
The possible influence of the environment on respiratory allergy: a survey on immigrants to Italy

Carlo Lombardi, MD^{*}; Giorgio Walter Canonica, MD[†]; Giovanni Passalacqua, MD[‡]; and the IGRAM, Italian Group on Respiratory Allergy in Migrants[‡]

Background: Respiratory allergy is influenced and determined by genetic and environmental factors. Migration is a good model to indirectly evaluate the possible influence of environment.

Objective: To assess the clinical characteristics of respiratory allergy in immigrants to Italy, in comparison with the Italian population.

Methods: The clinical/demographic data of those immigrants stably living in Italy and referred for the first time to allergy services for respiratory allergy were collected in a multicenter survey. All the patients underwent a standard diagnostic workup. A matched Italian population was also examined.

Results: Six hundred ninety-eight immigrants and 859 Italians had at least one positive skin test and were analyzed. Most of the patients were referred to the allergy units by their general practitioners. In those patients, the demographic characteristics were not different, except for family size. Immigrants had less family history of atopy. Only 16% had a clinical history of allergy before migration. The time elapsed between migration and onset of symptoms was 5.3 ± 3.1 years, with a minimum of 0.5 and a maximum of 7 years. A higher rate of monosensitization was seen among immigrants, and the severity of their asthma/rhinitis was greater than in Italians. No difference was seen in the pattern of sensitizations.

Conclusion: In this population of immigrants, environmental factors play a relevant role in the onset of respiratory allergies. *Ann Allergy Asthma Immunol.* 2011;106:407–411.

INTRODUCTION

Respiratory allergy (namely, allergic asthma and allergic rhinitis) is the most common clinical presentation of the “atopic status,” which is characterized by an ongoing production of specific IgE toward ubiquitous and usually non-noxious substances. The atopic status is, in turn, the result of a complex interaction among genetic and environmental factors.^{1,2} These latter include feeding, infections, gastrointestinal flora, and exposure to allergens.^{3–6} All of the mentioned factors can influence the development of allergy, but the relative weight of each of them, taken separately, is not

known. In general, the “westernization” of lifestyle, with more vaccinations, less infections, consumption of sterile foods, and better medical care, could be responsible for the increase in prevalence of allergic disorders. This is encompassed under the definition of “hygiene hypothesis.”⁷ The hygiene hypothesis, in fact, can explain at least in part⁸ the rising prevalence of allergy in both adults and children. This can be more easily observed in immigrants, who undergo a sudden and radical change in their environment and lifestyle.^{9,10} Thus, immigrants can be regarded as an interesting epidemiological model to demonstrate the overall influence

Affiliations: ^{*} Allergy Unit, Department of Internal Medicine, Sant’Orsola Hospital, Brescia, Italy; [†] Allergy and Respiratory Diseases, DIMI, University of Genoa, Italy.

[‡]The IGRAM: Italian Group on Respiratory Allergy in Migrants: Leonardo Antonicelli, Allergy Unit, Ospedali Riuniti, Ancona. Renato Ariano, Department of Internal Medicine, ASL 1 Imperia. Riccardo Asero, Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano. Daniele Berra, Division of Pneumology Ospedale di Busto Arsizio. Donatella Bignardi, Allergy Unit, S. Martino Hospital, Genoa. Angelo Corsico, Respiratory Medicine, Policlinico San Matteo, University of Pavia. Maria Teresa Costantino, Respiratory Division, Carlo Poma Hospital, Mantua. Mariangiola Crivellaro, Occupational and Environmental Medicine, University of Padua. Federica Gani, Respiratory Disease Division, Allergy Unit, S. Luigi Hospital, Turin. Ilenia Folletti, Occupational and Environmental Allergology, University of Perugia. Cristoforo Incorvaia, Allergy/Pulmonary rehabilitation, ICP Hospital, Milan. Gennaro Liccardi, Division of Pneumology and Allergology, A. Cardarelli Hospital, Naples. Guido Marcer, Occupational and Environmental Medicine, University of Padua. Maurizio Marogna, Allergy Unit, Macchi Foundation, Cuasso al Monte Hospital, Varese. Manlio

Milanese, Division of Pneumology, S. Corona Hospital, Pietra Ligure. Paola Minale, Allergy Unit, S. Martino Hospital, Genoa. Antonino Musarra, Allergy Unit, National Healthcare, Reggio Calabria, Italy. Franco Nebiolo, Allergy & Clinical Immunology, University of Turin & AO Ordine Mauriziano. Erminia Ridolo, Internal Medicine, University of Parma. Giovanni Rolla, Allergy & Clinical Immunology, University of Turin & AO Ordine Mauriziano. Gianenrico Senna, Allergy Unit, Verona General Hospital. Michele Schiappoli, Allergy Unit, Verona General Hospital. Andrea Siracusa, Occupational and Environmental Allergology, University of Perugia. Susanna Voltolini, Allergy Unit, S. Martino Hospital, Genoa. Mona Rita Yacoub, Allergy and Immunology Department, IRCCS San Raffaele Hospital, Milan. Pietro Zanon, Division of Pneumology Ospedale di Busto Arsizio.

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of the environment itself on the development of respiratory allergic disorders.

During the last 15 years, Italy has undergone a large immigration influx, because of the presence of numerous factories and farms, offering the opportunity for stable employment. In 2008, an estimated 4 million immigrants lived stably in Italy, approximately 14% of the total population.¹¹ The immigrants are not uniformly distributed over the territory, with the industrialized areas in the north of the country accounting for more than 60% of stably living immigrants. Based on this background, we attempted to assess whether clinical differences between the immigrants to Italy and the native population exist, such as a more recent onset of sensitization in immigrants, or a difference in atopic background. We performed a large cross-sectional survey of immigrants with a matched Italian population used for comparison.

METHODS

Population and Data Collection

Twenty-one allergy units, distributed over the Italian territory, and located in areas with high migration pressure, were recruited. Physicians were asked to collect the data from 40 to 50 consecutive adult immigrants seen for the first time between January 2009 and June 2009 and suffering from respiratory allergy symptoms (rhinitis or asthma). Patients who came spontaneously, or who were referred by an emergency care unit after an acute episode, or referred by their general practitioner (GP) were included. Only those subjects stably living in Italy, that is, residing in the areas surrounding the allergy units, having residence permission, and being assisted by the National Healthcare System were considered. Those patients seen for follow-up visits (ie, not the first visit) were excluded. Those inclusion criteria also applied to the control population of Italian patients. The data recorded in a standard database were demographics, date of immigration, region of origin, family history (allergic diseases in one/both parents), previous symptoms of asthma/rhinitis, onset of actual symptoms, time elapsed from migration, history of adverse reactions to food or drugs or atopic dermatitis, and results of skin tests. When needed, an interpreter helped in collecting the clinical history. The countries of origin were grouped for convenience into four macro-regions (Asian-Pacific, Africa, Latin America, and Eastern Europe). The diagnostic workup was standard and included clinical history, examination, allergy skin prick tests (or CAP-RAST), and pulmonary function tests. Rhinitis was diagnosed according to Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines¹² and defined as allergic if one or more of the skin prick test results were positive. It was graded as intermittent/persistent, or mild/moderate-severe. Asthma was diagnosed according to Global INitiative on Asthma (GINA),¹³ and the diagnosis was confirmed, when required, by pulmonary function tests with either reversibility assessment or methacholine challenge. The tests were performed with computerized spirometers, always according to current recommendations.¹⁴ The extracts

used for skin tests were only 2 across the centers (ALK Abell , Lainate, Italy, or Stallergenes, Milan, Italy). The panel included those allergens commonly responsible for respiratory symptoms in Italy: grasses, *Parietaria*, birch, olive, hazelnut, dust mites, ragweed, *Blattella germanica*, *Alternaria*, and cat and dog dander. Skin tests with food allergens were carried out only in the presence of a suggestive clinical history. These tests were carried out and read according to European recommendations.¹⁵ All the involved centers notified their Ethics Committees of the study. According to the Italian law, no formal approval is required for observational studies.

Statistical Analysis

The frequency of characteristics, such as sex ratio, family size, and monosensitization, were analyzed using the χ^2 test. Mean values have been compared by the Mann-Whitney test for independent samples. The association between duration of symptoms and duration of migration was estimated by a linear regression analysis.¹⁶ The probability levels were computed using a complete randomization method (permutation or exact test; P_{exact}), or by a Monte Carlo simulation based on a 10,000 sampled table ($P_{Monte Carlo}$)¹⁷ when computation was not possible. The type I error (α) has been set at the 0.01 level. The means (age, symptom duration, and so forth) have been reported with the standard error of mean ($\pm$ SEM). All statistical analyses were computed using the Statistical Package for Social Sciences ver. 17.01 for Windows (SPSS Inc, Chicago, Illinois).

Results

Complete medical records were obtained for 802 immigrants (42% male; mean age, 34.4 ± 10.7 years) and 960 Italian patients (47% male; mean age 35.0 ± 15.2 years). The macro-regions of origin of the immigrants were distributed as follows: Africa 28%, Eastern Europe 29%, Asia 15%, and Latin America 28%. Most patients (approximately 80%) were referred to the allergy units by their GPs. The remaining came spontaneously or were sent by other specialists or after an emergency care visit for acute symptoms. Only those patients with at least one positive skin prick test (that is, allergic patients) were considered for the subsequent analysis. Thus, 698 immigrants (87%) and 859 (89.4%) Italians were analyzed. The demographic characteristics of the 2 groups of allergic subjects were not different, except for the family size, and for a slightly but significantly higher prevalence of females in the Italian population (Table 1).

Concerning the medical history of atopic diseases, a significantly lower prevalence of positive family history was found in immigrants than in the Italian population. A significant difference also was seen in the rate of previous adverse reactions to foods/drugs and of atopic eczema, which were more frequent ($P < .001$) in the Italian population than in immigrants (Table 2). Rhinitis was diagnosed in almost all patients, with no difference between immigrants and Italians, whereas asthma was less frequent in Italians ($P = .004$). The

Table 1. Demographic Characteristics of the Allergic Patients

	Immigrants (n = 698)		Italian population (n = 859)		P
	N	%	N	%	
Male	302	43	414	48	$\chi^2 = 5.8$ $P = .016$
Mean age $\pm$ SD	34.0 $\pm$ 10.1		34.2 $\pm$ 13.8		$T = -0.4$ $P = .7$
Age range, years	18–67		18–64		—
Sent from					$\chi^2 = 9.5$ $P = .08$
GP	550	79	687	80	
Emergency Dept	4	0.6	4	0.4	
Other specialists	59	8.4	44	5	
Spontaneous	84	12	124	14.6	
Family size					$\chi^2 = 147.3$ $P < .0001$
1–2	119	17	141	16.4	
3–4	351	50	632	74	
5–6	191	27	81	9	
>6	47	6	5	0.6	
Smoking habit					$\chi^2 = 8.3$ $P = .1$
Never	440	63	593	69	
Ex	77	11	78	9	
Current	181	26	188	22	

distribution of severity of rhinitis and asthma was also different between Italian patients and immigrants, with the immigrant group demonstrating a greater prevalence of more severe asthma and rhinitis ($P = .002$ for both asthma and

Table 2. Medical History of Atopic Diseases and Clinical Characteristics of the Allergic Patients

	Immigrants (n = 698)		Italian population (n = 859)		P
	N	%	N	%	
Family history of atopy					$\chi^2 = 110$
No	507	73	401	46	$P < .0001$
1 Parent	173	24	384	45	
Both parents	18	3	74	9	
History of food allergy	73	11	127	15	$\chi^2 = 6.4$ $P = .012$
History of drug reactions	26	4	76	9	$\chi^2 = 17.6$ $P < .0001$
History of eczema	52	7.4	121	14	$\chi^2 = 17.7$ $P < .0001$
Diagnosis of rhinitis	651	93	812	95	$\chi^2 = 4.5$ $P = .41$
Diagnosis of asthma	383	55	408	47	$\chi^2 = 8.3$ $P = .004$
Monosensitized	275	39	235	27	$\chi^2 = 26.6$ $P < .0001$

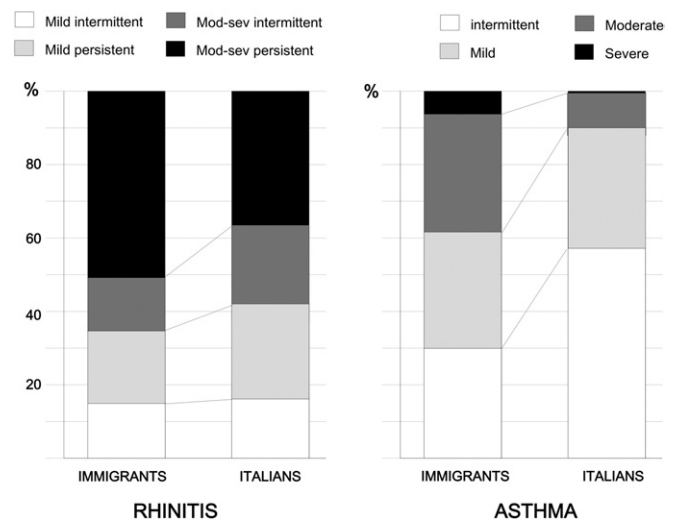


Figure 1. Frequency distribution of the severity of rhinitis (according to ARIA) and asthma (according to GINA).

rhinitis), as shown in Figure 1. Only 116 of the immigrants reported the presence of asthma or rhinitis before their arrival in Italy. In other words, in 83% of the immigrants, the symptoms appeared invariably only after immigration.

The rate of monosensitized subjects was higher in immigrants than in Italians (39% vs 27%; ($P < .001$) (Table 2). Among monosensitized subjects, house dust mite, grasses, *Parietaria*, and birch were the most common positive allergens, and the pattern of sensitization was overall similar in Italians and immigrants. Nonetheless, sensitization to *Alternaria* and ragweed was significantly more common in Italians than in immigrants (4.8% vs 0.7% and 8.6% vs 2.9%, respectively) (Fig 2). The pattern of skin sensitizations was also similar in the polysensitized subjects of the two populations (Fig 3), with the exception of cypress, which was more frequently positive in the Italians (37.8% vs 13.4%, $P = .01$).

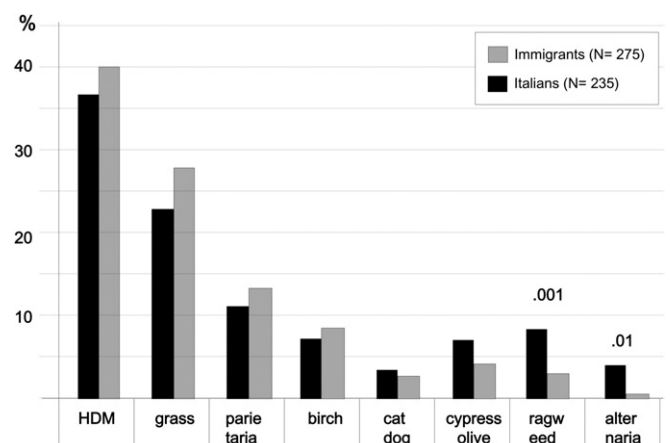


Figure 2. Percentage of subjects with skin prick test positivity to each allergen within the monosensitized Italians and immigrants.

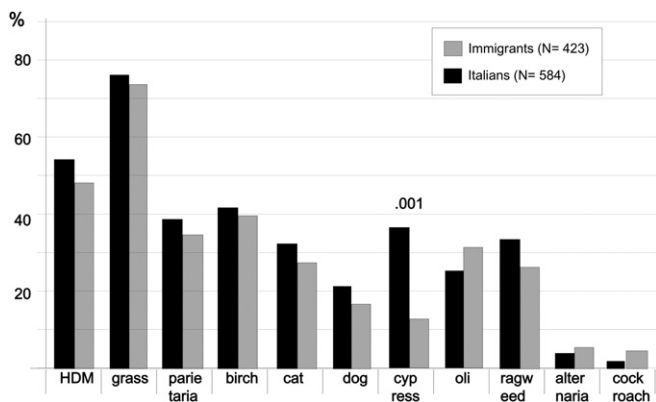


Figure 3. Percentage of subjects with skin prick test positivity to each allergen within the polysensitized Italians and immigrants.

Cockroach (*Blattella germanica*) sensitization (always in association with other sensitizations) was found in 3.3% of immigrants and 2.5% of Italians. Overall, the immigrants without a previous history of respiratory allergy appeared to be sensitized to local allergens. For instance, 80% of the subjects sensitized to birch pollen came from areas where birch is not present. The same happened for 74% of the ragweed-sensitized and for 70% of the *Parietaria*-sensitized subjects.

The 582 immigrants with no clinical history of asthma or rhinitis before migration had a mean duration of habitation in Italy of 9.5 ± 5 years, and the time elapsed from the appearance of symptoms was 5.3 ± 3.1 years (range, 0.5–7). This duration of symptoms is significantly shorter than that of the native population (9.9 ± 6.7 years; $P < .001$). Conversely, in the 116 immigrants with a positive clinical history before migration, the duration of symptoms was not different from that of the Italian population (10.4 ± 7.1 vs 9.9 ± 6.7 years; $P = .21$). In addition, a significant positive association was seen between the time elapsed from immigration and the duration of symptoms ($R^2 = 0.384$, $P < .001$) (Fig 4). No difference in the distribution of family history, clinical history, clinical presentation, and allergen sensitization among the four macroregions of origin of the immigrants could be detected.

DISCUSSION

Immigrants represent a special population, because they undergo a sudden and usually long-lasting change in lifestyle/environment. Thus they can be regarded as a natural epidemiological model to indirectly assess environment/lifestyle influences on diseases.¹⁸ In general, the immigrant populations differ from the local populations as far as asthma is concerned. For instance, the European Community Respiratory Health Survey showed that the prevalence of asthma is, on average, greater in migrants than in resident people,¹⁹ although it is lower in immigrant children.²⁰ Also, some previous cross-sectional surveys, performed in limited geographical Italian regions, showed that a positive clinical his-

tory for respiratory allergy was present in only less than 20% of migrants vs more than 65% in Italians, and that the allergic disease appeared after a latency of some years after migration.^{21–23} Based on those previous observations, we extended the survey to the whole Italian territory, to have a large population of immigrants to compare with the Italian population. Several interesting results concerning the characteristic of respiratory allergy emerged from our study. First, the rate of positive family history is lower as compared with the general population, and in 85% of immigrants, the symptoms appeared only some years after the immigration, the mean time being 5.3 ± 3.1 years, with a direct relationship between the duration of staying and the onset of symptoms. This is in agreement with previously reported observations: in the study by Tedeschi et al,²² the average interval between immigration to Milan and onset of allergy was 4 years 7 months, and in our previous study on immigrants in the town of Brescia the time was 5 years 2 months.²³ Second, the percentage of monosensitized subjects was greater in immigrants than in Italians. This would be in agreement with the observation that the number of sensitizations tends to increase with time.²⁴ Another intriguing observation was that the distribution of sensitizations was overall not different between immigrants and local population. In particular, in immigrants a relevant rate of sensitization to local allergens, such as *Parietaria* or birch pollen, which are not present in most of the regions of origin, was found. In this regard, the observation that individuals become sensitized to local allergens was reported more than 50 years ago.²⁵ Concerning cockroach, a nontypical Italian allergen,²⁶ which is an important cause of allergy in South America, as well as in Asia,^{27,28} its presence as a sensitizing allergen was low in both immigrants and Italians. Third, the severity of rhinitis or asthma symptoms was, on average, greater in immigrants than in the local population. In this regard, the treatment is not expected to be a confounding variable, because the level of therapy was similar in both groups.

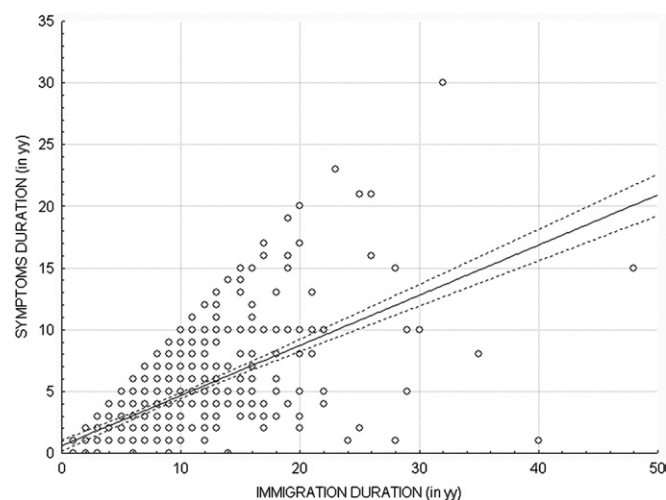


Figure 4. Correlation between the duration of staying in Italy and the duration of symptoms. Each circle may represent more than 1 patient.

Some information biases (eg, underreporting of clinical history or family history) may have occurred, although the data collection was accurate at the best, and validated questionnaires were used. On the contrary, an overreporting, if any, would not have affected the results.

Taken together, the findings of our study suggest that environmental factors are relevant in favoring allergic sensitization in immigrants. Some of these factors, as analyzed by von Hertzen and Haahtela,⁴ are part of the hygiene hypothesis, and include changes in indigenous microbiota, reduced exposure to parasites/endotoxins, and increased use of antibiotics. This may result in immunological changes such as reduced expression of Toll-like receptors and reduced stimulation of regulatory T cells. Also, the exposure to allergens, either new or ubiquitous, intervene in this process. Conversely, genetic factors still may play a fundamental role in dictating which individuals will become atopic within a population, when the whole population is moving to a western lifestyle. The hygiene hypothesis, which applies mainly to the early years of life, cannot fully explain the development of atopy, because our population of immigrants developed their sensitization in adulthood.²⁹

In summary, in the considered population of immigrants, the clinical characteristics of respiratory allergy are partially different from those of the local population, and the disease seems to develop ex novo a few years after coming to Italy. Our data support an epigenetic^{30,31} nature of respiratory allergy and indirectly suggest that the environment may sometimes overtake the genetic background (familiarity), or better actively interact with it in the development of allergic diseases.

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Requests for reprints should be addressed to:

Giovanni Passalacqua, MD

Allergy & Respiratory Diseases, Dept of Internal Medicine

Padiglione Maragliano, L.go R. Benzi 10, 16132 Genoa ITALY

E-mail: passalacqua@unige.it