# **INVESTIGATIVE REPORT**

# Prevalence of Atopic Dermatitis in Italian Schoolchildren: Factors Affecting its Variation

Luigi NALDI1, Fabio PARAZZINI1,2, Silvano GALLUS1,3 and GISED study centres

<sup>1</sup>Centro Studi GISED, USC of Dermatology, University Hospital, Bergamo, <sup>2</sup>Clinica Mangiagalli, University of Milan, IRCCS Fondazione Policlinico Mangiagalli Regina Elena, and <sup>3</sup> "Mario Negri" Institute for Pharmacological Research, Milan, Italy

The frequency of atopic dermatitis in Italian children and its relationship with selected variables were analysed in a large survey of skin health conducted in Italy. In 1997 we conducted a survey on schoolchildren aged 12-17 years from 13 areas of northern, central and southern Italy. For the present analyses, 3179 Caucasian children (1618 males, 1561 females) were considered. A diagnosis of atopic dermatitis was reported in 224 cases (7.0%). The frequency of reported atopic dermatitis was significantly higher in children with asthma (rate ratio (RR) 4.5; 95% confidence interval (CI) 3.1-6.5). The lifetime prevalence of a diagnosis of atopic dermatitis was higher among schoolchildren reporting a diagnosis of psoriasis (RR 5.5, 95% CI 3.0-10.1) and vitiligo (RR 16.1, 95% CI 6.5-39.5). This study gives estimates of the lifetime prevalence of atopic dermatitis in adolescents in Italy and emphasizes the direct association between the condition and other immune-related skin diseases. Key words: atopic dermatitis; children; survey.

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Silvano Gallus, Centro Studi GISED, U.O. Dermatologia, Ospedali Riuniti, Largo Barozzi 1, IT-24128 Bergamo, Italy. E-mail: gallus@marionegri.it

Atopic dermatitis (AD) is a common condition in children. Prevalence studies indicate large variability among countries, with a ratio between low and high prevalence greater than 10-fold (1–14). In the large worldwide International Study of Asthma and Allergies in Children (ISAAC) study, which included more than 190,000 children aged 6–7 years and 300,000 aged 13–14 years in 56 countries, the one-year prevalence in children aged 6–7 years ranged from approximately 2% (Indian subcontinent, Iran) to more than 22% (Sweden). The values for children aged 13–14 years ranged from approximately 1% (Albania, China) to more than 20% (Morocco) (14). Studies conducted in different countries have reported prevalence rates in children ranging from less than 1% to 25% (3, 5, 15).

Data from the ISAAC study aside, scanty information have been published on the prevalence of AD in Italy and, more generally, in southern European countries. In the context of the ISAAC study, these countries have generally reported intermediate rates, lower than those reported from northern European countries, but higher than those reported from eastern Europe.

Genetic determinants apart, these differences may be attributable to different exposure to risk factors or to methodological issues (16). For example, some studies have reported the point prevalence, while others have reported the lifetime risk of AD.

In order to provide data on the lifetime risk of AD in children aged 12–17 years and to quantify the association between selected diseases and AD, we analysed data collected in the framework of a large survey on the skin health of Italian schoolchildren (17, 18).

# MATERIALS AND METHODS

During the spring of 1997, we conducted a multicentre study among schoolchildren attending the third class of a number of secondary schools in Italy. The methods of the present study have already been described (18). Briefly, we selected 13 provinces according to the presence of a dermatological centre participating in the clinical network of the Italian Group for Epidemiological Research in Dermatology (GISED). The provinces were located in northern (Bergamo, Cremona, Ferrara, Verona, Reggio Emilia, Ravenna, and Cesena), central (Florence, Ancona, and San Marino Republic) and southern Italy (Naples, Benevento, and Bari).

The study was co-ordinated locally by a dermatologist, who obtained a list of the schools in each district. Two or three schools per district, according to a preliminary agreement by the local study co-ordinator, were selected randomly from the list. Within each school, all the children attending the third class were eligible.

Permission to conduct the study was obtained by the schools contacting the parents and their children. A standard questionnaire was distributed to parents and written permission to examine the children was requested. Overall, 99% of the parents consented to participate to the study. Of these, 2% were non-Caucasian. For the present analyses, we considered a total of 3179 European Caucasian children (1618 boys and 1561 girls), with written permission, examined by dermatologists, whose parents filled in the questionnaire and with information on AD. The age range of the children was 12–17 years, but most of the children were aged 13 (73%) or 14 (23%) years.

The questionnaire included information about the parents' education, family residence, children's anthropometric characteristics including height and weight, family history of malignant melanoma, and dietary habits. Further, detailed information were collected on the history of selected skin diseases including AD, vitiligo, psoriasis, diabetes, asthma, hepatitis and thyroid diseases, including date at onset and date at first diagnosis by a physician. In a preliminary exercise involving approximately 300 children, the questionnaire was assessed for reliability showing consistent results in terms of inter-rater and intra-rater reliability with kappa values ranging from 0.8 to 0.9 for all the examined items. For each medical condition assessed, a diagnosis by a medical doctor was required. The diagnosis was taken as reported in the medical charts. Lifetime prevalence was defined as "the total number of persons known to have had the disease for at least part of their life."

#### Statistical analysis

Rate ratios (RR) and corresponding 95% confidence intervals (CI) were derived by unconditional logistic regression models after allowance for age (<14 or  $\geq$ 14 years) and sex (19).

#### RESULTS

Table I shows the reported lifetime prevalence of a diagnosis of AD in the overall series and in strata of sex, age, anthropometric factors and geographic area of residence. A diagnosis of AD was reported in 224 cases (7.0%). The lifetime prevalence of AD was apparently higher in males (7.6%) than in females (6.5%): this difference, however, was not significant (p=0.21).

Table I. Distribution of 3179 Italian schoolchildren (1618 males and 1561 females) by history of atopic dermatitis according to selected characteristics. Corresponding rate ratios (RR) and 95% confidence intervals (CI)

	History of atopic dermatitis		
	Yes n (%)	No n	RR <sup>a</sup> (95% CI)
Total series	224 (7.0)	2955	
Sex			
Male	123 (7.6)	1495	1.00 <sup>b</sup>
Female	101 (6.5)	1460	0.82 (0.62-1.10)
Age (years) <sup>c</sup>			
<14	170 (7.8)	2008	1.00 <sup>b</sup>
$\geq 14$	36 (5.0)	687	0.61 (0.42-0.88)
BMI (kg/m <sup>2</sup> ) <sup>c</sup>			
<18.7	85 (7.9)	989	1.00 <sup>b</sup>
18.7-21.0	63 (6.0)	981	0.77 (0.54-1.09)
≥21.1	75 (7.1)	978	0.93 (0.67-1.31)
BSA (m <sup>2</sup> ) <sup>c</sup>			
<1.49	85 (7.9)	987	1.00 <sup>b</sup>
1.49-1.62	66 (6.3)	983	0.74 (0.52-1.05)
≥1.63	72 (6.9)	978	0.93 (0.66-1.32)
Weight (kg) <sup>c</sup>			
< 50	89 (7.8)	1050	1.00 <sup>b</sup>
50-56	58 (6.1)	889	0.74 (0.51-1.06)
≥57	76 (7.0)	1011	0.94 (0.67–1.31)
Height (cm) <sup>c</sup>			
<160	78 (7.4)	983	1.00 <sup>b</sup>
160-164	55 (6.6)	778	0.97 (0.67-1.40)
≥165	90 (7.0)	1188	1.02 (0.72–1.43)
Geographic area			
North	141 (7.3)	1779	1.00 <sup>b</sup>
Centre	33 (5.9)	529	0.79 (0.53-1.17)
South	50 (7.2)	647	0.94 (0.66–1.32)

<sup>a</sup>Estimated by unconditional logistic regression models after allowance for age and sex.

<sup>b</sup>Reference category.

<sup>e</sup>The sum does not add up to the total because of some missing values. BMI: body mass index; BSA: body surface area.



*Fig. 1.* Distribution of 208 children with atopic dermatitis according to age at diagnosis (16 subjects had missing information for age at diagnosis).

No relationship emerged between anthropometric variables and frequency of AD. The frequency was consistent in strata of area of residence. Fig. 1 shows the distribution of subjects with a diagnosis of AD according to age at onset of the condition: most of the subjects reported that the diagnosis was made during the first year of life.

Table II shows the frequency of AD according to history of selected diseases. The frequency of children reporting AD was significantly higher in children with asthma (RR 4.5, 95% CI 3.1–6.5). In particular, 50 subjects reported AD and asthma. Of these, 13 reported that AD was diagnosed before and 14 after the diagnosis of asthma, 16 that asthma and AD were diagnosed at the same age and in 7 cases age at diagnosis of AD and/or asthma was missing.

The lifetime frequency of a diagnosis of AD was higher among schoolchildren reporting a diagnosis of psoriasis (RR 5.5, 95% CI 3.0–10.1) and vitiligo (RR 16.1, 95% CI 6.5–39.5).

Table II. Distribution<sup>a</sup> of 3179 Italian schoolchildren (1618 males and 1561 females) by history of dermatitis, according to history of selected skin and general diseases. Corresponding rate ratios (RR) and 95% confidence intervals (CI)

	History of at	History of atopic dermatitis	
	Yes	No	-
	n (%)	п	RR <sup>b</sup> (95% CI)
Asthma			
No	153 (5.3)	2753	1.00°
Yes	50 (20.0)	200	4.46 (3.07-6.46)
Psoriasis			
No	186 (6.0)	2901	1.00°
Yes	16 (23.5)	52	5.48 (2.98-10.1)
Vitiligo			
No	191 (6.1)	2934	1.00°
Yes	10 (47.6)	11	16.1 (6.52–39.5)

<sup>a</sup>The sum does not add up to the total because of some missing values. <sup>b</sup>Estimated by unconditional logistic regression models after allowance for age and sex.

°Reference category.

# DISCUSSION

This study indicates that the lifetime prevalence of AD at age 13–14 years was approximately 7% in this population. AD was more frequent among children reporting a history of asthma, vitiligo and psoriasis.

The main strengths of the study include the uniquely large sample size, the large number of centres involved and the fact that it was conducted in different Italian geographic areas, giving a more representative estimate of the prevalence of AD in Italy.

Some limitations of the study should be thoroughly considered. The questionnaire was not formally validated for assessing AD or the other medical conditions considered. In fact, the study was originally designed in order to assess the frequency of various melanocytic naevi in Italian schoolchildren. However, it should be noted that only diagnoses supported by medical documentation were accepted and, at most, the study may have underestimated the true prevalence. Moreover, it is reassuring that, in a preliminary exercise, intra- and inter-observer reliability was guite satisfactory for all the items considered in the questionnaire. Even if examination by an experienced dermatologist was considered in our study design, this was restricted to naevus count and we did not collect information on the point-prevalence of AD based on dermatologist's assessment.

The schoolchildren enrolled in the study are not a random sample of Italian schoolchildren aged 12–17 years. However, they were identified in schools located in northern, central and southern Italy, and the prevalence of some medical conditions considered in the analysis, e.g. asthma (20), is largely similar to the one reported in other epidemiological studies from Italy.

The reported point prevalence for Italian children aged 6–7 and 13–14 years in the ISAAC study was approximately 7% (14). In a study conducted in seven Italian cities on 1369 children aged 9 years, the self-reported lifetime prevalence of AD was 15%, and the estimated point prevalence was 5.8% (1).

For most of the cases in our study, a first diagnosis of AD was reported during the first year of life. Although recall bias cannot be excluded, these data indicate that AD is a condition with a very early age at diagnosis.

We observed a strong association between the frequency of AD and history of vitiligo and psoriasis. Recall bias cannot be completely ruled out, and the associations may also be a chance effect due to multiple statistical testing. However, it is interesting to note that the skin conditions considered recognize an immunological even if heterogeneous background (21).

Psoriasis is a chronic inflammatory skin disease that affects 2–4% of the general population (22, 23). In our study, 68 children had psoriasis (2.1%). The observation of an association between AD and psoriasis is at variance with previous observations that pointed to a negative association suggesting divergent pathways for the two conditions (24). Although AD is distinct from psoriasis, both diseases may share similar characteristics, including dry, scaly skin, and misdiagnosis is possible especially in young children. On the other hand, psoriasis and AD are inflammatory diseases associated with various immunological abnormalities. Genomewide linkage scans have revealed overlap between psoriasis and AD susceptibility loci on chromosomes 1q21, 3q21, 17q25 and 20p12 (25). Even if the genes from these loci have not yet all been identified, these locations suggest that some susceptibility factors lie within genes or gene families with common effects upon epithelial immunity.

To the best of our knowledge, only case reports exist concerning the association of AD and vitiligo (26).

It is well known that children with AD are at higher risk of allergenic asthma (27). We confirmed this association, but no clear time–risk relationship emerged between the two conditions (data are, however, limited).

In conclusion, this large study gives estimates of the lifetime prevalence of a physician-confirmed diagnosis of AD in Italian schoolchildren. Furthermore, it emphasizes the association between the condition and other immunologically related skin diseases and asthma.

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