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Changes in atopy prevalence and sibship effect in rural population at all ages

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Abstract

Background: We examined the associations of family size and birth order with atopy prevalence in rural Poland at two time periods.
Methods: Two cross-sectional surveys were conducted in the same villages and a small town of lower Silesia at an interval of 9 years. In 2003, 1700 (88% of eligible individuals), and in 2012, 1730 (86%) inhabitants aged 5 years or more completed a questionnaire and had a skin prick test for atopy.
Results: There was an inverse association between family size and atopy in the village population in 2003; the prevalence of atopy was the highest for those with no siblings (15.2%) and decreased to 5.4% for those with three and more siblings (OR = 0.22; 0.07–0.66). In contrast, there was little or no such protective effect in the town population where the prevalence of atopy was much higher (7.3% in the villages, 20.0% in the town). Nine years later, the prevalence of atopy had increased in the village to be similar to that in the town (19.6% and 19.9% respectively), and the protective effects of family size and birth order in the villages were much weaker (OR = 0.64; 95% CI 0.33–1.27 for three or more siblings). Both protective effects were strongest among children.
Conclusions: The protective effects of family size and birth order on atopy were much stronger in children than in adults and among those living in a village. They largely disappeared with the steep increase in atopy prevalence at all ages; this followed environmental changes on the village farms.

One of the more intriguing phenomena following the increased prevalence of atopy and allergic diseases in the last few decades is their unequal distribution, not only across westernized and nonwesternized parts of the world, but also within small communities living in close proximity but under different environmental conditions (1, 2). The well-known protective effect of rural living is the most typical example. Children brought up on farms have less atopy, asthma, and atopic eczema than their nonfarm neighbors (3–5). In addition, the risk of atopy may differ depending on the birth order and number of siblings. Larger family size and/or birth order may protect against allergic sensitization (6), hay fever (7), and asthma (8). The reasons for these associations, first reported nearly 30 years ago (9) and confirmed in many later studies, are still unclear.

Both protective effects – farming and family size/birth order – appear to be independent (10). However, both are consistent with the 'hygiene' hypothesis (11), which states that improvements in hygiene may promote allergy development. More recent observations suggest that the mechanisms may be more complex involving gene–environment interactions for the farm effects (12) and hormones and prenatal programming for the family size effects (13).

In 2003, we reported a striking difference in atopy prevalence between village inhabitants and those living in a nearby small town in southwest Poland; the differences occurred at all ages, with an overall prevalence of 7.3% in the villages and 20.0% in the town (14). Shortly afterward, a rapid and distinct change in farming practices took place in these communities, following Polish accession to the European Union. Nine years later, we repeated the survey in the same area and found a strong increase in atopy prevalence in the village population; this occurred at all ages, with an overall prevalence of 19.6% in the villages and 19.9% in the town (15).

We proposed that this may mean that the atopic state is more plastic than was previously believed and is not programmed once for the whole of life and that changes in exposure to risk/protective factors may influence immunological responses at any age (15).

In this study, we examine the associations of family and family size/birth order with atopy prevalence in the village and town populations at all ages and at two time periods, before and after the steep increase in atopy prevalence in the rural population.

Methods

Two cross-sectional surveys were conducted in the same rural areas of lower Silesia in Poland in 2003 and 2012. The study design has been described in detail previously (15). All inhabitants aged 5 years or more in seven small villages and two randomly selected areas of a nearby quiet, small town with 4000 inhabitants and no large-scale industry were eligible. We used exactly the same instruments in both surveys. All family members completed, with the aid of a nurse interviewer, a questionnaire on respiratory and allergic symptoms and on early-life and current exposures to a farming environment. Mothers supplied information on behalf of the children younger than 15 years. In addition, each person was invited to undergo skin prick testing with extracts of four common local aeroallergens, house dust mite, cat fur, mixed grass, and tree pollens (ALK-Abello, Hungerford, Berkshire, UK), and with negative (saline) and positive (histamine) control solutions. The nurses each surveyed approximately equal numbers of urban and village households. Atopy was defined as a positive result (wheal of mean diameter 3 mm or more than the response to saline) of skin prick tests; we considered an individual to be atopic if they had a positive response to one or more of the test allergens.

We defined household size as the number of individuals currently living in the home; this incorporates information on nonparticipants, but results are only reported for surveyed participants. Family size was defined as the number of siblings an individual has, regardless of whether or not they currently live in the same household. Farming was defined by the response to the question: Do you currently live on farm?

Ethical approval was obtained from the Ethics Committee at Wroclaw Medical University; each participant provided signed consent and/or did so on behalf of their child.

Statistical methods

We estimated crude and adjusted prevalence odds ratios for atopy using logistic regression, adjusting for age, sex, maternal age, current smoking, and farming (identified *a priori* as potential confounders). All analyses were performed with IBM SPSS Statistics for Windows, Version 20.0. (IBM Corp., Armonk, NY, USA).

Results

A total of 1700 (88% of eligible individuals) inhabitants in 2003 and 1730 (86%) inhabitants in 2012 completed a questionnaire; skin prick tests were conducted in 1664 participants (97%) in 2003 and 1676 (97%) in 2013. The response rate was similar in villages and town (in 2003: 87% in villages *vs* 90% in town; and in 2012: 84% *vs* 90%, respectively); 908 people (560 villagers and 348 town inhabitants) participated in both surveys.

The characteristics of the village and town participants are shown in Table 1. Townspeople were slightly older than those from the villages. Participants in 2012 were older than in 2003 in both locations. Village families were larger than those in the town (median five members compared with four

Table 1 Characteristics of the village and town study population in the two surveys

	Villages			Sobotka		
	2003	2012	*P*	2003	2012	*P*
Surveyed (questionnaire + SPT), *n*	973	868		691	808	
Age, median (range)	34 (5–92)	40 (5–92)	<0.001	40 (5–86)	46 (5–99)	<0.001
Female, *n* (%)	515 (52.9)	479 (55.2)	0.33	383 (55.4)	471 (58.3)	0.26
Household size, median (range)	5 (1–13)	4 (1–12)	<0.01	4 (1–8)	3 (1–8)	<0.01
Live on a farm? *n* (%)	534 (54.9)	429 (49.4)	0.02	7 (1.0)	18 (2.2)	0.07
Contact with farm animals (pigs, cows or poultry) (%)	516 (53.0)	340 (39.2)	<0.01	30 (4.3)	31 (3.8)	0.43
Number of siblings (%)						
0	46 (4.7)	61 (7.0)	<0.01	65 (9.4)	68 (8.4)	0.42
1	211 (21.7)	220 (25.3)		235 (34.0)	267 (33.0)	
2	250 (25.7)	232 (26.7)		166 (24.0)	224 (27.7)	
>3	466 (47.9)	355 (40.9)		225 (32.6)	249 (30.8)	
Birth order (%)						
1	307 (31.6)	308 (35.5)	0.15	272 (39.4)	320 (39.6)	0.68
2	276 (28.4)	244 (28.1)		230 (33.3)	282 (34.9)	
>3	390 (40.1)	316 (36.4)		189 (27.4)	206 (25.5)	
Atopy (%)	71 (7.3)	170 (19.6)	<0.001	138 (20.0)	161 (19.9)	0.98

Table 2 Prevalence and adjusted odds ratio of atopy stratified by place of living and number of siblings or birth order in 2003 and 2012 (total surveyed population)

	Village 2003		Village 2012		Sobotka 2003		Sobotka 2012	
	n (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*
Number of siblings								
0	7 (15.2)	1.00	17 (27.9)	1.00	17 (26.2)	1.00	12 (17.6)	1.00
1	23 (10.9)	0.54 (0.19–1.55)	55 (25.0)	0.89 (0.46–1.70)	61 (26.0)	0.98 (0.37–2.60)	65 (24.3)	1.38 (0.69–2.75)
2	16 (6.4)	0.30 (0.10–0.89)	46 (19.8)	0.66 (0.34–1.29)	33 (19.9)	0.88 (0.32–2.48)	47 (21.0)	1.41 (0.69–2.87)
≥3	25 (5.4)	0.22 (0.07–0.66)	52 (14.6)	0.64 (0.33–1.27)	27 (12.0)	0.90 (0.30–2.70)	37 (14.9)	1.07 (0.51–2.27)
Birth order								
1	29 (9.4)	1.00	70 (22.7)	1.00	63 (23.2)	1.00	65 (20.3)	1.00
2	25 (9.1)	0.67 (0.32–1.38)	52 (21.3)	0.96 (0.62–1.46)	47 (20.4)	0.89 (0.47–1.68)	62 (22.0)	1.09 (0.73–1.63)
≥3	17 (4.4)	0.25 (0.10–0.63)	48 (15.2)	0.72 (0.44–1.16)	28 (14.8)	0.60 (0.25–1.42)	34 (16.5)	0.87 (0.51–1.50)

*Adjusted for age, sex, maternal age, current smoking, and farming.

in 2003 and four compared with three in 2012, $P < 0.01$). Household size decreased over time in both locations. There were no changes in family size or birth order in the town population, whereas in the villages there were more individuals with no siblings and fewer with three or more in 2012 than in 2003.

As we reported previously, atopy prevalence increased significantly among village inhabitants between the two surveys (7.3% in 2003 *vs* 19.6% in 2012, $P < 0.001$) but did not change in the town (20.0% *vs* 19.9%, respectively, $P = 0.98$).

There was an inverse association between family size and atopy prevalence in the village population in 2003 (Table 2). For those villagers who had no siblings, the prevalence of atopy was the highest (15.2%) and decreased to 5.4% for those with three and more siblings (OR = 0.22; 0.07–0.66). After 9 years, the prevalence of atopy increased significantly in all groups independently of number of siblings, and the protective effect of family size was much weaker than in 2003 (OR = 0.64; 95% CI 0.33–1.27 for three or more siblings). A similar pattern was observed for birth order among villagers. The prevalence of atopy was the highest among firstborns and lower among those with higher birth order, but once again the protective effect was much more pronounced in 2003 than in 2012 (0.25; 0.10–0.63 for people with three or more older siblings in 2003; and 0.72; 0.44–1.16 in 2012). The protective effect was stronger for older than younger siblings but was still present for the latter (0.64; 0.23–1.80 for those with three or more younger siblings in 2003; and 0.68; 0.36–1.30 in 2012, data not shown in the table).

In contrast, among townspeople, there was little or no association between family size or birth order and atopy in either 2003 or 2012; the one possible exception is that the odds ratio for atopy in 2003 was nonsignificantly reduced among those who had three or more older siblings.

Very similar results, both in villages and in the town, were observed when we restricted the analyses to those who participated in both surveys (Table 3).

Table 2 also shows that atopy increased in the villages between 2003 and 2012 in each category of family size and birth order. For example, in those with no siblings, atopy prevalence in the villages increased from 15.2% to 27.9%; there were corresponding increases for those with 1 (10.9–25.0%), 2 (6.4–19.8%), or 3 or more siblings (5.4–14.6%).

Table 3 Prevalence and adjusted odds ratio of atopy stratified by place of living and number of siblings or birth order in 2003 and 2012 (population taking part in both surveys)

	Village 2003		Village 2012		Sobotka 2003		Sobotka 2012	
	n (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*
Number of siblings								
0	6 (23.1)	1 (ref.)	8 (23.5)	1 (ref.)	6 (25.0)	1 (ref.)	5 (21.7)	1 (ref.)
1	16 (13.2)	0.56 (0.19–1.64)	32 (27.8)	1.41 (0.56–3.57)	24 (25.0)	0.90 (0.30–2.66)	30 (29.4)	1.10 (0.33–3.63)
2	8 (5.8)	0.22 (0.07–0.73)	26 (19.0)	0.72 (0.28–1.84)	17 (18.3)	0.86 (0.28–2.65)	19 (19.6)	0.91 (0.27–3.07)
≥3	13 (5.1)	0.21 (0.07–0.66)	30 (11.8)	0.58 (0.23–1.48)	15 (12.3)	0.70 (0.21–2.31)	19 (16.7)	1.14 (0.33–3.95)
Birth order								
1	21 (12.4)	1 (ref.)	40 (21.7)	1 (ref.)	23 (20.4)	1 (ref.)	23 (20.4)	1 (ref.)
2	13 (8.4)	0.54 (0.25–1.18)	18 (19.6)	0.93 (0.52–1.66)	25 (21.7)	0.99 (0.49–1.98)	30 (24.6)	1.13 (0.58–2.20)
≥3	9 (4.1)	0.19 (0.07–0.50)	28 (13.1)	0.57 (0.31–1.07)	14 (13.1)	0.57 (0.22–1.49)	20 (19.8)	1.20 (0.53–2.72)

*Adjusted for age, sex, maternal age, current smoking, and farming.

Table 4 Prevalence and adjusted odds ratios (95% CI) of atopy in villagers and townspeople by number of siblings or birth order stratified by age in 2003 and 2012

	Village 2003		Village 2012		Sobotka 2003		Sobotka 2012	
	n (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*	*n* (%)	OR (95% CI)*
5–20 years old								
Number of siblings								
≤1	13 (10.6)	1 (ref.)	29 (27.9)	1 (ref.)	38 (32.5)	1 (ref.)	19 (20.2)	1 (ref.)
2	7 (7.5)	0.65 (0.24–1.72)	17 (29.8)	0.87 (0.40–1.86)	10 (30.3)	0.67 (0.27–1.64)	8 (40.0)	3.09 (0.89–10.73)
≥3	2 (2.6)	0.21 (0.04–1.06)	8 (20.0)	0.71 (0.26–1.97)	3 (17.6)	0.36 (0.09–1.41)	2 (12.5)	0.47 (0.09–2.49)
Birth order								
1	13 (12.1)	1 (ref.)	25 (29.4)	1 (ref.)	25 (34.7)	1 (ref.)	18 (28.1)	1 (ref.)
2	7 (7.4)	0.43 (0.15–1.21)	19 (31.1)	1.12 (0.52–2.42)	19 (29.7)	0.48 (0.19–116)	9 (17.6)	0.54 (0.20–1.47)
≥3	2 (2.2)	0.08 (0.01–0.42)	10 (18.2)	0.54 (0.21–1.42)	7 (22.6)	0.26 (0.07–0.93)	2 (13.2)	0.44 (0.07–2.55)
21–60 years old								
Number of siblings								
≤1	16 (13.9)	1 (ref.)	38 (27.0)	1 (ref.)	40 (23.4)	1 (ref.)	57 (28.6)	1 (ref.)
2	8 (6.1)	0.41 (0.16–0.99)	26 (17.0)	0.59 (0.33–1.06)	22 (17.5)	0.97 (0.52–1.81)	36 (21.7)	0.80 (0.49–1.32)
≥3	20 (6.8)	0.53 (0.25–1.11)	36 (16.2)	0.72 (0.41–1.28)	20 (12.3)	0.78 (0.39–1.55)	26 (19.8)	0.72 (0.40–1.31)
Birth order								
1	15 (9.0)	1 (ref.)	37 (21.5)	1 (ref.)	37 (20.2)	1 (ref.)	46 (24.5)	1 (ref.)
2	16 (11.0)	1.19 (0.54–2.59)	30 (20.1)	0.99 (0.56–1.75)	27 (17.5)	0.77 (0.43–1.40)	50 (27.8)	1.10 (0.68–1.79)
≥3	13 (5.7)	0.47 (0.18–1.24)	33 (16.9)	0.84 (0.44–1.59)	18 (14.6)	0.73 (0.32–1.68)	23 (18.0)	0.51 (0.26–1.03)
>60 years old								
Number of siblings								
≤1	1 (5.3)	1 (ref.)	5 (13.9)	1 (ref.)	0	1 (ref.)	1 (2.4)	1 (ref.)
2	1 (3.8)	0.42 (0.02–11.43)	3 (13.6)	1.05 (0.22–5.02)	1 (14.3)	N/A	3 (7.9)	3.32 (0.32–34.44)
≥3	3 (3.1)	2.14 (0.11–42.21)	8 (8.6)	0.59 (0.18–1.96)	4 (8.9)	N/A	9 (8.8)	3.18 (0.38–26.82)
Birth order								
1	1 (3.0)	1 (ref.)	8 (15.7)	1 (ref.)	1 (5.9)	1 (ref.)	1 (1.5)	1 (ref.)
2	2 (5.7)	2.31 (0.16–34.35)	3 (8.8)	0.47 (0.11–1.98)	1 (8.3)	0.76 (0.03–16.79)	3 (5.9)	5.27 (0.47–59.85)
≥3	2 (2.7)	7.59 (0.31–183.9)	5 (7.6)	0.36 (0.10–1.31)	3 (8.6)	1.04 (0.06–16.71)	9 (14.3)	13.97 (1.39–140.19)

*Adjusted for age, sex, maternal age, current smoking, and farming.

We have also conducted analyses stratified by age for the 2003 and 2012 surveys (Table 4). We used ≤1 sibling as the reference category because there were relatively few people with no siblings. The protective effects of family size and birth order were mainly seen among children and young people, but once again it was stronger in village than town children in 2003, but not in 2012 and stronger in 2003 than in 2012. In village children surveyed in 2003, the odds ratio for atopy was 0.08 (0.01–0.42) among those with three or more older siblings and 0.21 (0.04–1.06) for those with three or more siblings. In 2012, the protective effects of family size and birth order were much weaker (0.54 (0.21–1.42) and 0.71 (0.26–1.97), respectively).

In adults, the association of sibling number or birth order with atopy was much weaker than in children. Both among village and town inhabitants, there was a trend for the prevalence of atopy to decline with increasing family size or birth order, but the associations were much weaker and did not reach statistical significance.

Discussion

We found negative associations between atopy and both family size and birth order in the village population, particularly in children. This protective effect was much weaker after the strong increase in atopy prevalence in this population between 2003 and 2012 both in total surveyed population and among those who took part in both surveys. The increase in atopy prevalence in the villages occurred across all age-groups and occurred in all categories of family size and birth order. The association between atopy and family size and birth order was much weaker in the town than in the village population in both surveys and at all ages and did not change over time.

Some of the limitations of these data should be considered. Firstly, the small sample size limits the precision of the analyses, especially those stratified by age. Secondly, discrepancies in measurements between surveys cannot be excluded. However, it is unlikely that such discrepancies would be major as we used the same protocol and allergen source and checked for histamine response comparability in both surveys. Moreover, the increase of atopy was confined only to villagers, and the specificity of this effect makes any systematic bias unlikely. It is also unlikely that there would be differences in the validity of the skin prick tests by birth order or family size. On the other hand, the response rates, in both studies, were relatively high, and most of the participants (53.4% of the participants in the first survey) took part in both studies.

Most observations of the associations between sibship size, birth order, and atopy come from studies in children. In our study, the strongest protection against atopy from living in the villages was seen in children. Although in 2003 the prevalence of atopy was extremely low in this population, we still observed protective effects of family size and birth order. These results are in accordance with another larger study of children living in a rural environment where the combination of family size and farm exposure significantly reduced the prevalence of atopy (10). The protective effects of living on a farm (in the village) were present in all categories of birth order and family size, which suggests that these two protective factors act independently. In our study, it is clearly seen in 2003 but no longer in 2012 when the prevalence of atopy increased significantly at all ages, and in all groups independently of number of siblings or birth order. It suggests that both variables (farm, siblings) showed independent effects in 2003, and both showed little or no effect in 2012. Thus, the changes in the environment 'removed' the independent effects of both variables. It is of interest that the protective effect of larger family size was much stronger in the village than in the town population. The reasons for this are unclear, and the findings are not completely consistent with those shown recently in the International Study of Asthma and Allergies in Childhood (ISAAC) Phase III study of the protective effects of family size on asthma, rhinoconjunctivitis, and eczema in affluent and nonaffluent countries (16). In that study, the protective effect of older siblings on hay fever and eczema was unequal. It varied between countries with different level of affluence and was significantly stronger in more affluent countries than in less affluent centers. In contrast, in our study, the effect was observed in the more traditional (and generally less affluent) populations (i.e., the villages in 2003) and largely disappeared as these populations became more Western and urban.

Other previous studies of the associations between family size and birth order and atopy in adulthood have yielded inconsistent results; very little is known, in this context, about adults living in the rural environment. The ECRHS study of young adults (aged 20–44 years) found a negative association between sensitization to grass pollen and family size but not birth order (8). In another large study of young men (aged 18–24 years), a protective effect of family size on atopic sensitization was found (17). In our population, the family size effect was much less evident in adults than in children, both in the villages and in the town. It should be noted that most of the surveyed adults, regardless of whether they nowadays live in the village or in the town, spent their first years of life on farms.

The mechanism of the protective effects of village life, family size, and birth order is unclear. With regard to the family size effect, two main hypotheses have been proposed. Both are focused on the events which occur at the early stages of our life. The first hypothesis relates to repeated infections in childhood protecting against the development of allergy and allergic asthma. However, it is not clear whether the frequency and profile of early infections really depend on family structure, and the association of family size with early infection has not been proven (18). The apparent protective effects of younger siblings mean that not only the first years of life are important, but also later events may be so (17). As an alternative explanation, the role of subsequent pregnancies on fetal immune system maturation and the ways in which newborn or fetal immunological systems react to their environment has been proposed (19). Making the picture even more complex, previous studies showed that the sibling effect may depend on different phenotypes of allergic diseases and different populations (8, 20, 21).

In summary, the findings of our study confirm the protective effects of family size and birth order on atopy. This protective effect was much stronger in children than in adults and much stronger among those living in villages than among town inhabitants. The strong increase in atopy prevalence at all ages presented in the repeated survey, which supposedly followed environmental changes on farms, was independent of family size and birth order. With this overall increase in atopy, the protective effects of family size and birth order largely disappeared.

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Author contributions

BS, NP, and PC designed the study. BS, NP, AB, and PC conducted the study. BS and PC managed data collection. MB performed the statistical analyses. BS, NP, and PC wrote the manuscript. All authors contributed to the interpretation of the results and editing of the manuscript and have approved the final manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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