure during the first year						
Pets	340/598 (56.9)	51/92 (55.4)	354/627 (56.5)	37/63 (58.7)	303/517 (58.6)	88/173 (50.9)*
Cigarette smoke	64/595 (10.8)	13/91 (14.3)	65/623 (10.4)	12/63 (19.0)**	56/513 (10.9)	21/173 (12.1)
Antibiotics	377/593 (63.6)	60/92 (65.2)	390/624 (62.5)	47/61 (77.0)**	318/512 (62.1)	119/173 (68.8)
Day-care	501/598 (83.8)	71/92 (77.2)	517/627 (82.5)	55/63 (87.3)	432/517 (83.6)	140/173 (80.9)
Siblings	336/594 (56.6)	46/92 (50.0)	337/623 (54.1)	45/63 (71.4)	288/513 (56.1)	94/173 (54.3)
Mould or moisture at home	19/587 (3.2)	2/89 (2.2)	17/615 (2.8)	4/61 (6.6)	18/505 (3.6)	3/171 (1.8)
Recurrent cold	355/584 (60.8)	49/87 (56.3)	357/613 (58.2)	47/58 (81.0)**	299/502 (59.6)	105/169 (62.1)
Allergic diseases of the mother						
Atopic sensitization	234/579 (40.4)	39/91 (42.9)	244/610 (40.0)	29/60 (48.3)	190/500 (38.0)	83/170 (48.8)**
Eczema	95/581 (16.4)	18/87 (20.7)	100/606 (16.5)	13/62 (21.0)	78/499 (15.6)	35/169 (20.7)
Asthma	45/589 (7.6)	6/91 (6.6)	44/619 (7.1)	7/61 (11.5)	35/509 (6.9)	16/171 (9.4)
Allergic diseases of the father						
Atopic sensitization	193/448 (43.1)	42/68 (61.8)**	213/470 (45.3)	22/46 (47.8)	166/388 (42.8)	69/128 (53.9)**
Eczema	47/573 (8.2)	9/87 (10.3)	53/600 (8.8)	3/60 (5.0)	33/493 (6.7)	23/167 (13.8)**
Asthma	36/588 (6.1)	9/91 (9.9)	44/617 (7.1)	1/62 (1.6)*	28/508 (5.5)	17/171 (9.9)**
Birth weight of the child in grams, median (range)	3400 (830–4980)	3300 (2300–4720)	3400 (830–4980)	3430 (2270–4510)	3400 (830–4980)	3330 (1850–4300)
Maternal age at birth in years, median (range)	30.6 (18–42)	30.2 (21–39)	30.6 (18–42)	30.4 (24–40)	30.6 (18–42)	30.5 (21–41)

Associations tested by Pearson's chi-square test or by Mann-Whitney *U*-test.

p* < 0.10; *p* < 0.05.

Table 3. Distribution (frequency and percentage) of explanatory variables by parental educational level

Characteristic	High education (n = 573)	Low education (n = 117)	p-value
Gender (male vs. female)	311/573 (54.3)	58/117 (49.6)	0.353
Breastfeeding	472/573 (82.4)	75/117 (64.1)	<0.001
Exposure during pregnancy			
Pets	243/571 (42.6)	69/117 (59.0)	0.001
Cigarette smoke (active)	37/572 (6.5)	22/117 (18.8)	<0.001
Cigarette smoke (passive)	138/589 (18.9)	15/90 (40.4)	<0.001
Antibiotics	105/558 (18.8)	23/116 (19.8)	0.801
Exposure during the first year			
Pets	308/573 (53.8)	83/117 (70.9)	0.001
Cigarette smoke	41/570 (7.2)	36/116 (31.0)	<0.001
Antibiotics	363 (63.7)	74/115 (64.3)	0.893
Day-care	494/573 (86.2)	78/117 (66.7)	<0.001
Siblings	315/569 (55.4)	67/117 (57.3)	0.706
Mould or moisture at home	15/560 (2.7)	6/116 (5.2)	0.159
>2 periods of cold	338/560 (60.4)	66/111 (59.5)	0.860
Diseases of the mother			
Atopic sensitization	235/558 (42.1)	38/112 (33.9)	0.108
Eczema	97/552 (17.6)	16/116 (13.8)	0.324
Asthma	47/564 (8.3)	4/116 (3.4)	0.069
Diseases of the father			
Atopic sensitization	192/425 (45.2)	43/91 (47.3)	0.718
Eczema	45/546 (8.2)	11/114 (9.6)	0.624
Asthma	35/563 (6.2)	10/116 (8.6)	0.343
Birth weight of the child in grams (median and range)	3410 (830–4980)	3270 (1810–4480)	0.061
Maternal age at birth in years (median and range)	30.7 (23.0–42.0)	29.8 (18.0–41.0)	0.006

Associations tested by Pearson's chi-square test or by Mann–Whitney *U*-test.

the child at the age of 1 yr. Children with at least one highly educated parent tend to be more atopic than children with low-educated parents. When atopic sensitization was separated into sensitization to food allergens and inhalant allergens, only the associations between PEL

and sensitization to food allergens were statistically significant. After adjusting for potential confounders the odds ratios went up, indicating that the associations could not be explained by these PEL-related determinants. While maternal education was positively associated with atopic sensitization and sensitization to food allergens of the child, no significant associations were found with paternal education. There was no interaction between maternal and paternal educational level in the logistic regression models for atopic sensitization; therefore, this interaction term was not included in the regression models.

The association between PEL on the occurrence of recurrent wheezing of the child during the first year of life is shown in Table 5. According to univariate analyses, children with highly educated parents had significantly less recurrent wheezing than children with low-educated parents (crude OR: 0.4, 95% CI 0.2–0.8). After adjustment for potential confounders this association remained unchanged (adj. OR: 0.4, 95% CI: 0.2–0.8). When differentiating recurrent wheezing according to the atopic status of the child, it appeared that all children with atopic wheeze had at least one highly educated parent, however, the number of children with atopic wheeze was low (*n* = 8). In contrast, children with at least one highly educated parent had significantly less non-atopic wheeze than children with both low-educated parents (crude OR: 0.4, 95% CI 0.2–0.6). After adjustment for potential confounders, this association remained significant (adj. OR: 0.3, 95% CI: 0.1–0.6). We found significant interaction between maternal and paternal education in the logistic regression

Table 4. Crude and adjusted* odds ratios (ORs) with 95% confidence intervals (CIs) for association between parental education (high vs. low) and atopic sensitization, sensitization to food and inhalant allergens at the age of 1 yr

Outcome	Parental education		Maternal education		Paternal education	
	High	Low	High	Low	High	Low
Atopic sensitization n/N (%)	81/573 (14.1)	11/117 (9.4)	75/517 (14.5)	17/173 (9.8)	58/459 (12.6)	33/230 (14.3)
Crude OR (95% CI) p-value	1.6 (0.8–3.1)	0.170	1.6 (0.9–2.7)	0.117	0.9 (0.5–1.4)	0.531
Adj. OR* (95% CI) p-value	2.1 (1.0–4.4)	0.054	2.4 (1.2–4.7)†	0.011	0.7 (0.4–1.2)‡	0.211
Sensitized to food allergens n/N (%)	65/557 (11.7)	9/115 (7.8)	61/503 (12.1)	13/169 (7.7)	45/446 (10.1)	28/225 (12.4)
Crude OR (95% CI) p-value	1.6 (0.8–3.2)	0.231	1.7 (0.9–3.1)	0.111	0.8 (0.5–1.3)	0.355
Adj. OR* (95% CI) p-value	2.2 (1.0–5.0)	0.061	2.9 (1.3–6.3)†	0.007	0.6 (0.4–1.1)‡	0.122
Sensitized to inhalant allergens n/N (%)	21/513 (4.1)	3/109 (2.8)	19/461 (4.1)	5/161 (3.1)	16/417 (3.8)	8/205 (3.9)
Crude OR (95% CI) p-value	1.5 (0.4–5.1)	0.509	1.3 (0.5–3.7)	0.565	1.0 (0.4–2.3)	0.968
Adj. OR* (95% CI) p-value	2.2 (0.5–9.0)	0.273	1.7 (0.5–5.9)†	0.377	1.1 (0.4–3.1)‡	0.839

*Adjusted for: gender, birth weight, maternal age, breastfeeding ever, active and passive smoking during pregnancy, exposure to cigarette smoke in the first year, exposure to pets during pregnancy and in the first year, day-care attendance, atopic sensitization of the father.

†Also adjusted for paternal education.

‡Also adjusted for maternal education.

Table 5. Crude and adjusted* odds ratios (ORs) with 95% confidence intervals (CIs) for the association between parental education (high vs. low) and different forms of recurrent wheezing at the age of 1 yr

Outcome	Parental education		Maternal education		Paternal education	
	High	Low	High	Low	High	Low
Recurrent wheeze n/N (%)	44/573 (7.7)	19/117 (16.2)	40/517 (7.7)	23/173 (13.3)	39/459 (8.5)	24/230 (10.4)
Crude OR (95% CI) p-value	0.4 (0.2–0.8)	0.003	0.5 (0.3–0.9)	0.028	0.8 (0.5–1.4)	0.405
Adj. OR* (95%CI) p-value	0.4 (0.2–0.8)	0.010	1.1 (0.4–3.4)†	0.882	2.1 (0.8–6.1)†	0.154
			0.2 (0.1–0.7)‡	0.008	0.4 (0.1–1.4)‡	0.158
RW with atopy n/N (%)	8/573 (1.5)	0/98 (0.0)	8/485 (1.6)	0/98 (0.0)	6/426 (1.4)	2/208 (1.0)
Crude OR (95%CI) p-value	–	–	–	–	1.5 (0.3–7.4)	0.636
Adj. OR* (95%CI) p-value	–	–	–	–	–	–
RW without atopy n/N (%)	36/565 (6.4)	19/117 (16.2)	32/509 (6.3)	23/173 (13.3)	33/453 (7.3)	22/228 (9.6)
Crude OR (95%CI) p-value	0.4 (0.2–0.6)	<0.001	0.4 (0.2–0.8)	0.003	0.7 (0.4–1.3)	0.285
Adj. OR* (95%CI) p-value	0.3 (0.1–0.6)	0.002	0.8 (0.3–2.6)†	0.755	3.3 (0.9–12.5)†	0.082
			0.1 (0.1–0.4)‡	0.002	0.4 (0.1–1.4)‡	0.162

*Adjusted for: gender, birth weight, maternal age, breastfeeding ever, active and passive smoking during pregnancy, exposure to cigarette smoke in the first year, exposure to pets during pregnancy and in the first year, antibiotics in the first year, day-care attendance, older siblings, mould / moisture, recurrent cold, asthma of mother and father.

†With a high educational level of the other parent.

‡With a low educational level of the other parent.

model for recurrent wheeze. This means that the association of the education of one parent depends on the education of the other parent. Therefore, OR's were calculated for both high and low educational levels of the other parent. A high maternal education was significantly protective for recurrent wheeze. This effect was strongest when the paternal educational level was low. Again only a significant effect of maternal education was seen.

Table 6 presents the associations between PEL and eczema of the child during the first year of life. According to univariate analyses eczema of

the child is positively associated with a high educational level of the parents (crude OR: 1.7, 95% CI: 1.0–2.7). After adjustment for potential confounders, this association remained (adj. OR: 1.9, 95% CI: 1.1–3.4). When atopic and non-atopic eczema were analysed separately, similar trends were seen for both types of eczema: children with at least one highly educated parent had more atopic as well as non-atopic eczema than children with low-educated parents. However, the association of PEL was stronger with atopic eczema than non-atopic eczema. The effect of maternal educational level on eczema

Table 6. Crude and adjusted* odds ratios (ORs) with 95% confidence intervals (CIs) for the association between different definitions of eczema at the age of 1 yr and parental education level (high vs. low)

Outcome	Parental education		Maternal education		Paternal education	
	High	Low	High	Low	High	Low
Eczema n/N (%)	152/573 (26.5)	21/117 (17.9)	140/517 (27.1)	33/173 (19.1)	120/459 (26.1)	52/230 (22.6)
Crude OR (95% CI) p-value	1.7 (1.0–2.7)	0.051	1.6 (1.0–2.4)	0.036	1.2 (0.8–1.8)	0.312
Adj. OR* (95% CI) p-value	1.9 (1.1–3.4)	0.023	1.8 (1.1–3.0)†	0.013	1.3 (0.8–2.0)‡	0.202
Eczema with atopy n/N (%)	45/466 (9.7)	4/100 (0.4)	42/419 (10.0)	7/147 (4.8)	32/371 (8.6)	16/194 (8.2)
Crude OR (95% CI) p-value	2.6 (0.9–7.3)	0.068	2.2 (1.0–5.1)	0.051	1.1 (0.6–2.0)	0.878
Adj. OR* (95% CI) p-value	3.2 (1.0–10.1)	0.045	3.2 (1.2–8.2)†	0.018	1.2 (0.6–2.4)‡	0.640
Eczema without atopy n/N (%)	107/528 (20.3)	17/113 (15.0)	98/475 (20.6)	26/166 (15.7)	88/427 (20.6)	36/214 (16.8)
Crude OR (95% CI) p-value	1.4 (0.8–2.5)	0.202	1.4 (0.9–2.2)	0.163	1.3 (0.8–2.0)	0.252
Adj. OR* (95% CI) p-value	1.6 (0.9–3.0)	0.122	1.6 (0.9–2.6)†	0.104	1.4 (0.9–2.2)‡	0.197

*Adjusted for: gender, birth weight, maternal age, breastfeeding ever, active and passive smoking during pregnancy, exposure to cigarette smoke in the first year, prenatal antibiotics, exposure to pets during pregnancy and in the first year, day-care attendance, paternal eczema.

†Also adjusted for paternal education.

‡Also adjusted for maternal education.

was also stronger than the effect of paternal educational level, on both atopic and non-atopic forms. There was no interaction between maternal and paternal education in the logistic regression models for eczema, thus the interaction term was not included in the regression model.

Discussion

The results of our study in a prospective birth cohort showed that the occurrence of atopic sensitization and atopic eczema is higher among 1-yr-old children with highly educated parents. Furthermore, in our study population all children with atopic wheeze had highly educated parents. However, children with low-educated parents had significantly more non-atopic recurrent wheeze. When maternal and paternal educational level were considered separately, the effects were almost entirely explained by maternal education.

In general, we found that 1-yr-old children with at least one highly educated parent had more atopic sensitization and eczema, but had less recurrent wheeze than children with low-educated parents. Similar positive associations between SES/educational level and atopic sensitization (23, 24) and eczema (5, 25) have been reported previously in children and adults. However, the results concerning the relationship between asthma (or wheezing) and SES/educational level are conflicting. Some study groups found a positive association (6), whereas others found a negative association (9, 25) or no clear relationship (11). These inconsistent findings may arise from studies that do not make a distinction between allergic and non-allergic forms of asthma or wheeze.

To our knowledge this is the first study that investigates associations between PEL on the one hand, and atopic and non-atopic forms of eczema and recurrent wheeze on the other hand in children up to the age of 1 yr. We found that children with at least one highly educated parent had more atopic as well as non-atopic eczema than children with low-educated parents, though this association was statistically significant for atopic eczema only.

After differentiating between atopic and non-atopic recurrent wheezing, opposing effects were found for these two forms. Children with low-educated parents had significantly more non-atopic wheeze than children with highly educated parents, even after adjustment for potential confounders. In contrast, it appeared that all eight atopic wheezers had highly educated parents. A similar effect was found in an American

and a Swedish study in adults; i.e. a positive relationship of allergic asthma with increasing levels of education but an inverse relationship of non-allergic asthma (26, 27). However, both studies used symptomatic definitions of allergic status, namely hay fever and allergic rhinitis. In the ECRHS comprising young adults from 15 countries, objective specific IgE measures were used to assess atopy. They found, similar to our results, that the occurrence of non-atopic asthma was higher in lower socioeconomic groups, whereas no relationship was found between educational level and atopic asthma (8). The conflicting results of studies, which did not differentiate between atopic and non-atopic wheeze, may be explained by differences in the prevalence of non-atopic wheeze. In populations with a high prevalence of non-atopic wheeze, it is more likely to find a negative association between wheezing and PEL. On the other hand, in populations with a low prevalence of non-atopic wheeze, it is more likely to find a positive association.

A possible explanation for a lower prevalence of atopic wheeze, atopic eczema and atopic sensitization among those with a lower SES/educational level is that poorer living conditions and more childhood infections may exert a protective effect on the development of atopy (cfr. hygiene hypothesis) via the preferential stimulation of T-helper (Th) 1 lymphocytes, with an inhibitory effect on IgE synthesis and, by consequence, atopic sensitization (28). In turn, non-atopic wheeze is shown to be associated with viral infections, exposure to tobacco smoke *in utero*, environmental tobacco smoke, and low birth weight, which are all associated with lower SES/educational level (16). Nevertheless, after controlling for these characteristics the correlation between non-atopic wheeze and educational level remained.

Many possible risk factors for asthma and allergies are related to educational level (or SES) and have been proposed to explain associations between SES and asthma and allergic diseases. According to our results, children with low-educated parents were significantly more exposed to cigarette smoke and pets during pregnancy and the first year of life than children with highly educated parents. We also found that children with highly educated parents received more breastfeeding and were more likely to attend day-care. These findings agree with previous studies (29, 30). Associations between PEL and the use of antibiotics, the number of siblings, exposure to mould or moisture and allergic diseases in the parents were less clear. Although

we accounted for all the afore-mentioned potential explanatory variables in our analyses, the relationship between PEL and recurrent wheezing and eczema did not change substantially and remained statistically significant. Other, not measured, components associated with educational level (or SES) may also contribute to the development of asthma and allergic diseases. Aspects of the indoor environment such as central heating, use of carpets, type of bedding and decreased air circulation because of better insulation may increase the risk of allergic diseases by influencing house dust mite populations in wealthier groups (31). Other possible risk factors in higher socioeconomic classes are the overuse of showers or soaps and the greater use of synthetic clothing fabrics and greater exposure to ultraviolet light (32).

After differentiation between atopic sensitization to food and inhalant allergens, only the association with food allergens remained significant. Almqvist et al. (33) also did not find a significant association between SES and atopic sensitization to inhalant allergens in 4-yr-old children. However, in that study, there were decreasing risks of sensitization to food allergens with increasing SES, which is in contrast to our results. This difference may be as a result of the diverse sensitization patterns in 1 and 4-yr-old children (more food atopy in 1-yr-olds vs. more inhalant atopy in 4-yr-olds). When interpreting these results, one also has to take into account that a large proportion of the children sensitized to food allergens at the age of 1 yr have a transient atopic sensitization, and that transient sensitizations are found more often in children with lower specific serum IgE levels (34).

In general, we found that the education of the mother had a much stronger influence than the education of the father. Only in the models for recurrent wheeze, interaction between maternal and paternal education was retained. We found that children with either a highly educated mother or father had less risk for (non-atopic) recurrent wheeze. However, a high maternal educational level was significantly protective for (non-atopic) recurrent wheeze, only when paternal education was low. Different effects of maternal and paternal education have been described previously (35). This may be explained by the important role of the perinatal environment (20). In our analyses, we took several exposures of the mother during pregnancy into account, such as exposure to pets, cigarette smoke (active and passive) and antibiotics. Yet, the significant influence of maternal education remained.

The strengths of the present study are the prospective data collection, the availability of pre- and postnatal data and specific IgE measurements for atopic status. The prospective data collection reduces the chance of recall bias. Pre- and postnatal data collection allows accounting for exposures before the onset of disease. The quantification of specific serum IgE represents an objective measurement for the atopic status of the children as well as the parents. Furthermore, to our knowledge, this is the first study that investigates associations between PEL on one hand, and atopic and non-atopic forms of eczema and recurrent wheeze on the other hand, in children up to the age of 1 yr.

However, this study has some methodological limitations. The chance of selection bias has to be considered in the interpretation of the results. For example, higher educated parents may be more likely to participate in an epidemiological study than those with a lower education. This may explain the high percentage of highly educated parents in this study. Parents with allergic diseases also tend to participate more in a study on asthma and allergies. Consequently, the prevalence of allergic diseases is likely to be higher than in the general (Belgian) population. However, as this is not a prevalence study on atopy, recurrent wheezing and eczema, we believe that this selective participation does not have an important influence on the studied associations. Also according to non-responder analysis children with incomplete information were not significantly different compared to children with complete information as regards outcome and educational variables (data not shown). Furthermore, parents with a high educational level may be more likely to recognize and report symptoms than parents with a low educational level, resulting in information and reporting bias. As a result, parent-reported information on the history of allergic diseases may be a source of misclassification, which may have led to an overestimation of the associations between PEL and allergic symptoms. Finally, some minor misclassification may also have occurred in defining the children (and parents) as non-atopic because of the limited number of inhalant and food allergens tested (which is common in most epidemiological studies).

In conclusion, even after correcting for several PEL-related confounders we found that PEL is positively associated with atopic disorders (atopic sensitization, atopic eczema and atopic wheezing). A negative association was seen between PEL and non-atopic wheezing. When maternal and paternal education were considered

separately, maternal education had a stronger effect on the outcomes. Future research should explore how maternal education affects the risk of atopy, asthma (-like symptoms) and eczema, and which potential mechanisms are involved. Additionally, future studies on asthma and eczema should take into account that atopic and non-atopic forms are two different phenotypes with different risk factors and prognosis.

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