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Prevalence of allergic disorders in Italy: the Cotignola population study

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SUMMARY

Background: The worldwide prevalence of allergic diseases such as rhinitis, asthma, and atopic dermatitis is continuously increasing, while other allergic disorders such as urticaria and angioedema are less investigated. We performed a population study evaluating the prevalence of any kind of allergic disorders. **Methods:** The entire population of 7,201 inhabitants of Cotignola (Ravenna, Italy) was surveyed by a questionnaire assessing symptoms related to rhinitis, asthma, anaphylaxis, skin symptoms and insect sting allergy as well as the features of clinical presentations, diagnosis, and treatment received. **Results:** Valid questionnaires were obtained by 6,676 inhabitants (92.7%). The sample was formed by 3,266 males and 3,495 females, the mean age was 45.6 years; 1,035 subjects (15.5%) were aged less than 18 years; 404 subjects (6%) had at least one episode of wheezing/breathlessness in their lifetime, and 243 of them (60.1%) had a diagnosis of asthma; 1,002 subjects (14.8%) had nose symptoms in their lifetime, and 375 of them (37.4%) had a diagnosis of allergic rhinitis or rhinoconjunctivitis. For other allergic manifestations, data were obtained from 5,730 subjects; of them, 178 (3.1%) had skin symptoms, 59 (1.1%) had oral symptoms, and 37 (0.6%) had anaphylaxis; 207 (3.6%) had reactions to insect stings. There were no significant differences in prevalence between Italians and immigrants. Only 51.7% of subjects with asthma, 46.5% of those with rhinitis, 22.7% of those with other allergies, but 97.1% of those with insect allergy, received treatment. **Conclusions:** These findings confirm recent data on epidemiology of allergic diseases in Europe, particularly in Italy, and add some details on how such diseases are managed.

Introduction

Allergic diseases, including both the IgE and non-IgE-mediated disorders have a high prevalence throughout the world. The International Study of Asthma and Allergies in Childhood (ISAAC), in its different phases, provided significant advances in the knowledge of epidemiology of the atopic disease, i.e. atopic eczema/dermatitis, asthma, and rhinitis generally affecting 10-20% of children (1),

and demonstrated that the prevalence of atopy is still rising. In fact, in phase 3, which was completed a mean of 7 years after phase 1, more countries showed an increase in all three disorders more often than showing a decrease; with asthma showing a decrease in the 13-14-year age group (2). The European Community Respiratory Health Survey (ECRHS), addressed the adult population (20-44 year olds) concerning asthma and found a prevalence of wheeze at about 20% and of diagnosed asthma at about

5% (3). Studies investigating the epidemiology of other clinical manifestations of allergy are also available. Anaphylaxis is estimated to affect about 1–2% of the general population (4). A recent survey on 4,093 inhabitants of Berlin reported a lifetime prevalence of urticaria of 8.8% (5), while there are no reliable data on the prevalence of angioedema. Allergy to insect stings, and particularly to Hymenoptera venom, though with some variations in different climatic areas, generally showed a prevalence of around 3% of systemic reactions of any kind and of less than 1% of anaphylaxis (6, 7).

We designed a population study to evaluate the prevalence of allergic disorders in Italy, by administering a questionnaire covering a number of allergic manifestations, including rhinitis, asthma, skin symptoms, and anaphylactic symptoms.

Methods

The entire population of Cotignola (Ravenna), formed by 7,201 inhabitants, was screened for allergic disorders by a questionnaire dealing with symptoms concerning the different expressions of hypersensitivity and their history. Table 1 reports the symptoms related to rhinitis/conjunctivitis, asthma, other manifestations of allergy, and insect sting allergy. The questions concerned:

- 1) For rhinitis, conjunctivitis and asthma, the occurrence of symptoms (at least once in their lifetime, in the previous 12 months, or current), the causative factors (when known), the use of drugs, a previous diagnosis of allergy, and for asthma, if it occurred following physical exercise, the number of attacks of breathlessness and wheezing, and the number of night awakenings in the previous 12 months.
- 2) For other manifestations of allergy, the symptoms considered are reported in table 1. The other questions concerned the occurrence of symptoms (at least once in their lifetime, in the previous 12 months, or current) and the use of drugs.

- 3) For insect sting allergy, the questions concerned the occurrence of insect stings in their lifetime, the number of stings received prior to a reaction, the occurrence of a single or more than one reaction, the number of stings received for a reaction, the time elapsed from the sting to the symptoms, the kind of symptoms, the environment and activity associated with the sting, the kind of first aid received, the performance of diagnostic tests, and if venom immunotherapy was carried out. The kinds of symptoms were classified according to Mueller's method in four grades of increasing severity (8).

Statistical analysis

The only continuous parameter was age that was reported as mean, median, and standard deviation, while all the other parameters were categorised and analysed in contingency tables, setting a p value of <0.05 as significant.

Results

Valid questionnaires were returned by 6,676 inhabitants (92.7% of the total population). The population sample was formed by 3,266 males and 3,495 females. The mean age was 45.6 years in the entire sample; 44.3 ± 23.1 years for males and 46.8 ± 24.2 years for females, this difference being significant ($p < 0.01$). The median age was 44 years for males and 47 years for females; 1035 subjects (15.3%) were aged less than 18 years, 368 (5.4%) were aged less than 5 years. According to occupation, 1,989 subjects (29.4%) were retired, 849 (12.5%) were students, 842 (12.4%) were workers, 661 (9.8%) were employees, 336 (5%) were housewives, 199 (2.9%) were farmers, 123 (1.8%) were children in pre-school age, 97 (1.4%) were business men, 90 (1.3%) were teachers, 81 (1.2%) were craftsmen, and 92 (1.3%) reported no occupation. The data concerning the different allergic disorders were as follows.

Respiratory allergy: 404 subjects (6%) had had at least one episode of wheezing/breathlessness in their lifetime, and in

Table 1 - Symptoms indicated in the questionnaire related to clinical manifestations of allergy

Rhinitis	Sneezing, runny nose, nasal stuffiness, eye itching and tearing
Asthma	Breathlessness, wheezing
Other manifestations of allergy	Itching in the mouth, urticaria, angioedema, eczema, laryngeal oedema, cardiovascular collapse
Insect sting allergy	Large local reaction, urticaria, angioedema, gastrointestinal disturbance, dyspnoea, chest tightness, laryngeal oedema, cardiovascular collapse, loss of consciousness

267 of them (66%) wheezing occurred in the last 12 months; 243 subjects (60.1%) had a diagnosis of asthma. Table 2 shows the characteristics of subjects regarding acute attacks, nocturnal awakenings, causative factors, and the use of drugs. One thousand and two subjects (14.8%) had nose symptoms (sneezing, runny nose, and nasal obstruction) in their lifetime, and in 852 of them (85%) the symptoms occurred in the last 12 months; 375 subjects (37.4%) had a diagnosis of allergic rhinitis or rhinoconjunctivitis. Table 3 reports the characteristics of subjects regarding concomitant eye symptoms (itching and tearing), causative factors, and the use of drugs. No significant difference was detected between the females and males about asthma and rhinitis characteristics.

Other manifestations of allergy: Data were obtained from 5,730 subjects. Of them, 240 (4.2%) had had such symp-

toms. There were significantly more females than males in this group (167 vs. 73, $p < 0.0001$). In 130 subjects (54.2%), the symptoms occurred at least once in their lifetime, in 110 (45.8%) occurred in the last 12 months, and in 98 of them (40.8%) were current. Table 4 shows the prevalence of the different kind of symptoms. The most common presentation was urticaria, followed by oral itching, angioedema, eczema, laryngeal oedema, and cardiovascular collapse. There were no significant differences between females and males for any of the symptoms. Only 63 subjects (26.2%) received drug treatment.

Insect sting allergy: Data were obtained from 5,730 subjects. Of them, 2,289 (39.9%) were stung at least one time, and 207 (3.6%) had reactions of the allergic type. These reactions affected significantly more males than fe-

Table 2 - Clinical features in the 404 subjects reporting asthma symptoms

Feature	Females (%)	Males (%)	Total (%)
No acute attacks	100/210 (47.6%)	94/194 (48.5%)	194/404 (48%)
Acute attacks	110/210 (52.3%)	100/194 (51.5%)	210/404 (52%)
Less than one attack/month	76/210 (36.2%)	51/194 (26.3%)	127/404 (31.4%)
More than one attack/month	14/210 (6.7%)	18/194 (9.3%)	32/404 (7.9%)
More than one attack/week	24/210 (11.4%)	13/194 (6.7%)	37/404 (9.2%)
Less than one nocturnal awakening /month	76/210 (36.2%)	70/194 (36.1%)	146/404 (36.1%)
More than one nocturnal awakening /month	24/210 (11.4%)	24/194 (12.4%)	48/404 (11.9%)
Seasonal allergens as a causative factor	79/210 (37.6%)	78/194 (40.2%)	157/404 (38.8%)
Perennial allergens as a causative factor	114/210 (54.2%)	92/194 (47.4%)	206/404 (50.9%)
Irritants as a causative factor	24/210 (11.4%)	25/194 (12.9%)	49/404 (12.1%)
Infections as a causative factor	50/210 (23.8%)	33/194 (17%)	83/404 (20.5%)
Physical exercise as a causative factor	38/210 (18.1%)	37/194 (19.1%)	75/404 (18.6%)
Drug use in the previous 12 months	108/210 (51.4%)	101/194 (52.1%)	209/404 (51.7%)

Table 3 - Clinical features in the 1,002 subjects reporting nose/eye symptoms

Feature	Females (%)	Males (%)	Total (%)
Eye symptoms	318/525 (60.6%)	280/474 (59.1%)	598/1,002 (59.7)
Seasonal allergens as a causative factor	285/525 (54.3)	270/474 (57%)	555/1,002 (55.4%)
Perennial allergens as a causative factor	252/525 (48%)	213/474 (44.9%)	465/1,002 (46.4%)
Irritants as a causative factor	29/525 (5.5%)	21/474 (4.4%)	50/1,002 (4.9%)
Drug use in the last 12 months	226/525 (45%)	230/474 (48.5%)	466/1,002 (46.5%)

Table 4 - Kind of symptoms in the 240 subjects reporting other manifestations of allergy

Symptom	Females (%)	Males (%)	Total (%)
Oral itching	37/167 (22.2%)	22/73 (30.1%)	59/240 (24.6%)
Urticaria	90/167 (53.8%)	24/73 (32.9%)	114/240 (47.5%)
Angioedema	28/167 (16.8%)	11/73 (15.1%)	39/240 (16.2%)
Eczema	15/167 (9%)	10/73 (13.7%)	25/240 (10.4%)
Laryngeal oedema	19/167 (11.4%)	10/73 (13.7%)	29/240 (12.1%)
Cardiovascular collapse	7/167 (4.2%)	1/73 (1.4%)	8/240 (3.3%)

males (116 vs. 91, $p = 0.029$). Table 5 reports the kind of reactions presented. Most reactions (79.8%) occurred within 30 minutes from the sting, and in most cases (81.6%), the reaction was caused by a single sting; 149 subjects (72%) had only one reaction, 14 (6.8%) had two reactions, 25 (12.1%) had three reactions, and 17 (8.2%) had more than three reactions. Concerning the time elapsed from the last tolerated sting to the reaction, the highest frequency (12.1%) was detected for a time interval of less than three months. Table 6 shows the details on subjects with reactions regarding the time elapsed from the last tolerated sting, the place where the sting occurred, the kind of aid received, the number of subjects undergoing diagnostic tests, and the number of subjects undergoing venom immunotherapy. Significant differences between females and males were detected concerning the more frequent occurrence of reactions at home for females ($p = 0.003$), the more frequent referral to a family doctor for females ($p = 0.017$), and the more frequent applying of the venom immunotherapy for males ($p = 0.006$).

Data from immigrants: among the screened population, 549 (8.2%), 270 males, 279 females, were immigrants. Of them, 451 (82.1%) returned valid questionnaires, showing the fol-

lowing data: 19 subjects (4.2%) had wheezing, 10 (2.2%) had a diagnosis of asthma, 59 (13.1%) had nose symptoms, and 28 (6.2%) had a diagnosis of rhinitis. Concerning the other clinical manifestations, 436 valid questionnaires (79.4%) were obtained: 8 subjects (2.3%) had skin symptoms, 3 (0.7%) had oral symptoms, 2 (0.5%) had anaphylaxis, and 12 (2.7%) had reactions to insect stings.

Discussion

The prevalence of allergic diseases has long been investigated, but most studies dealt with small populations, where a non-Gaussian distribution affecting the reliability of data is likely to occur. In the 1990s, studies evaluating large population in different world regions became available, providing reliable worldwide data regarding asthma, rhinitis, and atopic dermatitis (1) as well as asthma in Europe (2). The ISAAC Phase One was addressed on about 464.000 children and found extremely variable prevalence in the world, from less than 1% to more than 35%, with a 20-fold variation for asthma, a 30-fold variation for rhinoconjunctivitis, and 60-fold variation for atopic dermati-

Table 5 - Kind of allergic reactions to insect stings

Symptom	Females (%)	Males (%)	Total (%)
Overall reactions	91/2,976 (3.1%)	116/2,754 (4.2%)	207/5,730 (3.6%)
Large local reactions	54/2,976 (1.8%)	53/2,754 (1.9%)	107/5,730 (1.9%)
Systemic reactions	32/2,976 (1.1%)	61/2,754 (2.2%)	93/5,730 (1.6%)
Grade I reactions	20/2,976 (0.7%)	28/2,754 (1.2%)	48/5,730 (0.8%)
Grade II reactions	5/2,976 (0.2%)	9/2,754 (0.3%)	14/5,730 (0.2%)
Grade III reactions	4/2,976 (0.1%)	14/2,754 (0.5%)	18/5,730 (0.3%)
Grade IV reactions	3/2,976 (0.1%)	10/2,754 (0.4%)	13/5,730 (0.2%)
Unusual reactions	1/2,976 (0.03%)	0/2,754 (0%)	1/5,730 (0.02%)

Table 6 - Details on the 207 subjects reporting allergic reactions to insect stings

Feature	Females (%)	Males (%)	Total (%)
Environment where the reaction occurred			
At home	11/91 (12.1%)	1/116 (0.9%)	12/207 (5.8%)
Outdoors	76/91 (83.5%)	108/116 (93.1%)	184/207 (88.9%)
While eating	1/91 (1.1%)	0/116 (0%)	1/207 (0.5%)
While sporting	0/91 (0%)	4/116 (3.4%)	4/207 (1.9%)
While working	3/91 (3.3%)	7/116 (6%)	10/207 (4.8%)
While gardening	1/91 (1.1%)	4/116 (3.4%)	5/207 (2.4%)
Kind of aid received			
E.R.	39/91 (42.9%)	75/116 (64.7%)	114/207 (55.1%)
Family doctor	23/91 (25.3%)	11/116 (9.5%)	34/207 (16.4%)
Other doctor	3/91 (3.3%)	2/116 (1.7%)	5/207 (2.4%)
Other health-care worker	2/91 (2.2%)	2/116 (1.7%)	4/207 (1.9%)
Auto-medication	18/91 (19.8%)	22/116 (19%)	40/207 (19.3%)
No aid	3/91 (3.3%)	3/118 (2.6%)	6/207 (2.9%)
Performance of allergy tests	18/91 (19.8%)	40/116 (34.5%)	58/207 (28%)
Performance of venom immunotherapy	3/91 (3.3%)	21/116 (18.1%)	24/207 (11.6%)

tis (1). The ISAAC Phase Three surveyed 193,404 children and was completed a mean of 7 years after Phase One, reporting increases in prevalence with the exception of asthma in older age-group children (2). In Italy, the application of the ISAAC framework produced the Studi Italiani sui Disturbi Respiratori dell'Infanzia e l'Ambiente (SIDRIA) studies that showed a prevalence of asthma of about 9% in children and 10% in adolescents, of rhinitis of about 12% in children and 20% in adolescents, and of atopic dermatitis of about 16% in children and 12% in adolescents (9, 10). A comparison of two cross-sectional surveys conducted in 1994 and 2002, in northern and central Italy (11) detected a small increase in children (0.8%) and stable values in adolescents for asthma but a significant increase of rhinitis both in children (5.2%) and adolescents (4.1%), and for atopic dermatitis in children (4.4%), and less pronounced in adolescents (2.1%). Evaluation of changes in the prevalence of asthma and rhinitis in adults in 1991–1993 compared with 1998–2000 offered substantial confirmation to such a trend, because asthma showed a slight decrease (from 9.8% to 9.6%), while rhinitis increased from 15.4% to 18.3% (12). The prevalence we found in the present survey, that is 6% for asthma and 14.8% for rhinitis, is lower than that reported in the above-cited studies in Italy. Some characteristics concerning the environment and the population may account for such difference. First, Cotignola is a small city of 7,200 inhabi-

tants surrounded by a country, and such an environment seems less favourable than an urban area for developing allergic disorders (13). However, it is hard to explain our observation of the so-called 'farming effect', which is an important component of the hygiene hypothesis (14), because only 3% of the population we studied were farmers. Second, the number of children, who are especially affected by atopic diseases, was relatively small in the studied population, and in particular 1,035 subjects (15.3%) were aged less than 18 years, and 368 (5.4%) were aged less than 5 years. Differently from most epidemiologic surveys on allergy that considered only asthma, rhinitis, and atopic dermatitis, we included in the investigation other possible manifestations of allergy, i.e. urticaria, angioedema, oral allergy syndrome, and anaphylactic symptoms such as laryngeal oedema and cardiovascular collapse. Urticaria was reported by about 2% of the subjects; this is in line with the prevalence commonly estimated in the general population (15) but is much lower than the value of 8.8% reported in a recent study in Germany (5). In our study, 0.7% of subjects reported angioedema, but this finding cannot be argued with because other studies on angioedema prevalence are lacking. This warrants further epidemiologic studies on both urticaria and angioedema. Instead, the prevalence of 0.6% of life-threatening anaphylactic symptoms such as laryngeal oedema and cardiovascular collapse agree with values lower than 1% generally

reported in the available studies (4, 16). Epidemiology of allergy may be studied also according to its causative factor. This gives reliable results when the cause is the venom of stinging insects that elicit true allergic reactions, while the value of questionnaire-based surveys is low when the suspected causes are food. In fact, it is known that up to 33% of people have a self-perception of food allergy (17) but less than 1% actually react to the suspected food when a placebo-controlled food challenge is performed (18). These observations lead us to limit to insect stings the evaluation of allergic reactions according to its cause. The prevalence of systemic reactions to insect stings of 1.6%, we found, is in the low end of the reported values that range from 0.9–8.9% (7), and is slightly lower than in the previous studies in Italy, where a prevalence of 2.7% in conscripts (19) and 2.8% in a population of factory workers and foresters (20) were reported. However, the general population surveyed in the present study included more females (52%) than males, while the previous studies addressed only males or a population sample with a male preponderance, and it is known that males are more frequently concerned by an insect venom reaction, mainly because of higher exposure to stings (21). The answers to the questionnaire provided some other details on this kind of allergy. Confirmation was obtained regarding the fact that most reactions (79.8%) develop within 30 minutes from the sting and are caused (81.6%) by a single sting (21). Also, the observation on the shortness of time interval between a tolerated sting and the reaction, as a risk factor to develop hypersensitivity to insect venom (22), is confirmed from our findings. New observations concern the management of patients with Hymenoptera venom allergy: only 28% of subjects had a diagnostic evaluation, and 11.6% underwent venom immunotherapy that is the optimal preventive treatment. However, considering that admission criteria to venom immunotherapy include systemic but not large local reactions (23), the rate of treated subjects among those with systemic reactions rises to 25.8%. About 97% of the subjects received a medical treatment, mostly (55%) not only in the E.R. department but also by physicians and other health-care workers, and 19% by self-administered drugs. This differs from the treatment of other allergic disorders that was performed in 51.7% of subjects with asthma, in 46.5% of subjects with rhinitis, and in 22.7% of subjects with other allergic reactions. Concerning asthma, the data confirms recent observations reporting that about half of the asthmatic patients follow an adequate and regular drug treatment (24, 25).

In this survey, data from immigrants were also obtained: the prevalence of the various clinical manifestations was similar for some of them, such rhinitis symptoms (13.1%), asthmatic symptoms (4.2%), reactions to insect stings (2.7%), and anaphylaxis (0.5%), while was lower for others, such as skin symptoms (2.3%), and oral symptoms (0.7%). A number of studies evaluated the characteristics of immigrants referring to allergy units in Italy compared to those of Italian patients, the most recent by Lombardi et al. (26), but to our knowledge only one study – concerning children and adolescents – assessed the prevalence of allergy in immigrants (27). In such study, asthma and other atopic diseases were on the whole significantly less common among immigrant children than among Italians, while in our study, that addressed the general population, the prevalence of allergy in immigrants was not significantly different from Italian people. In fact, it was reported that subjects who migrate tend with time to embrace the prevalence of the area to which they migrate (28). In conclusion, the findings from this survey, conducted on the population of the city of Cotignola in Italy, substantially confirm the recent epidemiological data on asthma, rhinitis, anaphylaxis, and insect sting allergy in Europe, and add some data on the prevalence of urticaria and angioedema and on the management of allergic reactions.

Conflict of Interest Statement

Stallergenes Italia srl partially supported the submitted work.

Author Contribution Statement

All authors have contributed to the manuscript.

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