

Original article

The epidemiology of atopic dermatitis in Italian schoolchildren

Background: Atopic dermatitis (AD) is common in children in industrialized countries. Only one large population study on its prevalence has been conducted in Italy, based on self-report questionnaire. The present study was designed to estimate the prevalence of AD in schoolchildren in Italy by dermatologists' assessment and by UK Working Party criteria, and to investigate associated symptoms and factors.

Methods: Cross-sectional survey on a random sample of 9-year-old schoolchildren from seven Italian cities. Children were examined by experienced dermatologists. Parents and teachers answered standardized questionnaires.

Results: Of the 1369 children examined, 88 had a diagnosis of AD, with an estimated point prevalence of 5.8% (95% CI 4.5–7.1) in the reference population. The reported lifetime prevalence was 15.2 (95% CI 12.2–18.2) for AD, 11.9% (95% CI 9.0–14.8) for asthma, and 17.6% (95% CI 14.6–20.7) for rhinoconjunctivitis. The strongest associated factor was the presence of AD in at least one parent. No association of AD with maternal smoking during pregnancy, birth weight, maternal age at the time of the child birth and breast-feeding was observed. The environmental characteristics of the house and the school did not correlate with the prevalence of AD. Episodes of lower respiratory tract infections were associated with asthma, and to a lower extent also with AD and rhinitis.

Conclusions: The prevalence of doctor-diagnosed AD in Italian schoolchildren is comparable to those reported for other developed countries. Family history of atopy was the single most important associated factor, while the complex interplay of environmental factors remains to be elucidated.

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Atopic dermatitis (AD) is a chronic relapsing disorder, which is most prevalent in childhood. It is a distressing condition for both the patients and their families, and has a considerable impact in health care utilization, including direct medical costs, direct family care costs, and indirect costs associated with loss of productivity of carers (1–4). Several studies on the prevalence of AD have been conducted in industrialized countries, mainly in UK and Northern Europe (3). However, only a few studies have addressed this issue in countries with a temperate climate, including those of the Mediterranean area (5–9), and the most important of them, the International Study of Asthma and Allergies in Childhood (ISAAC) study, was based on self-report questionnaires (10).

The present study was undertaken to estimate the prevalence of AD in a population of schoolchildren throughout Italy, examined by trained dermatologists and using a standardized questionnaire to elicit information on associated diseases, characteristics of the family and other environmental factors. Specificity and sensitivity of the diagnosis according to the UK Working Party criteria (11) were also assessed in this population.

Material and methods

Sample design and recruitment

The study was carried out between January and June 2000 in seven Italian cities. The population living in these urban areas on January 1, 2000, comprised 54 066 9-year-old children (the reference population) representing 9.4% of Italian 9-year-old children, according to the data obtained from the National Institute for Statistics (ISTAT). The study population consisted of children attending the fourth grade elementary school. A sample size of 1400 was selected to enable the determination of a true prevalence of AD in the range of 10%, with a 95% confidence interval (CI) of $\pm 1.5\%$. Two levels of sampling were used: first, the 1223 public schools (clusters) present in the seven cities were stratified by three geographical areas (282 in the north, 579 in the centre, and 372 in the south), and schools were randomly selected from each area (13 in the north, 10 in the centre, and 13 in the south); secondly, within each school, children were randomly selected with a different sampling fraction for each geographical area, in order to obtain a distribution of the children in the sample similar to that of the reference population. The overall sampling fraction represents the likelihood to be included in the sample for a child of the reference population (Table 1).

After obtaining consent from the schools for participation in the study, the teachers distributed the questionnaires along with an

Table 1. Characteristic of sample design and response rate

City	Reference population		Sample population		Sampling fraction*	Response rate
	Total schools	Children 9 years old	Sampled schools	Sampled children		
Milan	180	8974	7	260		88%
Modena	40	1415	3	79		68%
Padua	62	1557	3	90		83%
North	282	11946	13	429	3.6%	82%
Rome	508	23558	6	188		70%
Florence	71	2535	4	158		69%
Centre	579	26093	10	346	1.3%	70%
Neaples	286	12592	7	357		51%
Bari	86	3435	6	237		69%
South	372	16027	13	594	3.2%	57%
Total	1233	54066	36	1369		71%

* Mean overall sampling fraction of the children within the cluster.

information sheet, an informed consent form and a reminder of the time of examination. On the day of examination, the children returned the completed consent form and questionnaire, and were then given a complete physical assessment by a trained dermatologist. The criteria for the diagnosis of AD, which were standardized in a consensus conference before the beginning of the study, were: presence of itching dermatitis characterized by erythema, papules, vesicles, excoriations, scaling, and/or lichenification at typical sites. The physician recorded the examination data together with a positive or negative response to each of the UK Working Party diagnostic criteria (11). In addition, the presence of palmar hyperlinearity, keratosis pilaris, pityriasis alba, infraorbital folds, itch when sweating, intolerance to wool, hand eczema, and nummular eczema was registered (12).

Questionnaires

The parental questionnaire was self-administered. It was designed to elicit demographic and health information on the child and the parents, including parental educational level and occupation, as well as personal and family history of atopic disorders, previous infectious diseases, and vaccinations. Prenatal and perinatal variables such as maternal smoking during pregnancy, maternal age at the time of the child birth, birth weight, and duration of breast-feeding were recorded. Environmental factors such as smoking habits of the parents, the type of housing (e.g. apartment or house, size, dampness, and type of heating), type, and intensity of vehicular traffic were asked about. Finally, parents were asked to record medicines and products purchased for their children, specialist consultations and tests, days off school, and other social activities in the previous 15 days. Teachers also completed a questionnaire, which included information on environmental factors related to the location and building characteristics of the school.

Statistical analysis

All data were analysed using the Statistical Package for the Social Sciences version 8.0 for Windows (13). The analysis included all the variables listed previously. The prevalence rate and its variance were computed coherently with the stratified two-stage clustered sampling design used (14). The three geographical areas constituted the

strata, the schools were the cluster, the children the second level unity, and they were weighted inversely to the sampling fraction of each stratum. All prevalence data were computed excluding missing answers. The diagnostic validity of the UK Working Party's criteria and of other skin signs and symptoms associated with AD was analysed against the clinical diagnosis using contingency tables. Results have been expressed in terms of sensitivity, specificity, positive and negative predictive values. The association between risk factors with the clinical diagnosis were quantified using sex- and centre-adjusted odds ratios (OR), and 95% CI from multiple logistic models. The statistical significance of the difference of lifetime prevalence of atopic diseases in relatives of AD index cases and unaffected controls was assessed using the formula reported by Fleiss (15).

Results

Prevalence of AD

The parents of 1369 of 1928 contacted children gave consent for the clinical examination, with an overall response rate of 71%. AD was clinically diagnosed in 88 of the 1369 children examined, with a point prevalence of 6.4% (95% CI 4.5–7.1) in the study population. When the sampling design and fractions were accounted for, the resulting point prevalence in the reference population was 5.8% (95% CI 4.5–7.1), with a prevalence of 6.0% (95% CI 4.1–7.8) in the girls, and 5.7% (95% CI 4.0–7.3) in the boys. No differences in prevalence by month of investigation have been observed. When applying the UK Working Party's criteria, AD was diagnosed in 77 of the 1331 children with complete information on all criteria. The UK Working Party's criteria showed a sensitivity of 77.6%, a specificity of 99.1%, a positive predictive value of 85.7%, and a negative predictive value of 98.5% in our study population, assuming the direct clinical diagnosis as the gold standard. The strongest predictor was the presence of flexural dermatitis, followed by the history of involvement of skin creases, onset under the age of 2 years and itch. History of dry skin in the last year, and history of asthma or hay fever were less strongly associated with AD (Table 2). One hundred eighty-nine of the 1360 parents who answered to this question reported that their children had suffered from 'atopic dermatitis/eczema', with an overall lifetime prevalence of 15.2% (95% CI 12.2–18.2), higher in girls than in boys (Table 3). The reported lifetime prevalence of bronchial asthma and rhino-conjunctivitis is presented in Table 3. In the children with and without AD, respectively, asthma was reported in 46.0 and 10.1% (OR 6.8, 95% CI 4.2–11.0) and rhino-conjunctivitis in 35.6 and 15.1% (OR 3.2, 95% CI 2.0–5.1).

Minor cutaneous clinical signs associated with AD

Among minor clinical signs, hand eczema and nummular eczema were strongly associated with AD. Infraorbital folds, intolerance to wool, itch when sweating, and

Table 2. Sensitivity, specificity, predictive values, and prevalence odds ratios of individual features used in the UK diagnostic criteria for AD against dermatologist's clinical diagnosis

UK Working Party's criteria	Sensitivity %	Specificity %	PPV* %	NPV† %	Prevalence OR (95% CI)‡
Visible flexural dermatitis	36.8	99.5	84.2	95.8	132.1 (51.6–342.6)
History of involvement of skin creases	85.2	93.8	49.0	98.9	91.1 (47.3–175.6)
Onset under age of 2 years	63.2	94.9	45.8	97.4	33.6 (19.8–56.9)
Itch	82.8	82.6	24.5	98.6	29.8 (15.7–56.7)
History of generally dry skin in last year	83.0	73.2	17.6	98.4	14.7 (8.1–26.7)
Personal history of asthma or hay fever	55.7	83.8	19.2	96.5	6.6 (4.2–10.6)

* Positive predictive value.

† Negative predictive value.

‡ Odds ratios adjusted for sex and city.

Table 3. Lifetime prevalence of AD, asthma, and allergic rhinitis based on questionnaire information

	Yes	No	% Total population (n = 1360)	% Girls (n = 651)	% Boys (n = 709)
AD	189	1171	15.2 (12.2–18.2)*	17.6 (13.3–21.9)	13.0 (10.1–15.8)
Asthma	168	1192	11.9 (9.0–14.8)	10.1 (7.3–13.8)	13.2 (9.7–16.7)
Allergic rhinitis	223	1137	17.6 (14.6–20.7)	16.0 (12.0–20.0)	19.2 (15.9–22.4)

* 95% CI are reported in parenthesis.

Table 4. Sensitivity, specificity, predictive values, and prevalence odds ratios of skin signs and symptoms associated with AD against dermatologist's clinical diagnosis

Skin signs and symptoms	Sensitivity %	Specificity %	PPV* %	NPV† %	Prevalence OR (95% CI)‡
Hand eczema	14.9	97.5	28.9	94.4	9.1 (4.3–18.1)
Nummular eczema	2.3	97.7	33.3	93.8	7.6 (1.3–45.8)
Infraorbital folds	60.5	75.4	14.2	96.6	5.4 (3.3–8.9)
Intolerance to wool	78.4	53.9	10.6	97.3	4.5 (2.6–7.8)
Itch when sweating	49.4	82.0	16.0	95.9	4.0 (2.5–6.4)
Palmar hyperlinearity	27.3	92	19	94.8	3.8 (2.3–6.5)
Pityriasis alba	30.2	87.2	13.8	94.8	2.5 (1.4–4.3)
Keratosis pilaris	58.6	68.7	11.4	96.0	2.3 (1.8–4.8)

* Positive predictive value.

† Negative predictive value.

‡ Odds ratios adjusted for sex and city.

palmar hyper linearity showed comparatively moderate levels of association, and an even weaker association was observed between AD and pityriasis alba or keratosis pilaris (Table 4).

Factors associated with AD

The prevalence of AD was higher among children whose parents had both suffered AD (OR 3.9, 95% CI 1.2–12.3), with the mother AD slightly more relevant (OR 2.6, 95% CI 1.5–4.4) than father AD (OR 2.1, 95% CI 1.1–4.1), and sibling AD not significantly associated (OR 1.4, 95% CI 0.7–2.7). The presence of asthma or rhinitis in parents or siblings was not significantly associated with AD, with the exception of asthma in siblings (OR 2.7, 95% CI 1.5–4.9). Asthma in at least one parent (OR 3.7, 95% CI

Table 5. Higher lifetime prevalence of atopic diseases in relatives of AD index cases than in relatives of unaffected controls

	N	Doctor-diagnosed AD (yes)	Reported AD (yes)	Allergic rhinitis (yes)	Asthma (yes)
Index cases	82	100.0	64.6*	25.9*	43.9*
Fathers	82		16.3*	28.8	10.0
Mothers	82		26.0*	29.9	9.1
Siblings	88		16.5	24.1	20.3*
Index controls	1252	0.0	10.8	15.2	10.1
Fathers	1252		7.5	19.9	6.3
Mothers	1252		12.1	20.9	6.2
Siblings	1380		12.5	15.8	0.9

* $P < 0.05$ vs relatives of unaffected controls.

2.5–5.7) or sibling (OR 3.5, 95% CI 2.2–5.6) predicted instead the presence of asthma in children. Finally, rhinitis in both parents or in at least one sibling was associated with increased risk of both rhinitis and asthma in children. Table 5 shows the higher lifetime prevalence of atopic disease in relatives of AD index cases than in relatives of unaffected controls.

A higher socioeconomic class, as reflected by educational level of both parents, white-collar occupation of the mother and ownership of the house, showed a trend towards an association with AD, although no statistical significance was measured. No association was found with maternal smoking during pregnancy, birth weight, maternal age at the time of child birth and breast-feeding, neither for AD nor for respiratory atopy. The type of housing (apartment or house, size, dampness, type of heating, and air pollution of the area), as well as the location and building characteristics of the school did not correlate with the prevalence of AD. Episodes of lower respiratory tract infections (recurrent bronchitis, pneumonia, and whooping cough) were significantly associated with asthma, and to a lower extent with AD and rhinitis (Table 6). However, association between infections and AD was mainly due to confounding by associated asthma, and was no longer significant after controlling for that. No association was found with vaccinations or other common viral infection (herpes simplex, measles, viral warts, and parotitis), while rubella was found to be negatively associated (OR 0.4, 95% CI 0.2–0.8).

Table 6. Prevalence of AD, asthma, and rhinitis by lower respiratory tract infections*

	No. of lower respiratory tract infections		
	0	1	2–3
AD†			
Rate (%)	5.8	6.4	12.7
OR (95% CI)¶	1.0	0.8 (0.5–1.4)	1.1 (0.5–2.6)
Asthma‡			
Rate (%)	7.7	16.7	40.8
OR (95% CI)¶	1.0	2.2 (1.5–3.2)	8.4 (4.6–15.5)
Rhinitis‡			
Rate (%)	13.8	19.3	28.2
OR (95% CI)¶	1.0	1.3 (0.9–1.9)	1.4 (0.8–2.6)

* Whooping cough, recurring bronchitis, bronchial pneumonia.

† Diagnosed by dermatologists.

‡ Reported by parents.

¶ Odds ratios adjusted for sex, city, and for the other two atopic diseases.

Socioeconomic impact of AD

When compared with their nonaffected counterparts, AD children were more likely to have undergone prick or radioallergosorbent tests (52.3 vs 16.2%) or specialist consultations (63.4 vs 50.6%). Their families were more likely to have purchased special products for personal hygiene (52.4 vs 35.9%), over-the-counter medicines (56.1 vs 40.1%) and special clothing (17.1 vs 5.1%). These differences were statistically significant ($P \leq 0.003$) by chi square test.

Discussion

The results of this study indicate that AD is common in Italian schoolchildren, with an estimated point prevalence of 5.8% as assessed by expert dermatologists and a lifetime prevalence of 15.2 as reported by parents, in 9-year-old children in the year 2000. Many difficulties arise in directly comparing findings across studies, because the estimates have been shown to be dependent upon the disease definition and methods of assessment (11), age ranges (16, 17), and year of birth of the children studied or period of time in which the study was conducted (18–21), besides geography (22). However, our data confirm those obtained by questionnaire in the ISAAC study in Italy (1-year period prevalence of 5.8% in 6–7-year-old children in 1994) (10) and are comparable with those obtained in other westernized lifestyle developed countries in similar populations (9, 21, 23, 24). The influence of warmer temperatures on the prevalence of the disease (25) in comparison with Northern European countries is difficult to assess, given the complex interplay of multiple risk and trigger factors (26). The sex ratio for AD was approximately equal, as already reported in other studies (27), but in contrast to previous studies that

showed a female preponderance (23, 28–30). To date, ours is the largest and most comprehensive study in Italy reporting on physician-diagnosed AD, and we believe our figures are representative of the actual prevalence of AD among schoolchildren living in urban areas of Italy, due to accurate sampling and accounting for sampling design in the analysis of the data. However, due to the response rate of only 71% the prevalence could be overestimated, as children with cutaneous complaints might be more likely to participate in the study than children without it. Our sample design was, however, unsuitable for estimating differences in regional prevalence.

The UK Working Party criteria (11) showed very good sensitivity and specificity, with high positive and negative predictive values when compared with clinical diagnosis in Italian 9-year-old schoolchildren, as previously reported for other populations (31, 32), and are confirmed to be a practical and reliable epidemiological tool in the investigation of AD in population settings. However, minor diagnostic criteria for AD, as suggested by Hanifin and Raika (12), were only moderately associated with AD in our study population, confirming scarce utility for diagnosis in this setting (33, 34), in contrast to selected hospital-based AD populations. Parents reported on lifetime prevalence of AD, while the dermatologists assessed the period prevalence of the disease, thus measuring the same phenomenon on different time scales. However, when compared with the diagnosis by the dermatologist, parental reporting of AD showed a moderate sensitivity of 62.1% and a surprisingly high specificity of 89.4%, which is reassuring as far as lifetime prevalence estimate is concerned. In other words, the parents were unlikely to report AD for any kind of dermatitis experienced by their children, and their awareness of the disease was instead surprisingly low. This would result in a conservative estimate of the real lifetime prevalence of the disease.

A higher lifetime prevalence of atopic diseases (AD, asthma, and allergic rhinitis) was found in the relatives of children with current AD than in relatives of unaffected controls (Table 5), as reported in many studies focused on the familial association of atopy (35, 36). As information was obtained by history taking, accuracy of recall should remain a point of concern (37). Also the stronger association with the mother AD, although confirming the findings of other authors (38–40), could be biased by the fact that usually the mothers complete the questionnaires regarding the children's health (37). However, the real importance of a family history of atopy as a risk factor for the development of AD is well documented in cohort studies (41–43). Although cohort studies are also better suited to ascertain risk factors, our cross-sectional survey was designed to collect information at least on factors that were not modifiable on the basis of the child status, such as prenatal and perinatal variables and building characteristics of the house and the school: none of the variables tested was associated with AD, including birth

weight, breast feeding – as already suggested in the literature (43–45) – and type of heating. A higher prevalence of AD in higher socioeconomic classes was confirmed (40, 46, 47), although differences were not statistically significant. The high prevalence of AD in Italy and little differences observed between different socioeconomic groups could reflect the fact that the prevalence of AD in each group had reached almost saturation level, with most of the genetically susceptible cases becoming symptomatic, given the thorough distribution of modern urban lifestyle in the study population, as already described in Japan (21). No association was found with the number of siblings (40) but information on birth order in the sibship (39–42), and age of entry to day nursery (48) was not available, and controlling for these potentially confounding factors was impossible.

Epidemiological and clinical studies have provided compelling evidence that viral/microbial infections may

result in the inhibition or exacerbation of atopy, depending on the infectious agent and the time-point of the infection (49). Our data support the hypothesis that episodes of lower respiratory infections are associated with asthma (Table 6), although the possibility of parental recall bias should be kept in mind.

Finally, although a detailed economical analysis was not conducted, the socioeconomic impact of the disease was somewhat indicated by the qualitative data collected, showing that AD is an important cause of economic burden both to the National Health Service and the families, as in other developed countries (1–4).

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