

Prevalence of self-perceived allergic diseases and risk factors in Italian adolescents

Brescianini S, Brunetto B, Iacovacci P, D'Ippolito C, Alberti G, Schirru MA, Stazi MA, Pini C, Di Felice G, Barletta B. Prevalence of self-perceived allergic diseases and risk factors in Italian adolescents. *Pediatr Allergy Immunol* 2008.

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The aim of the study was to assess the symptoms prevalence of allergic diseases in a population of 11–15 yr old schoolchildren, to evaluate the associations between asthma and other symptoms and identify risk factors for asthma, rhinitis and eczema syndromes. A sample of 481 students was studied using an International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Prevalence of different kind of self-reported symptoms was calculated. Using a logistic regression approach, we tried to identify risk factors for three syndromes – rhinitis, eczema and asthma. The highest and the lowest prevalence rates of self-reported symptoms were recorded for rhinitis (43.6%) and for eczema (8.1%), respectively. The prevalence of asthma was 15.7%. Univariate analysis showed a mutual association between wheeze and rhinitis symptoms. Multivariate logistic regression model for eczema syndrome revealed female gender as a significant risk factor. The polytomic logistic multivariate regression revealed female gender and family history of allergy as significant risk factors for rhinitis syndrome only, and maternal smoking and familial allergy for rhinitis and asthma together. In particular, familial allergy yields a 400% higher chance of developing asthma and rhinitis together. The synergistic effect of familial allergy on rhinitis and asthma syndromes suggests the implementation of preventive measures in children with family history of these diseases.

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Key words: adolescents; allergic diseases; comorbidity; prevalence; risk factors

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Accepted 1 July 2008

The reasons for the global increase in prevalence of allergic diseases are still unknown, and epidemiological surveys have the potential to explore the overall degree and trend over the time of allergic diseases in a given population. However, they need steady updates and methodological uniformity (1–3).

Comparison studies report that the prevalence of allergic diseases is increasing in many countries worldwide, particularly among children and adolescents and confirm that allergy begins early in life, usually in the form of atopic dermatitis (most often linked to food allergy). The first symptoms of seasonal allergic rhinitis (hay fever) appear at about the age of 3 and its incidence increases by 1–3% per year during the first 10 yr of life (4).

Allergic diseases are the major illness and the most common cause of school absence among children (5) and they have now become the most common chronic childhood medical conditions in developed countries. Hence, allergic diseases have a comprehensive impact on each affected child, its family and society as a whole.

The majority of epidemiological evidence relating to allergic diseases is derived from questionnaire surveys and health care utilization data. Specific questionnaires have been developed and validated providing a comprehensive tool (approach to patients) with the aim of identifying and quantifying what patients experience about allergic symptoms.

The International Study of Asthma and Allergies in Childhood (ISAAC) was developed to

provide a standardized methodology and a standardized questionnaire to compare the prevalence of atopic diseases in children, both within and between countries, and across time (6). Most epidemiological surveys performed on adolescents are derived from parent-completed questionnaires (7). However, more recent studies, including the large multicentre ISAAC protocol, obtained the information directly from adolescents, inviting them to complete the questionnaire either on their own or with the help of their parents if necessary (8, 9). Comparison studies have shown that, although parents remain a crucial source of information on clinical and familial history, for epidemiological and medical purposes, direct information from adolescents is essential for a correct evaluation of respiratory and allergic disorders.

This study represents an update of the prevalence rates and the risk factors of allergic diseases in schoolchildren aged 11–15 yr by means of an ISAAC questionnaire. Questionnaires were completed independently by the children themselves during school hours focussing our attention on how adolescents themselves perceive allergic diseases rather than on diagnoses performed by a physician. This makes the results independent by differences in diagnostic processes and accessibility of medical assistance. In particular, we will explore how rhinitis and asthma syndromes may or may not share the same risk factors.

Materials and methods

Study area

A cross-sectional study was carried out between December 2003 and January 2004, outside the main pollen season, in two small semi-urban towns in the south-east of Rome (central Italy), Ciampino and Marino both with about 35,000 residents. Ciampino is the second airport of Rome and recently, airport and heavy car traffic have substantially contributed to the air pollution in this area.

Study population and design (cross-sectional study)

The study population included 481 students aged 11–15 yr old attending three different secondary schools, located in Ciampino ($n = 99$) and Marino ($n = 382$). All students were asked to and did fill out a written questionnaire during school hours, under the supervision of a teacher and a researcher who briefly explained the procedures to answer questionnaires before distributing them.

Parental informed consent was obtained individually from schoolchildren through the Department of School's Administration. The study protocol was approved by the local Ethics Committee.

Questionnaire

An extended version of the questionnaire designed by the ISAAC (Phase I) has been translated according to defined guidelines (8) and used in the study. Additional questions include demographic characteristics (gender, age, height, weight and family structure) and lifestyle (exposure to environmental factors such as smoke and pets, sport practice, food habits, etc.).

Definitions

The definitions presented in Tables 2 and 3 concerning wheeze, rhinitis and eczema symptoms were labelled according to the responses to the ISAAC core questions on wheeze, rhinitis and eczema modules. Questions included the presence of symptoms in the last 12 months (current symptoms) and during their lifetime ('ever' symptoms). Asthma, hay fever and eczema symptoms were assessed by affirmative responses to the questions 'have you ever had asthma?', 'have you ever had hay fever?' and 'have you ever had eczema?'.

The definitions of asthma, rhinitis and eczema reported in Tables 4 and 5 were labelled as syndromes. In particular, asthma syndrome was based on at least one affirmative answer to any of the core questions 1 or 6 of the ISAAC questionnaire on wheezing module: 'have you ever had wheezing or whistling in the chest at any time in the past?', 'have you ever had asthma?'. Rhinitis was defined as a syndrome when adolescents reported sneezing or a runny or a blocked nose when they did not have a cold or the flu or ever had hay fever. Children who reported an itchy rash which was coming and going for at least 6 months or ever had eczema were labelled as having eczema syndrome.

Statistical analysis

Prevalence rates were computed using, as denominator, the whole sample for which there were valid answers for one of the three main questions on 'ever' wheezing ($n = 477$), 'ever' rhinitis ($n = 479$) and 'ever' itchy rash ($n = 479$), according to the ISAAC questionnaire methodology and to make estimates that are comparable with other studies. For prevalence rate, 95%

confidence intervals (95% CI) were computed using the exact binomial method implemented in the STATA software (v.9.2, StataCorp LP, College Station, Texas, USA). We computed prevalence rates separately for females and males, and we compared them using the Pearson's chi-squared test for association.

To explore possible associations between wheezing and any other symptom, univariate odds ratios (ORs) were computed for rhinitis and any other symptom and 95% CI and p-values are given.

Odds ratios were also computed to explore the univariate and multivariate association between each risk factor and the outcome of interest (asthma and/or rhinitis and eczema). We have adopted two different strategies for the different syndromes. For respiratory syndromes, we used a polytomous model using as reference group children that reported neither asthma nor rhinitis. Thus, the dependent variable had four levels: '0' if no asthma and no rhinitis, '1' if only rhinitis, '2' if only asthma and '3' if both asthma and rhinitis were reported. For skin syndromes, we have coded the outcome variable as 0/1: 1 if itchy rash or eczema were reported and 0 if not. Risk factors included in the analyses were: gender (female *vs.* male), age (in years), parental smoking (or mother and father smoking separately), obesity and overweight [we used the cut-off for children as defined by Cole et al. (10)], physical activity (at least 1 h of physical activity per week), familial allergy (at least one among mother, father or siblings reporting personal history of allergy), diet (fruit and vegetable consumption, yes/no) and municipality of residence (Marino *vs.* Ciampino). For parental smoking, we used two kinds of coding: parental smoking itself, defined as 'at least one of the parents smoking in child presence' and maternal or paternal smoking (according to which parent declared to smoke in child presence). The two kinds of exposure to passive smoking can have different effects on the child symptom. In all analyses, statistical significance was reached if p-values were <0.05.

Results

The characteristics of the study population are described in Table 1. Two hundred and forty-four (50.7%) subjects were females. The age range of children studied was 11–15 yr [mean (s.d.), 12.8 (0.7)]. More than half of the children (60.5%) had a family unit including two children, 17.2% three children, 4.5% four or more children, whereas 17.2% were only child.

Exposure to passive smoking (either paternal or maternal) was present in 48.2% of children.

Table 1. Characteristics of study population

Subjects (n)	481
Age: mean (±s.d.)	12.8 ± 0.7
n (%)	
Male	237 (49.3)
Female	244 (50.7)
Family unit: 2 children	291 (60.5)
3 children	83 (17.2)
>4 children	22 (4.6)
Town	
Ciampino	383 (79.6)
Marino	98 (20.4)
Passive smoking exposure	232 (48.2)
Familial allergy:	
Mother allergy	101 (21.0)
Father allergy	53 (11.0)
Siblings	116 (24.1)
Pet ownership	226 (47.0)
Physical activity	258 (53.6)
Overweight	84 (17.4)
Obesity	20 (4.16)

Pet ownership was recorded in 64.8% of questionnaires. Among pets, that could represent a risk factor for allergic diseases, 24.2% of children owned dogs, 18.6% cats, 9.3% birds, 7.7% hamsters and about 5% rabbits. Familial history of atopic diseases was reported by 29.8% of the students, of whom 20.9% concerning mothers and 10.9% from fathers.

Prevalence rates of allergic diseases calculated from written questionnaire are reported in Table 2. Among respiratory symptoms, asthma and wheeze 'ever' were reported by 75 (15.7%) and 83 children (17.4%), respectively. The reported nocturnal cough rate was 21.6% and exercise-induced wheeze was 10.9%. The highest prevalence rates were reported for nose symptoms: 209 of 481 children (43.6%) reported rhinitis apart from regular colds during lifetime and 166 (34.7%) in the last 12 months. The prevalence of rhinoconjunctivitis was 18.6%. 24.4% of enrolled children gave an affirmative answer to the question 'have you ever had hay fever?'. The overall prevalence of skin symptoms was 12.5% for itchy rash and 8.1% for eczema.

Females reported more rhinitis symptoms, itchy rash and eczema compared with males (51.2% *vs.* 35.4% $p < 0.001$; 16.8% *vs.* 8.0% $p < 0.002$; 11.1% *vs.* 5.1% $p = 0.017$, respectively). Wheeze 'ever' and rhinitis were reported significantly more often by children living in Marino than in Ciampino (54.08% *vs.* 41.05% $p < 0.02$ and 25.77% *vs.* 15.30% $p < 0.01$, respectively; data not shown).

Table 3 shows the strength of association between rhinitis or asthma and the following comorbidities: asthma, 'ever' wheeze, wheeze in the last 12 months, hay fever, itchy rash coming

Table 2. Prevalence rates with 95% confidence intervals of respiratory, nose and skin symptoms in schoolchildren aged 11–15 yr calculated from the written questionnaire

	Total			Male			Female			p-value
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
Respiratory symptoms										
Asthma	75	15.7	12.5–19.1	44	18.6	13.8–24.1	31	12.7	8.8–17.5	n.s.
Wheeze 'ever'	83	17.4	14.0–20.0	45	19.0	14.2–24.6	38	15.6	11.3–20.7	n.s.
Wheeze in last 12 months	40	8.4	6.0–11.1	19	8.0	4.9–12.2	21	8.6	5.4–12.9	n.s.
Exercise-induced wheeze	52	10.9	8.1–13.9	19	8.0	4.9–12.2	33	13.5	9.5–18.5	0.05
Nocturnal cough	103	21.6	17.8–25.3	48	20.3	15.3–25.9	55	22.5	17.5–28.3	n.s.
Nose symptoms										
Rhinitis 'ever'	209	43.6	38.9–48.0	84	35.4	29.4–41.9	125	51.2	44.8–57.7	<0.001
Rhinitis in the last 12 months	166	34.7	30.2–38.9	70	29.5	23.8–35.8	96	39.3	33.2–45.8	n.s.
Rhinoconjunctivitis in the last 12 months	89	18.6	15.1–22.2	32	13.5	9.4–18.5	57	23.4	18.2–29.2	n.s.
Hay fever	117	24.4	20.5–28.4	51	21.5	16.5–27.3	66	27.0	21.6–33.1	n.s.
Skin symptoms										
Itchy rash 'ever'	60	12.5	9.6–15.7	19	8.0	4.9–12.2	41	16.8	12.3–22.1	0.004
Itchy rash in the last 12 months	51	10.6	9.0–13.7	17	7.2	4.2–11.2	34	13.9	9.8–18.9	n.s.
Eczema	39	8.1	5.8–10.9	12	5.1	2.6–8.7	27	11.1	7.4–15.7	0.017
Recover in past 12 months	39	8.1	5.8–10.9	11	4.6	2.3–8.2	28	11.5	7.8–16.2	n.s.

n.s., not significant.

Table 3. Comorbidities in children reporting wheeze or rhinitis during their lifetime (univariate analysis)

	OR	95% CI	p-value
Lifetime wheeze			
Rhinitis 'ever'	4.6	2.6–8.2	<0.001
Rhinitis in last 12 months	1.2	0.8–1.9	0.326
Itchy rash 'ever'	1.9	1.0–3.6	0.039
Itchy rash in last 12 months	2.9	0.3–26.8	0.321
Hay fever	3.8	2.3–6.4	<0.001
Eczema	2.3	1.1–4.9	0.018
Lifetime rhinitis			
Asthma	2.9	1.7–4.9	<0.001
Wheeze 'ever'	5.0	2.9–8.8	<0.001
Wheeze in last 12 months	2.4	0.8–7.1	0.089
Itchy rash 'ever'	2.1	1.2–3.6	0.009
Itchy rash in last 12 months	1.5	0.3–6.8	0.597
Hay fever	5.3	3.2–8.6	<0.001
Eczema	2.8	1.4–5.7	0.003

Table 4. Combination of the three self-reported syndromes

	n	%
None	209	43.4
Asthma only	20	4.1
Rhinitis only	131	27.2
Eczema only	14	2.9
Asthma and rhinitis	66	13.7
Asthma and eczema	4	0.8
Rhinitis and eczema	25	5.2
Asthma and rhinitis and eczema	13	2.7

and going for at least 6 months and itchy rash in the last 12 months. Subjects reporting wheeze in their lifetime are more likely to report 'ever' rhinitis

(OR 4.6, 95% CI 2.6–8.2, $p < 0.001$), 'ever' itchy rash (OR 1.9, 95% CI 1.0–3.6, $p = 0.039$), hay fever (OR 3.8, 95% CI 2.3–6.4, $p < 0.001$) and eczema (OR 2.3, 95% CI 1.1–4.9, $p = 0.018$). Children reporting rhinitis in their lifetime are more likely to report asthma (OR 2.9, 95% CI 1.7–4.9, $p < 0.001$), 'ever' wheeze (OR 5.0, 95% CI 2.9–8.8, $p < 0.001$), 'ever' itchy rash (OR 2.1, 95% CI 1.2–3.6, $p = 0.009$), hay fever (OR 5.3, 95% CI 3.2–8.6, $p < 0.001$) and eczema (OR 2.8, 95% CI 1.4–5.7, $p = 0.003$).

Table 4 shows the frequency of combinations of asthma, rhinitis and eczema syndromes. The highest frequency of combination was recorded for asthma and rhinitis (13.7%).

Polytomic multivariate logistic regression for respiratory syndromes gave the results reported in Table 5. When looking at rhinitis only, we found an association with female gender (OR 1.74, $p = 0.034$, 95% CI 1.04–2.89) and with familial history of allergy (OR 1.63, $p = 0.050$, 95% CI 0.99–2.69). When looking at asthma only, none of the risk factors met the $p < 0.05$ criteria for significance probably because of power problems. When looking at rhinitis and asthma together, two factors resulted to be associated with these syndromes: maternal smoking (OR 2.37, $p = 0.014$, 95% CI 1.19–4.70) and familial allergy (OR 4.05, $p < 0.001$, 95% CI 2.11–7.75). Physical activity was negatively almost significantly associated with rhinitis only and with asthma only (OR 0.65, $p = 0.093$, 95% CI 0.39–1.07 and OR 0.41, $p = 0.072$, 95% CI 0.15–1.08, respectively).

Table 5. Multivariate analysis of risk factors for respiratory and eczema syndromes

	Respiratory syndromes											
	Rhinitis only			Asthma only			Rhinitis and asthma			Eczema syndrome		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Female vs. male	1.74	1.04–2.89	0.034	0.64	0.22–1.82	0.402	0.76	0.40–1.44	0.402	1.96	1.06–3.61	0.032
Age	1.18	0.69–2.02	0.539	1.04	0.38–2.89	0.931	1.06	0.56–2.01	0.856	0.84	0.46–1.56	0.591
Father smoking	1.36	0.77–2.39	0.279	0.90	0.29–2.76	0.854	1.08	0.53–2.20	0.824	1.55	0.81–2.97	0.186
Mother smoking	1.01	0.57–1.79	0.968	1.86	0.65–5.31	0.247	2.37	1.19–4.70	0.014	0.96	0.50–1.86	0.913
Familial allergy	1.63	0.99–2.69	0.050	1.34	0.50–3.58	0.561	4.05	2.11–7.75	<0.001	1.81	1.01–3.24	0.046
Overweight	0.77	0.40–1.49	0.439	1.11	0.33–3.73	0.866	1.12	0.52–2.40	0.770	1.71	0.85–3.44	0.130
Obesity	1.20	0.36–3.99	0.766	3.16	0.67–14.94	0.147	0.65	0.12–3.64	0.628	2.36	0.66–8.43	0.187
Pet keeping	1.46	0.89–2.39	0.129	1.44	0.55–3.79	0.450	1.07	0.58–1.99	0.826	1.57	0.88–2.79	0.127
Physical activity	0.65	0.39–1.07	0.093	0.41	0.15–1.08	0.072	0.68	0.36–1.29	0.245	0.77	0.43–1.38	0.375
Fruit and vegetable consumption	0.98	0.58–1.68	0.957	1.67	0.51–5.40	0.391	1.46	0.72–2.95	0.289	1.27	0.65–2.45	0.485
Marino vs. Ciampino	2.00	0.79–5.08	0.141	2.09	0.36–12.03	0.409	2.52	0.83–7.64	0.102	1.59	0.58–4.41	0.364

Bold values indicate statistical significance.

Multivariate logistic regression model for eczema syndrome revealed female gender (OR 1.96, $p = 0.032$, 95% CI 1.06–3.61) (Table 5). Also having ‘a family history of allergy’ was found to be statistically significant in predicting eczema (OR 1.81, $p = 0.046$, 95% CI 1.01–3.24).

Discussion

In this study, we focussed our attention on how adolescents themselves perceive allergic symptoms rather than on diagnoses performed by a physician. This makes the results independent by differences in diagnostic processes and accessibility of medical assistance.

As regards to respiratory symptoms, the findings suggest that around one-sixth (17.4%) of all participants reported ‘ever’ wheezing, 40 of these 83 reported wheezing in the last 12 months, giving a rate of current wheezing of 8.4%. These results are very similar to previous studies conducted in the same area (11).

For rhinitis, our study finds a prevalence of 43.6% and 34.7% for ‘ever’ and current, respectively. These high prevalence rates should be viewed in the context of other recent investigations on the changes in the prevalence of rhinitis symptoms. In fact, time trend prevalence studies have reported a clear increase in rhinitis prevalence among adults and adolescents in Italy as well as in other countries (12–14). The persistence of a high prevalence of self-reported allergic rhinitis deserves attention because rhinitis is actually considered a significant independent risk factor for asthma and it may appear as the first manifestation of a common allergic airway disease, leading eventually to the onset of asthma (15).

This survey reveals also an interesting gender difference with regard to nose and skin symptoms among adolescents. Indeed, girls reported higher rates of rhinitis, itchy rash and eczema compared with boys.

We find a mutual association between respiratory and nose symptoms. In fact, adolescents reporting rhinitis ‘ever’ and hay fever were more likely to report ‘ever’ wheeze as well as adolescents reporting asthma and wheeze ‘ever’ often reported symptoms of rhinitis during lifetime, indicating that wheeze and rhinitis symptoms frequently coexisted. Also adolescents reporting hay fever symptom showed a higher probability to experience wheeze or rhinitis at least once in their life. These findings are confirmed by frequency of combinations of wheeze, rhinitis and eczema syndromes, defined as described in detail in Material and methods section. Indeed, 13.7% of adolescents reported to experience asthma and rhinitis syndromes at same time. These findings are in agreement with previous studies reporting an overall association and combination between asthma and rhinitis (16). Cross-sectional studies of adult patients with both rhinitis and asthma suggest that onset of rhinitis often precedes that of asthma, even though there are some reports of cases of asthma preceding rhinitis. On the other hand, in children, rhinitis is usually diagnosed later than asthma (17). Results from longitudinal studies derived from adult populations consistently show a higher incidence of asthma in subjects with rhinitis than in those without (15). *Vice versa*, a high incidence of rhinitis symptoms is also recorded among asthmatic subjects (18–20).

To increase our understanding of the relationship between rhinitis and asthma, we used a

polytomic logistic regression model allowing us to estimate simultaneously the effect of risk factors both on the condition and on their association, without bias in the estimation of the common risk factors. Female gender is positively associated with rhinitis syndrome but not with asthma with or without rhinitis syndrome. Again, being female constitutes a risk category for eczema syndrome, in a standard logistic regression model. Our results are consistent with a large amount of data reported in literature: girls are at higher risk for nasal syndrome and eczema than boys and boys are at higher risk for asthma than girls (21, 22), even though, it has been reported that the male predominance in asthmatic children gradually diminishes, disappearing after puberty (23). In this study, we find an inverse association, although not reaching statistical significance, between female gender and asthma with or without rhinitis. However, several studies have outlined that gender-related perception differences might also have a role. In fact, physical symptoms are reported more often by females than males.

Among the environmental risk factors analysed, we paid particular attention to smoking exposure and its definition. We asked the children to report if one or both parents were smoking at home or in the car when they are riding together. If the parent smokes but not in these two circumstances, we coded the subject as not exposed to passive smoking. Surprisingly, in our population, half the students reported to be exposed to passive smoking, whereas recent studies indicated a decreasing trend in the levels of exposure to passive smoking, although it is still high (14, 24). We decided to analyse paternal and maternal smoking separately, given that they can have different influences on the child's risk of allergy (25). In the polytomic model on respiratory syndromes, maternal smoking was significantly associated with asthma and rhinitis together, while it did not reach statistical significance for asthma only and was not associated for rhinitis only. Paternal smoking did not show any association with the outcomes of interest.

One of the most interesting results of this study is the synergistic effect of family history of allergy on the two syndromes (asthma and rhinitis). For rhinitis only, we found a 60% higher chance for children with a positive family history of allergy, while for asthma only the increase was of 30% and not statistically significant. When looking at the two syndromes together, we found that the same chance increased of 400%, and, together with maternal smoking, represents the most

important risk factor among the ones taken into account in this cohort.

For asthma only, we did not find any significant risk factors most likely because of power problems (only 20 subjects reported asthma only). Only two factors were slightly associated with the outcome: obesity and physical activity. These findings are in line with recent prospective studies reporting that obesity increases prevalence, incidence, and possibly severity of asthma in adults, adolescents and children throughout the world, while weight loss in the obese improves asthma outcomes (26).

The weak but almost significant association between asthma and physical activity, might imply that asthmatic adolescents avoid physical activity. In the past, asthmatic subjects were advised to avoid activities to avert new attacks (27, 28). On the other hand, several recent literature reviews have supported the benefits and safety of exercise in asthmatic subjects (29). Overall, the strong association between rhinitis and asthma is probably explained by family history of allergies and other unmeasured risk factors.

A possible limitation of this study is that it was based only on a screening questionnaire and both overestimation and underestimation of real prevalences can occur according to the screening methodology and the population studied (30, 31). Although study population do not reach the sample size desirable to be included in the prevalence comparisons, the analysis has shown statistical power.

Moreover, the classification of allergic diseases are made only using subjective responses and reporting bias is a methodological problem not overlooked; however, ISAAC questionnaire has shown an acceptable level of sensitivity and specificity. In conclusion, the results of this cross-sectional survey provide an update supporting a high prevalence of allergic diseases in Italian schoolchildren and suggest that association between asthma and rhinitis is epidemiologically significant, as the risk of asthma in subjects with rhinitis is significantly higher than the risk in subjects without rhinitis and *vice versa*.

To offer an early diagnosis and consequent appropriate treatment to the patient, paediatricians should take into account that rhinitis and asthma syndromes together appear to be the most reliable indicators for identification of allergic adolescents. The synergistic effect of family history on the two syndromes suggests the implementation of preventive measures in children with family history of these diseases that represent about one of seven adolescents.

Acknowledgments

This work was supported by grant n.1AN/F3 from the Italian Ministry of Health.

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