

Pollen counts in relation to the prevalence of allergic rhinoconjunctivitis, asthma and atopic eczema in the International Study of Asthma and Allergies in Childhood (ISAAC)

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Summary

Background Although pollens are major allergens associated with allergic rhinoconjunctivitis and asthma, there is little information about the relative prevalence of these conditions in populations with different pollen exposures.

Objective The purpose of this study was to investigate the relationship between pollen exposure and allergic symptoms among children in different countries.

Methods An ecological analysis was conducted to see whether pollen exposure (pollen counts, and duration and severity of pollen seasons) is associated with symptoms of allergic rhinoconjunctivitis, asthma and atopic eczema in 28 centres within 11 countries (nine being in Europe). Data on the prevalence of symptoms in 13–14-year olds were based on the responses to the written questionnaires from the International Study of Asthma and Allergies in Childhood (ISAAC). The analysis was adjusted for gross national product and mean annual relative humidity.

Results There was little relationship between pollen exposure and symptom prevalence, except for a significant inverse association between grass pollen counts and lifetime prevalence of the symptoms of allergic rhinitis ($P = 0.03$). Almost all the regression coefficients were negative. The associations were even weaker and all non-significant when the analyses were conducted within countries, using a random intercept fixed slope model, but there was still no evidence of a positive association between pollen exposure and symptoms.

Conclusion There is a weak but consistent tendency for the prevalence of allergic symptoms to be inversely associated with pollen exposure. This finding accords with evidence from several countries, suggesting that the prevalence of hayfever and asthma tends to be lower in rural than in urban areas, and lowest among people living on farms. Exposure to allergenic pollen in early life does not appear to increase the risk of acquiring symptoms of respiratory allergy, and may even give some protection against them.

Keywords allergic rhinitis, asthma, atopic eczema, hayfever, pollen

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Introduction

The prevalence of atopic disorders varies widely throughout the world. In the International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence of symptoms of allergic rhinoconjunctivitis showed a 30-fold variation among the 155 participating centres in 56 countries, while the prevalence of asthma symptoms varied 20-fold [1]. Among the potential explanations for this variation, it seems reasonable to consider differences in exposure to the allergens that are known to provoke the symptoms of these diseases. Differential exposures might affect the prevalence of symp-

toms in three ways: by provoking symptoms to a different extent among persons who are already sensitive to those allergens; by influencing the prevalence of sensitivity to the allergens concerned; or by a non-specific effect on the prevalence of atopy.

Grass pollen is one of the major allergens associated with atopic disease worldwide. In many parts of the world, it is the allergen that is most often implicated in allergic rhinoconjunctivitis, and for asthma it is second only to the house dust mite [2, 3]. Other pollens are particularly important in some areas, e.g. birch pollen in Scandinavia, ragweed in the United States and some parts of Europe, and olive in Mediterranean countries.

It is common knowledge that the symptoms of hayfever become more frequent and more severe when the pollen count rises beyond a certain threshold [4–6]. However, there is less clarity about the geographical relationship between pollen

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exposure and the underlying prevalence of rhinitis. A growing body of evidence suggests that the prevalence of rhinitis and atopy is lower among communities that are likely to be most exposed to pollens. Surveys in several countries show that the prevalence of rhinitis and atopy tends to be lower in rural areas [7–9], particularly on farms [8, 10–13]. On the other hand, in some surveys the occurrence of rhinitis has been similar in urban and rural areas [14, 15], or higher in an area with high pollen exposure [16].

Pollen counts have been recorded in some of the centres that participated in ISAAC. We have conducted an ecological analysis in order to see whether differential pollen exposure contributes to the geographical variation in the prevalence of symptoms of allergic rhinoconjunctivitis, asthma and eczema.

Methods

Study participants

This analysis is based on the ISAAC data from school-children aged 13–14 years; details of the methods and response rates have already been published [1, 17]. The analyses in this paper are confined to those centres in which comparable pollen count data were available. The survey began in 1991, most of the data being collected during 1994–1995. One centre collected data during the pollen season and has been omitted from this analysis.

Symptom questionnaires

A self-administered questionnaire was completed by the children. The questions to which this study relates were as follows:

- Have you *ever* had a problem with sneezing, or a runny or blocked nose, when you DID NOT have a cold or the flu? ('allergic rhinitis ever').
- In the *past 12 months*, have you had a problem with sneezing, or a runny or blocked nose, when you DID NOT have a cold or the flu? ('allergic rhinitis in past year').
- In the *past 12 months*, has this nose problem been accompanied by itchy-watery eyes? ('allergic rhinoconjunctivitis').
- Have you *ever* had wheezing or whistling in the chest at any time in the past? ('wheeze ever').
- Have you had wheezing or whistling in the chest *in the past 12 months*? ('wheeze in past year').
- Have you *ever* had asthma? ('asthma ever').
- Have you *ever* had an itchy rash that was coming and going for at least 6 months? If yes: Have you had this itchy rash at any time *in the last 12 months*? If yes: 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? ('atopic eczema in past year').

Pollen data

All the pollen data relate to 1995. Pollen monitoring stations were selected within about 50 km of the ISAAC centres; evidence suggests that data from one site can be taken to

represent the general pollen spectrum over an area with a radius of this distance [18]. In countries such as UK, where the ISAAC centre covered a region, pollen sites were chosen that fell well within the region. Some ISAAC centres had no pollen monitoring station within 50 km and were therefore not used in the analysis. Pollen data were excluded if the data were incomplete (for example, not recorded at weekends or affected by equipment failure), or very low or otherwise unusual that year; a maximum of 5% 'non-reporting days' during the season was allowed if the pollen data were to be used. All the pollen monitoring sites used volumetric traps, situated on exposed roof tops, and broadly comparable techniques.

Nearly all the monitoring stations recorded grass pollen, so these counts are reported here. Pollens from individual grass species are not differentiated in the counts, since (with very few exceptions) they all cross react. Grass pollen was among the three allergenic pollens most frequently reported at all the sites, but in some places other types may be equally or more important locally, and the monitoring stations also collected data on them. In order to provide some estimates of overall exposure to allergenic pollens, the counts of the most important pollen types ('principal allergenic pollens') for each area were taken into consideration. A high grass pollen count was defined as a daily count exceeding 50 grains/m³; a high allergenic count was defined as occurring when any of the following daily counts were exceeded: grass or olive 50 grains/m³, birch 80 grains/m³, ragweed 15 grains/m³. Length of season was similarly defined with reference to the following thresholds: grass or olive 20 grains/m³, birch 30 grains/m³, ragweed 2 grains/m³. These levels were selected to reflect the relative allergenicity of the different pollens [5, 19–21].

Three criteria were used to summarize the severity of the pollen exposures:

- 1 For grass, total pollen count (the sum of the daily counts) during the season.
- 2 Number of days with a high pollen count.
- 3 Length of season, defined as starting when pollen counts reach the threshold defined above. The end of the season is when counts return to being consistently below the threshold.

Data analysis

For each question about symptoms and index of pollen exposure, the data were analysed by linear regression with one data point for each centre, weighted by the inverse variance of the prevalence estimate for the centre. The analyses were adjusted for the gross national product (GNP) per capita of the country in which each centre was situated, since this is a convenient marker for the degree of affluence (a potential confounder) and has been found to be associated with asthma prevalence in the ISAAC data [22]. Adjustments were also made for the mean annual relative humidity, since this was negatively associated with symptoms of rhinoconjunctivitis (unpublished ISAAC data). For some analyses, we also calculated a two-level, random intercept, fixed slope model, with the dependent variable modelled by the normality assumption. The model allows for random deviations

from the estimated overall prevalence for each country, but the influence of pollen counts is assumed to affect the prevalence non-differentially.

Results

Data on both symptoms and pollen counts were obtained from 28 centres in 11 countries. The centres were all in Europe, except for Sydney (Australia) and Kuwait. The questionnaires were answered by 80 050 children altogether.

Table 1 shows the location of the centres, together with the pollen data. The centres occupy a variety of climatic regions and latitudes (37°38'N to 60°27'N for the European pollen sites). There is a very wide range in the total grass pollen counts (available from all these centres), and in the numbers of days with high counts. Birch is monitored in northern and central Europe, olive in southern Europe, and ragweed in some central and southern European locations. In comparison with data from the same centres in other years, none of the data sets for 1995 were unusual.

Table 2 shows the results of the regression analysis for the indices of grass pollen exposure. Almost all the coefficients

are in a negative direction, and although most of the associations are fairly weak, one of them (for total count in relation to allergic rhinitis ever) is statistically significant. The associations with the principal allergenic pollens are shown in Table 3; all are in a negative direction, most being fairly weak. Adjusting for relative humidity made only marginal differences. In the multilevel analyses (not shown in the tables), the associations were weaker still; none were statistically significant, but they still showed negative or approximately zero regression coefficients.

Figures 1–3 display some of these relationships; total grass pollen count was selected for this purpose as being the least arbitrary of the pollen indices, and the three respiratory symptoms that related to the past year as being most likely *a priori* to show associations, if they exist. These figures illustrate how weak the negative relationships are.

Discussion

This study examines the possibility that the degree of pollen exposure influences the prevalence of the symptoms of allergic rhinoconjunctivitis and asthma. Symptoms of atopic eczema

Table 1. Location of centres with pollen data.

Country	ISAAC centre <i>Pollen site if different</i>	Grass pollen			Principal allergenic pollens		
		Total count	Days > 50 grains/m ³	No. of days in season	Types*	Days with high counts	No. of days in season
Austria	Salzburg	8762	58	108	BG	73	142
	Urfahr-Umgebung Linz	2919	19	95	BG	20	139
Belgium	Antwerp Brussels	2575	17	60	BG	29	101
Finland	Turku & Pori Turku	734	2	47	BG	22	75
France	West Marne Paris	4653	31	70	BG	51	107
	Montpellier Nimes	3413	23	138	GR	25	165
	Pessac Bordeaux	4516	30	102	BG	34	113
	Marseilles	3503	28	83	GR	30	130
Germany	Strasbourg	4083	29	89	BG	47	117
	Münster	12 404	52	123	BG	73	155
	Greifswald	3052	27	64	BG	33	81
Italy	Ascoli Piceno	1799	5	84	(G)	—	—
	Emilia-Romagna Bologna	7248	40	108	GOR	41	120
	Firenze	1492	5	60	GOR	15	83
	Milano	3783	20	84	GOR	32	124
	Roma	3546	29	85	GR	29	91
Poland	Torino	2380	14	70	GOR	17	100
	Poznan	5023	33	61	BG	42	77
Spain	Barcelona	1058	3	50	GOR	3	65
	Cartagena	150	0	10	GOR	9	28
UK	West Midlands Worcester	2653	15	77	BG	26	105
	Scotland Edinburgh	1545	11	43	BG	12	52
	North West Preston	4036	21	64	BG	28	76
	South & West Plymouth	3950	20	98	BG	21	105
	Anglia & Oxford Cambridge	3802	24	71	BG	29	86
	Wales Cardiff	5079	70	84	BG	88	113
Australia	Sydney	5978	42	128	(G)	—	—
Kuwait	Kuwait	21	0	1	(G)	—	—

*B, birch; G, grass; O, olive; R, ragweed. See text for definitions of length of season and high counts.

Table 2. Regression analysis of symptom prevalence (by centre) against grass pollen counts, adjusted for GNP and mean relative humidity, and weighted by the inverse variance of the prevalence in each centre

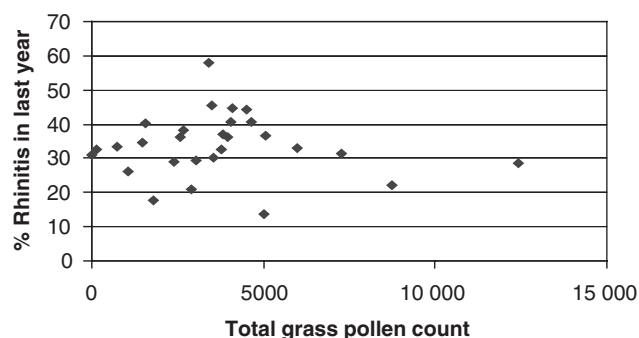
Symptom	Total count		Days > 50 grains/m ³		No. of days in season	
	Coefficient (SE)	P-value	Coefficient (SE)	P-value	Coefficient (SE)	P-value
Allergic rhinitis ever	-0.0014 (0.0006)	0.03	-0.1787 (0.1088)	0.11	-0.0342 (0.0671)	0.62
Allergic rhinitis in the past year	-0.0011 (0.0006)	0.07	-0.1263 (0.1032)	0.23	-0.0097 (0.0632)	0.88
Allergic rhinoconjunctivitis	-0.0003 (0.0003)	0.31	-0.0397 (0.0469)	0.41	-0.0063 (0.0287)	0.83
Wheeze ever	-0.0005 (0.0008)	0.53	0.0207 (0.1424)	0.89	-0.0210 (0.0831)	0.81
Wheeze in the past year	-0.0003 (0.0006)	0.67	0.0155 (0.1023)	0.88	-0.0099 (0.0602)	0.80
Asthma ever	-0.0004 (0.0004)	0.29	-0.0482 (0.0673)	0.07	-0.0107 (0.0432)	0.87
Atopic eczema in the past year	-0.0005 (0.0004)	0.15	-0.0521 (0.0652)	0.43	-0.0063 (0.0287)	0.83

See text for definition of season. GNP, gross national product.

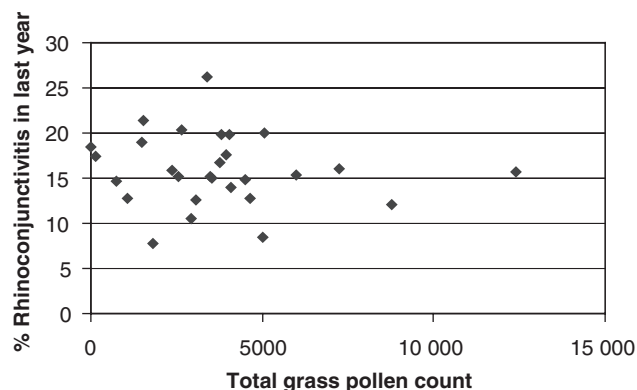
Table 3. Regression analysis of symptom prevalence (by centre) against principal allergenic pollen counts, adjusted for GNP and mean relative humidity, and weighted by the inverse variance of the prevalence in each centre.

Symptom	Days with high counts		No. of days in season	
	Coefficient (SE)	P-value	Coefficient (SE)	P-value
Allergic rhinitis ever	-0.1784 (0.0960)	0.06	-0.0599 (0.0705)	0.41
Allergic rhinitis in the past year	-0.1401 (0.0908)	0.14	-0.0358 (0.0661)	0.59
Allergic rhinoconjunctivitis	-0.0600 (0.0404)	0.15	-0.0180 (0.0296)	0.55
Wheeze ever	-0.1462 (0.1215)	0.24	-0.0853 (0.0833)	0.32
Wheeze in the past year	-0.0782 (0.0894)	0.39	-0.0439 (0.0591)	0.47
Asthma ever	-0.0802 (0.0582)	0.18	-0.0369 (0.0401)	0.37
Atopic eczema in the past year	-0.0619 (0.0610)	0.32	-0.0101 (0.0418)	0.81

See text for definitions of high counts and seasons. GNP, gross national product.

**Fig. 1.** Relationship between total grass pollen count and prevalence of allergic rhinitis in the last year.

were also studied, as a marker for non-respiratory atopic disease. There was an inverse association between pollen counts (particularly grass) and the prevalence of allergic rhinitis symptoms. There was also a non-significant inverse association between high allergenic pollen counts and a

**Fig. 2.** Relationship between total grass pollen count and prevalence of allergic rhinoconjunctivitis in the last year.

history of asthma. Almost all the associations examined were in a negative direction; none of them were very strong, and with multiple statistical tests it is possible that some will be

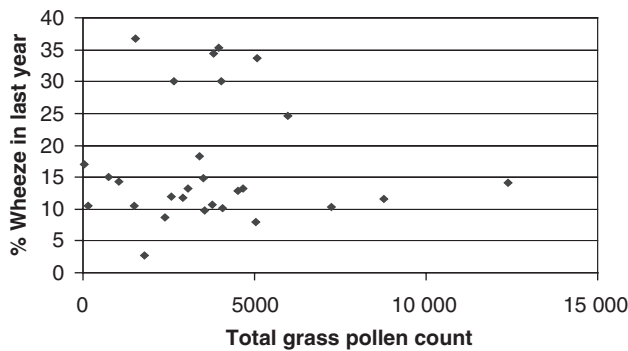


Fig. 3. Relationship between total grass pollen count and prevalence of wheeze in the last year.

significant by chance alone. Furthermore, the associations were weaker, but still negative, in the multilevel analyses that essentially involve controlling for country and comparing the findings for different centres within the same countries.

Thus there is no support here for the hypothesis that high exposure to pollen is a risk factor for developing hayfever [16]. It seems that either high pollen exposure has no effect on the risk of acquiring allergic rhinoconjunctivitis, or it may even confer some protection against it. This apparently paradoxical finding accords with evidence from several countries showing that the prevalence of hayfever and asthma tends to be lower in rural than in urban areas, and lowest among people living on farms [8, 10–13], who are presumably exposed to pollen more often and in higher concentrations than others. Children on livestock farms have a particularly low prevalence [11, 12], so that contact with animals is probably protective, but such children are also likely to be exposed to much grass pollen. It may be the case that continued exposure to pollen gives some protection against pollen allergy. Indeed, this possibility was suggested by Blackley in 1873:

‘One very curious circumstance in connection with hayfever is that persons who are most subjected to the actions of pollen belong to a class which furnishes the fewest cases of the disorder, namely the farming class. This remarkable fact may be accounted for in two different ways: it may, on the one hand, be due to the absence of the predisposition that mental culture generates; or, on the other hand, it may be that in this disease there is a possibility of a patient being rendered insusceptible to the action of pollen by continued exposure to its influence.’ [23]

There is some evidence that proximity to cats during infancy reduces the risk of cat sensitivity, allergic rhinitis and asthma in childhood [24], and the same mechanism could operate for pollen.

The study is restricted to those areas where data were available for both pollen and symptoms. Pollen was monitored in only 28 of the 155 ISAAC centres (representing 11 out of 56 countries), so that the power of the study is limited in the global context, although it does cover areas of major climatic differences in Europe. The analysis relates only to those pollens that were monitored in these locations. Grass is the most widely monitored pollen; although it comprises numerous species, they have similar allergenic properties and are found to some degree throughout the world. The clinical importance of grass pollen derives from its ubiquity and

allergenicity as well as the quantity of airborne grains in any one location. Allergic rhinoconjunctivitis can be provoked by a variety of pollens, many of which are much more important in some areas than in others. Birch, olive and ragweed pollens are major provoking factors in some parts of the world, and it seemed reasonable to consider them as well as grass in the overall picture. An attempt was made to weight them in relation to their known allergenicity. This procedure is admittedly imprecise, and other allergenic pollens could also be included. However, given the importance of these pollens and the overall consistency of the findings, it seems unlikely that addition of other pollens would greatly alter the pattern.

Pollen counts vary from year to year, so selecting data from a single year may reduce the sensitivity of the analysis. The data for 1995 were reasonably representative for each of the centres, so any loss of sensitivity on this account is unlikely to have been very great. In relation to sensitization, pollen counts during infancy are particularly important; in a Swedish study, children born during a year of exceptionally high birch pollen counts had a higher prevalence of birch pollen sensitivity 4–5 years later than others [25]. But the prevalence of asthma, allergic rhinoconjunctivitis and atopic dermatitis was no higher in these children, so the use of current pollen data may be adequate for the present purpose.

There are various potential confounders of the relationship between pollen exposure and allergy. Lifestyle factors (including ‘Westernization’) are believed to influence the risk of allergic disease; if they are also associated with pollen exposure (positively or negatively), they might give rise to misleading relationships. We attempted to allow for this effect by adjusting for GNP (as recommended for analyses of ISAAC data [22]), but it is possible that some residual confounding still occurs. Air pollution tends to occur in industrial areas; there is some evidence that it can potentiate the effects of aeroallergens and so raise the prevalence or severity of allergic rhinitis and asthma [26, 27]. Climate is another potential confounder, but the associations between climatic variables and atopic symptoms are rather weak and inconsistent (unpublished ISAAC data), and adjusting for relative humidity in the present analysis made very little difference.

Overall, it seems very unlikely that high exposure to pollen increases the risk of acquiring allergic rhinoconjunctivitis or asthma, despite its action in provoking attacks in susceptible persons. The associations in this study were very weak, and it may be that pollen exposure has no influence on the prevalence of atopic disease. Nevertheless, the degree of consistency in the negative direction of these associations suggests the possibility of a protective effect.

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