

Maternal atopy and parity

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Summary

Background Family size and high birth order were related to the prevalence of hayfever and positive skin prick test. However, this association may be explained by maternal atopy. We examined the relationship between maternal atopy and the number of offspring in three European cohorts of pregnant women.

Methods The mothers and their children ($n = 1487$) were recruited for the Asthma Multi-centre Infants Cohort Study (AMICS). The three concurrent cohorts (Ashford, Kent (UK); Menorca island (Spain) and Barcelona city (Spain) followed the same research protocol. Maternal and paternal atopy was identified by skin prick tests at different times at the three centres.

Results Maternal atopy was inversely related to the number of offspring, an association which occurred in each of the three cohorts and remained when atopy was defined separately for individual allergens (a positive response to testing with either Der p 1 or grass pollen) and which was not confounded by maternal age, smoking nor social class (the adjusted odds ratios were 0.71, 0.79 and 0.26 for increasing number of offspring, $P = 0.002$). Neither maternal asthma ($P = 0.43$) nor paternal atopy ($P = 0.58$) were associated with the number of offspring. Maternal atopy was not related to reproductive outcomes.

Conclusions The association between maternal atopy and parity challenges the role of family size on child atopy, which should be studied in other populations.

Keywords: atopy, family size, reproductive outcomes.

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Introduction

Family size and high birth order were related to the prevalence of hayfever and skin prick test responses to

common inhalant allergens in a British birth cohort [1,2], and in German [3] and Italian [4] school children. A plausible inference from these observations is that infection in early life confers protection against subsequent allergic disease. An alternative explanation is that maternal atopy which itself is a strong risk factor for childhood atopy is associated with fewer offspring. Although one of the studies on child allergy [4], and another on child wheezing [5], adjusted for familial atopy, they have used self-reported retrospective information to define parental atopy, with an insufficient evaluation of the role of maternal atopy. There is no single study testing whether there is an inverse association between parental atopy (particularly maternal) measured by skin tests reactivity or serum IgE

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against common allergens. We examined the relationship between maternal and paternal atopy and the number of offspring in three European cohorts of pregnant women.

Materials and methods

The mothers and their children were recruited for the Asthma Multi-centre Infants Cohort Study (AMICS), which aims to examine the effects of pre- and post-natal environmental exposures in the inception of atopy and asthma. The three concurrent cohorts (Ashford, Kent (UK); Menorca island (Spain) and Barcelona city (Spain)) followed the same research protocol. Cohorts were population-based in Ashford and Menorca, and hospital-based in Barcelona. We included all women presenting for antenatal care at three general practices in Ashford (Kent) ($n = 643$, 94% of eligible mothers) over 18 months beginning in January 1994; and, at all general practices in Menorca ($n = 500$, 95%) over 12 months starting in mid-1997. In Barcelona, women attending the obstetric department in the Hospital del March (this covers one of the health areas of the city) between 1996 and 1998, with permanent residence in the city and having a telephone were enrolled (476, around half of that eligible). In all centres women agreed to participate after they were told the objectives of the study and gave informed written consent. Overall, 1487 mothers (615, 477 and 395, respectively, for the three centres) consented to skin prick testing and were included in the present study.

Maternal and paternal atopy was identified by skin prick tests; performed during the first trimester of pregnancy in Ashford, third trimester in Barcelona, and six months after delivery in Menorca. A positive skin test was defined as a weal of 3 mm or greater (mean of perpendicular measures) to any of the allergens (cat, *Cladosporium*; *Dermatophagoides pteronyssinus* (Der p 1) or *pharynae*, mixed grass, tree mix or graminea (mix) in the presence of a positive histamine control and a negative uncoated control. Field workers were trained to follow the same procedure. After 15 min of individual antigen-coated lancets application, the outline of the weal was drawn on adhesive tape. The reproducibility of skin prick tests during and around 6 months after pregnancy was tested in 54 mothers of Barcelona and was high ($\kappa = 0.61$, proportion of positive agreement = 54%, and proportion of negative agreement = 82%) Paternal atopy was measured only in 60% of the fathers.

Peri-natal measurements, and data on previous spontaneous abortions in Barcelona and Menorca, were extracted from clinical records at delivery. The total number of live children for each woman, maternal asthma, smoking and socio-economic groups based on paternal occupation was obtained using a questionnaire administered during

pregnancy. Asthma was defined as a positive answer to the question 'have you ever had asthma', and hay fever to 'have you ever had hayfever or allergic rhinitis'.

Odds ratios were estimated by the maximum likelihood method using multiple logistic regression. Differences in continuous variables were compared by multiple linear regression. Heterogeneity between centres was assessed including an interaction term in the multivariate models. Since heterogeneity was non-significant ($P > 0.1$) in all of the models, a fixed effects model was used for the joint analysis of the three centres.

Table 1. Frequency of maternal atopy by selected variables

	Maternal atopy	
	Yes <i>n</i> (%)	No <i>n</i> (%)
Cohort		
Ashford	210 (34.1)	405 (65.9)
Barcelona	64 (16.2)	331 (83.8)
Menorca	135 (28.3)	342 (71.7)
Smoking		
Yes	79 (22.9)	266 (77.1)
No	329 (28.9)	809 (71.1)
Social class		
1 Professional	31 (35.2)	57 (64.8)
2 Managerial	72 (37.1)	122 (68.9)
3N Skilled non-manual	54 (22.9)	182 (77.1)
3M Skilled manual	145 (26.1)	411 (73.9)
4 Partly skilled	61 (29.6)	145 (70.4)
5 Unskilled	7 (19.4)	29 (80.6)
Maternal age in years		
< 27	114 (26.3)	319 (73.7)
27–32	192 (30.9)	430 (69.1)
> 32	103 (23.8)	329 (76.2)
Maternal asthma		
Yes	101 (66.5)	51 (33.5)
No	308 (23.1)	1025 (76.9)
Maternal hay fever		
Yes	209 (62.0)	128 (38.0)
No	200 (17.4)	949 (82.6)

Atopy defined as a positive specific skin test ≥ 3 mm to either cat, *Cladosporium*, *Dermatophagoides pteronyssinus* or *pharynae*, mixed grass, tree mix or graminea mix.

Comparisons between atopic and non-atopic mothers for all variables in the table had a $P < 0.05$ using chi-square test. Among these variables, only maternal age was heterogeneous between the three centres ($P < 0.1$), with a higher prevalence of atopy in women aged 27–32 in Ashford and Barcelona, and at age < 27 in Menorca.

Table 2. Frequency of maternal and paternal atopy by the number of offspring, and the corresponding adjusted association measured with the odds ratio (OR)

Offspring (<i>n</i>)	Ashford % (<i>n</i>) [†] OR	Barcelona % (<i>n</i>) [†] OR	Menorca % (<i>n</i>) [†] OR	All three centres		
				% (<i>n</i>) [†]	OR (95% CI)	Adj.‡ OR (95% CI)
By maternal atopy						
0	37.9% (261) 1	18.4% (185) 1	32.9% (246) 1	30.9% (692)	1	1
1	33.9% (224) 0.84	14.6% (151) 0.76	22.5% (173) 0.59*	25.0% (548)	0.74 (0.59, 0.96)*	0.71 (0.54, 0.94)*
2	29.4% (92) 0.68	13.5 (37) 0.69	29.4% (51) 0.85	26.1% (180)	0.79 (0.55, 1.14)	0.79 (0.52, 1.21)
≥ 2	21.1% (38) 0.44*	13.6% (22) 0.70	0% (7) 0	16.4% (67)	0.44 (0.23, 0.85)*	0.26 (0.11, 0.62)*
By paternal atopy**						
0	40.0% (230) 1	22.2% (90) 1	42.1% (133) 1	37.1% (453)	1	1
1	44.3% (194) 1.19	27.3% (55) 1.31	37.5% (64) 0.83	39.9% (313)	1.13 (0.84, 1.52)	1.16 (0.84, 1.60)
≥ 1	36.7% (109) 0.88	44.4% (18) 2.50	21.1% (19) 0.38	35.6% (146)	0.94 (0.64, 1.38)	1.03 (0.66, 1.60)

†Percentage of women with maternal (paternal) atopy and total number of women per each category of offspring.

‡Adjusting for age, smoking, social class and centre. *P* for heterogeneity between centres in the association with maternal atopy = 0.39, and with paternal atopy = 0.11.

**P* < 0.05

**Categories of Offspring (*n*) were collapsed due to small numbers.

Results

The prevalence of maternal atopy was higher in Ashford than in both Barcelona and Menorca (Table 1), and the mean numbers of offspring were 1.88, 1.80 and 1.62, for the corresponding centres. Maternal age and smoking were also related with atopy (Table 1). The prevalence of specific reactivity to Der p 1 was 20.4%, to cat fur, 6.5%, and to grass pollen, 10.5%.

Maternal atopy was inversely related to the number of offspring (Table 2), an association which occurred in each of the three cohorts and which was not confounded by maternal age, smoking nor social class (*P* for trend = 0.002)

(Table 2). The association remained when atopy was defined separately for individual allergens (*P* for trend with Der p 1 = 0.05 and with grass pollen = 0.003) (Table 3). The association between atopy and the number of offspring occurred both in mothers with asthma or hayfever and in mothers without either asthma or hayfever (*P* for interaction = 0.46) (Table 3). Paternal atopy was not associated with number of offspring (*P* for trend = 0.58) (Table 2). The association with maternal atopy remained unchanged when mothers without data on paternal atopy were excluded. Maternal asthma was not related to the number of offspring (*P* for trend = 0.43) (Table 3).

Table 3. Frequency of maternal atopy and asthma by the number of offspring, and the corresponding adjusted association measured with the odds ratio (OR)

Offspring (n)	Maternal atopy						Maternal asthma	
	To Der p 1		To grass		To any allergen, without asthma/hayfever		To any allergen	
	Prevalence	Adj. † OR (95% CI)	Prevalence	Adj. † OR (95% CI)	Prevalence	Adj. † OR (95% CI)	Prevalence	Adj. † OR (95% CI)
0	23.4%	1	11.7%	1	17.8%	1	10.8%	1
1	18.8%	0.75 (0.55–1.01)	10.4%	0.69 (0.45–1.05)	16.1%	0.89 (0.60–1.32)	9.9%	1.02 (0.69–1.54)
2	17.8%	0.85 (0.54–1.35)	10.6%	0.59 (0.32–1.10)	12.7%	0.77 (0.42–1.41)	11.4%	0.96 (0.51–1.81)
> 2	14.9%	0.46 (0.19–1.11)	7.5%	0.15 (0.03–0.66)*	9.6%	0.50 (0.17–1.52)	7.7%	0.51 (0.15–1.74)

†Adjusting for age, smoking, social class and centre.

**P* < 0.05

The number of women without asthma/hayfever per offspring were 484, 417, 134 and 52, respectively.

Table 4. Adjusted association between maternal atopy and reproductive outcomes

Outcome (unit)	Average	Adjusted† change due to maternal atopy (and SE)
Birth weight (g)	3287	– 19.3 (31.6)
Birth height (cm)	50.3	– 0.02 (0.17)
Cranial perimeter (cm)	34.1	0.04 (0.10)
Weight placenta (g)	608	– 14.5 (10.2)
Gestational age (wk)	39.2	– 0.01 (0.10)
	Percent	Odds ratio (95% CI) ‡
Prematurity (< 37 weeks)	6.6	1.06 (0.64–1.74)
Low birth weight (< 2500 g)	6.5	0.82 (0.52–1.28)
Previous abortion*	26	1.04 (0.70, 1.55)

†Adjusted for smoking, age, centre and social class.

*Data was only available for Barcelona and Menorca.

No peri-natal measurements were related to maternal atopy in any of the three cohorts (Table 4).

Discussion

Atopic mothers had a lower number of offspring in each of these three cohorts. Since maternal atopy is a strong risk factor for childhood atopy, this finding may in part explain the reported associations of child atopy with the number of siblings or the number of older siblings. Some of the studies on family size and child atopy attempted to control for the potential role of maternal atopy. One of the studies [4] adjusted for familial atopy (i.e. asthma, hayfever or eczema in any member of the family), self-reported by questionnaire during a survey among school children aged 9–11 years and the association between family size and child atopy was independent of parental atopy. A survey on wheezing among school children from 5 to 11 years of age found an independent association with family size after adjusting for maternal and paternal atopy (i.e. eczema, rhinitis, hayfever, wheezing or asthma) defined by questionnaire [5]. However, the measurement of familial atopy by a questionnaire may be susceptible to misclassification in the measure of maternal atopy. A recent survey in children aged 13 and 14 years found a positive association between maternal allergy (i.e. hayfever, allergic rhinitis, asthma or dermatitis), measured by questionnaire, and parity [6]. The discrepancy with our findings could be due to a problem of bias in the measurement of past history of atopy with questionnaire, or otherwise, that the history of clinical presentation of atopy and skin test reactivity are different phenomena. Nevertheless, we have found a negative association between

maternal atopy and the number of offspring when atopy was measured by reported hayfever ($P < 0.01$) (data not shown).

Explanations for a negative association between maternal atopy (but not paternal) and the number of offspring include the possibility that atopic mothers, as those with asthma [7], have a higher rate of poor pregnancy outcomes; however, we found no evidence for this. Alternatively, maternal atopy may be related to relative infertility (voluntary or otherwise). However, the average maternal age of atopic mothers at the time of their first child in these three cohorts (28.4-year-old) was not higher than that of non-atopic mothers (27.6) ($P = 0.08$). The mother's age when the first child is born is an indirect measure of time to pregnancy and thus of fertility. An alternative and more likely explanation could be that atopy in women may decrease with the number of pregnancies, since pregnancy has an effect on the immune system [8], although steroid hormones during pregnancy have not been related with immunosuppression [9].

The present study is the only one measuring maternal atopy by skin testing, rather than by questionnaire as in previous studies [4–6]. The present findings with a valid measurement of atopy deserve further confirmation in other populations and if the association between maternal atopy and the number of children were to be confirmed, the association between family size and child atopy should be reassessed. A second step would be to investigate possible explanations for the role of atopy on parity such as that atopy may reduce fertility or that pregnancy may have a permanent immunosuppressive effect.

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