

Onset of allergy and asthma symptoms in extra-European immigrants to Milan, Italy: possible role of environmental factors

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Summary

Background Allergy and asthma are typical disorders of the affluent societies. Migrants from developing to industrialized countries seem to be at increased risk of allergy and asthma development.

Objective To evaluate time of onset, spectrum of sensitization and clinical features in a population of extra-European immigrants to Milan, Italy, complaining of allergy and asthma symptoms.

Methods Data regarding 243 extra-European immigrants checked at an allergy clinic from 1994 to 2000 were collected retrospectively. The demographic data were compared with those of the extra-European immigrants living in Milan at the end of 1999.

Results The patients were complaining of asthma (63.7%), rhinoconjunctivitis (56.7%), rhinitis alone (21%) or urticaria (3%). One hundred and eighty-seven out of 222 patients (84.3%) declared they were healthy before migrating and allergy/asthma symptoms started to appear after their arrival in Italy, namely after an average period of 4 years and 7 months. The proportion of male patients was lower than the proportion of men in the extra-European immigrant population (48% vs. 55%), suggesting that in adult immigrants allergy and asthma are more common in women than in men. Furthermore, there was an over-representation of Central-South Americans attending the clinic, which seemed to be due to a genetic predisposition to allergy/asthma development. When data were analysed for single countries, a trend towards an increased risk of allergy and asthma was found in immigrants from all Central-South American countries. A skin test positivity for at least one inhalant allergen was found in 196 out of 232 patients (81%), and the spectrum of allergic sensitization was similar to that of the Italian population living in the North of Italy.

Conclusion Most extra-European immigrants declared that they were healthy at home and that allergy and asthma symptoms had appeared after immigration to Milan; lifestyle and environmental factors in a western industrialized city seem indeed to facilitate allergy/asthma onset in immigrants from developing countries. Allergy/asthma risk seems to be different in different ethnic groups.

Keywords allergy, asthma, extra-European immigrants, industrialized countries, Milan

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Introduction

In the last decades a progressive increase in asthma and allergy prevalence has occurred in all industrialized countries [1–4]. The International Study on Asthma and Allergies in Childhood (ISAAC), which has been carried out on 460 000 children and adolescents, has documented large variations in the prevalence of asthma and allergy among different populations [5, 6]. The highest prevalence has been found in English-speaking countries, like the United Kingdom, New Zealand, Australia and Ireland, whereas the lowest rates have been demonstrated in developing countries, such as Albania, China, Indonesia and Georgia. It seems indeed that asthma and allergy are typical

disorders of populations living in affluent countries. The results of the European Community Respiratory Health Survey (ECHRS) have recently confirmed that the prevalence of asthma and allergy is increasing world-wide, although there are large variations among populations living in different countries [7, 8]. This study has been performed on 140 000 persons aged between 20 and 44 years from nearly all the countries of the European Union, the United States of America, Australia, New Zealand, Estonia, Algeria and India. The highest prevalence has been found in English-speaking countries and the lowest prevalence in the Eastern European countries, India and the Mediterranean countries. The different genetic features cannot explain the large variations in the prevalence of asthma and allergy in the different countries. The studies carried out just after the reunification of Germany demonstrated that the prevalence of asthma and allergy was higher in the former Federal Republic than in the former Democratic Republic, although the genetic background of the two populations was

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the same [9, 10]. More recent studies have shown a rising trend of asthma and allergy in the population of the eastern regions in Germany, probably related to changes in lifestyle [11–13]. As genetic changes have not occurred in the population of former East Germany after reunification, it can be concluded that environmental factors play an important role in the development of asthma and allergy in those people genetically predisposed to them.

The evaluation of asthma and allergy in persons migrating from developing to industrialized countries provides a unique opportunity to investigate the role of environmental factors in the appearance of asthma and allergy [8, 14].

In the last 10 years a large number of people from developing countries have migrated to the industrialized countries of the European Union. Most of the immigrants in Italy come from North Africa, Central and South America, and Asian countries, such as Sri Lanka, the Philippines and China. Many of these immigrants have developed allergy and/or asthma when in Italy. We have analysed retrospectively the data regarding the immigrants from extra-European countries who have been under treatment at the Division of Internal Medicine and Pneumology of the Ospedale Fatebenefratelli in Milan in the years 1994–2000.

Subjects and methods

Subjects and data collection

The study was retrospective, taking into consideration the records of immigrants from extra-European countries treated at the outpatient clinic of the Division of Internal Medicine and Pneumology of the Fatebenefratelli Hospital in Milan, starting from January 1994 up to December 2000. The data cover 243 patients from Asia (30%), Central and South America (32%), and North Africa (26%). The demographic characteristics of the patients are reported in Table 1. All data concerning country of origin, time of stay in Italy, working conditions, smoking habits, presence of pets at home, family and personal history were recorded on the clinical report compiled on the occasion of their first visit at the clinic. All patients were able to speak Italian or were accompanied by an Italian-speaking relative.

Allergy was defined by allergic symptoms (rhinitis, conjunctivitis, asthma) and positive skin prick testing or specific IgE determination for one allergen at least. Any individual was considered asthmatic if he/she reported at least two episodes of wheezing, cough and dyspnoea in the last 12 months and was currently taking medications for asthma.

Skin prick testing and lung function evaluation

Skin prick tests were performed in 232 out of 243 patients (96%), using the method of Osterballe et al. [15]. The allergenic extracts used were house dust mites (*Dermatophagoides pteronyssinus* and *farinae*), grass pollens (*Lolium perenne*, *Cynodon*, *Phleum pratense*), birch, hazel, mugwort (*Compositae*), ragweed, wall pellitory (*Parietaria officinalis*), cat and dog epithelia, and moulds (*Cladosporium herbarum*, *Aspergillus*, *Candida*, *Penicillium*, *Alternaria alternata*), and were purchased from Stallergenes (Milan, Italy). Histamine (10 mg/mL) and saline were used as positive and negative controls, respectively. Lung function was measured by a spirometer (Vmax, Sensormedics, Baltimore, MD, USA) in 56 patients reporting asthmatic symptoms.

Statistical analysis

Statistical analysis was performed by chi-square test with Yates correction. The demographic characteristics of the patients were compared with those of the extra-European immigrants living in Milan during the year 1999 (data available from the Central Institute of Statistics, Rome, Italy). *P*-values were considered significant when lower than 0.05.

Results

Clinical and demographic characteristics of the patients

The extra-European immigrants seen at the outpatient clinic were affected by asthma (63.7%), rhinitis and conjunctivitis (56.7%), rhinitis alone (22.6%) or urticaria (3.2%) (some patients suffered from more than one disease). Continent of origin, male:female (M:F) ratio, mean ages and mean time spent in Italy are reported in Table 1. No significant differences were found among the patient populations from different continents regarding mean age and time of stay in Italy; conversely, M:F ratio was significantly lower among patients from Central-South America than among other populations ($P < 0.0001$). The demographic characteristics of the patients were different from those of the extra-European immigrants living in Milan in 1999 (total number 113 594). The proportion of male patients was lower than the proportion of men among the immigrants to Milan (48% vs. 55%, $P < 0.04$), and in fact the risk of allergy (OR 0.65, 95% CI 0.50–0.84, $P < 0.002$) and asthma (OR 0.63, 95% CI 0.46–0.87, $P < 0.01$) was significantly lower in men than in women. In addition, the proportion of patients from Central-South America was significantly higher

Table 1. Demographic characteristics of the extra-European patients treated at the outpatient clinic of the Division of Internal Medicine and Pneumology of the Ospedale Fatebenefratelli in Milan from January 1994 up to December 2000

Continent of origin	Men : women (ratio)	Mean age $\pm$ SD (years)	Time of stay in Italy (years, mean $\pm$ SD)
Central-South America	20/57 (0.35)	37 $\pm$ 0.3	11 $\pm$ 0.34
North America	6/2 (3)	38.1 $\pm$ 0.07	8.6 $\pm$ 0.18
North Africa	38/26 (1.46)	37 $\pm$ 0.8	11.4 $\pm$ 0.26
Central-South Africa	4/2 (2)	42.3 $\pm$ 0.09	14.2 $\pm$ 0.09
Asia	40/33 (1.21)	38 $\pm$ 0.2	11.4 $\pm$ 0.38
Oceania	1/0	42	19
Unknown	8/6 (1.33)	41.7 $\pm$ 0.26	13 $\pm$ 0

than the proportion of immigrants from that region (Fig.1). Over-representation of that patient population persisted also when data were analysed separately for men and women (Table 2). The ORs for allergy and asthma were significantly increased for both men and women originating from Central-South America. In contrast, the risk of allergy and asthma was significantly reduced in female immigrants from Asia and the risk of allergy was reduced in men from North Africa. When data were analysed for single countries, a trend towards an increased risk of allergy and asthma was found in male and female immigrants from all Central-South American countries, although a statistical significance was not reached for all national groups (Table 3). Immigrant behaviour from different countries, both Asian and North-African, was not homogeneous. The risk of allergy and asthma was significantly reduced in male immigrants from Morocco, but not in those coming from Egypt. Immigrants from the Philippines had a reduced risk of allergy and asthma, which in contrast was increased in male immigrants from Sri Lanka.

Allergic sensitization and lung function testing

Skin prick testing showed a positivity for at least one inhalant allergen in 196 out of 232 subjects (81%). As shown in Fig. 2, the patients were most commonly sensitized, in order of frequency, to grass pollens and house dust mites, followed by birch and wall pellitory (Fig. 2).

The spectrum of allergic sensitization in immigrants to Milan overlapped the one for the general population living in the north of Italy [16, 17]. Some differences were found among immigrants from different countries regarding the risk of sensitization to certain allergens: in particular, the people from North Africa had a reduced OR for sensitization to grass pollens (0.56, 95% CI 0.32–0.98, $P < 0.001$). As far as the relation between allergic sensitization and environmental factors is concerned, it is interesting to note that domestic work, the most common job among our patients (44%), did not bring about a significant increase in the risk of sensitization to house dust mites (OR 1.65, 95% CI 0.93–2.92). On the contrary, the presence of cats and dogs at home was associated with an increased risk of sensitization to the epidermal derivatives of these animals (OR 10.97, 95% CI 4.47–26.89, $P < 0.0001$). Smoking habits did not influence the risk of asthma development: the percentage of asthmatics among smoking and non-smoking patients was similar (68% vs. 63%).

Lung function tests showed bronchial obstruction in 48 out of 56 patients reporting asthmatic symptoms at the time of the clinical examination.

Relationship between time spent in Italy and appearance of allergy/asthma

The time elapsed between arrival in Italy and appearance of allergic/asthmatic symptoms was known only in 222 patients out of 243 (91%). One hundred and eighty-seven patients out of

Table 2. Odds ratios (ORs) for allergy and asthma among male (upper panel) and female (lower panel) immigrants to Milan divided according to the continent of origin

Continent of origin	OR (95% CI) for allergy	<i>P</i>	OR (95% CI) for asthma	<i>P</i>
Males				
Central-South America	1.81 (1.11–2.94)	0.02	2.09 (1.16–3.76)	0.02
Asia	0.93 (0.63–1.37)	NS	0.71 (0.42–1.2)	NS
North Africa	0.64 (0.43–0.96)	0.04	0.79 (0.48–1.29)	NS
Females				
Central-South America	2.16 (1.53–3.05)	< 0.0001	2.16 (1.41–3.31)	0.0004
Asia	0.39 (0.26–0.57)	< 0.0001	0.40 (0.24–0.65)	0.0002
North Africa	0.70 (0.46–1.08)	NS	0.87 (0.53–1.44)	NS

CI = confidence interval; NS = not significant.

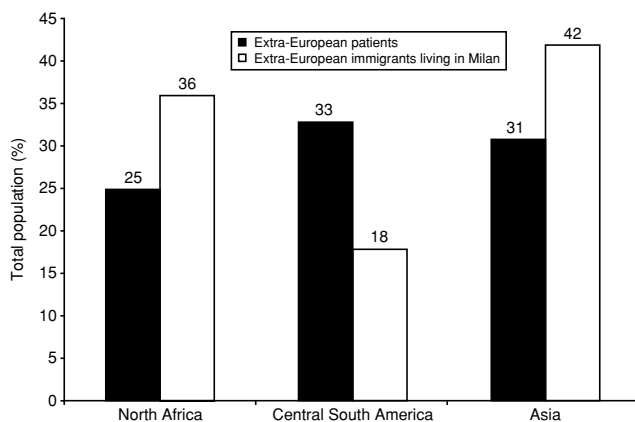


Fig. 1. Percentage distribution of extra-European patients and extra-European immigrants to Milan (year 1999) according to the continent of origin.

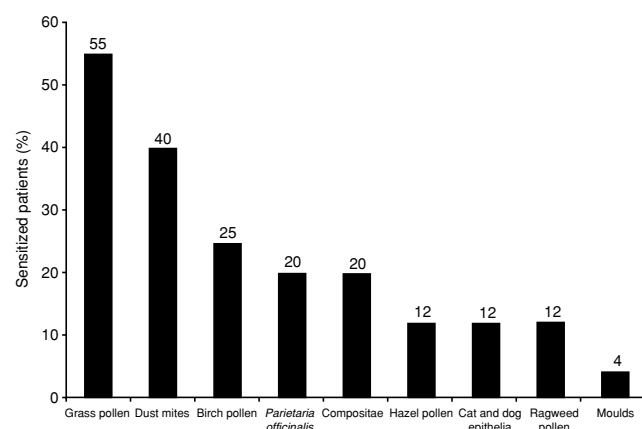
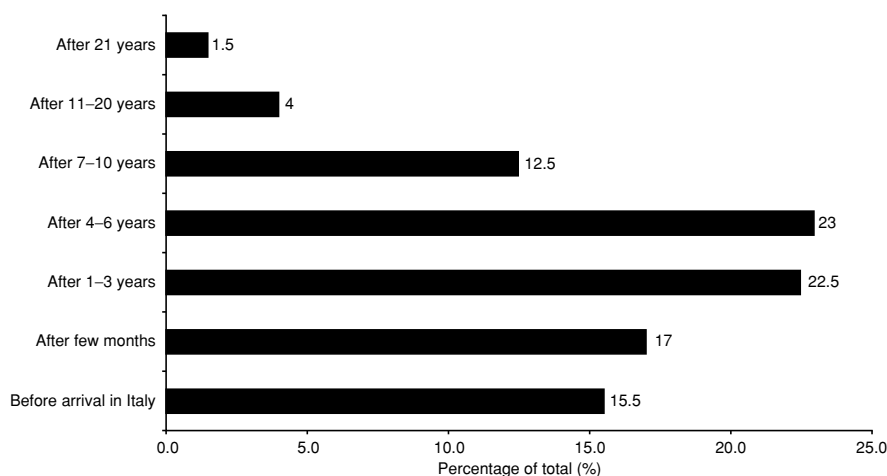


Fig. 2. Spectrum of allergic sensitization in the extra-European patients seen at the Fatebenefratelli Hospital in the years 1994 to 2000.

Table 3. Odds ratios (ORs) for allergy and asthma among male (upper panel) and female (lower panel) immigrants to Milan according to the country of origin

Country of origin	OR (95% CI) for allergy	P	OR (95% CI) for asthma	P
Males				
Egypt	1.09 (0.67–1.76)	NS	1.63 (0.95–2.79)	NS
Morocco	0.17 (0.05–0.56)	0.0015	0.04 (0.002–0.73)	0.0018
Brazil	1.92 (0.60–6.07)	NS	2.04 (0.49–8.34)	NS
El Salvador	3.7 (1.36–10.1)	0.02	4.45 (1.39–14.2)	0.03
Ecuador	2.98 (0.94–9.43)	NS	0.76 (0.04–12.32)	NS
Peru	1.25 (0.58–2.69)	NS	2.07 (1.14–2.93)	NS
China	1.16 (0.60–2.22)	NS	0.52 (1.16–1.67)	NS
Philippines	0.27 (0.10–0.74)	0.01	0.21 (0.05–0.88)	0.03
Sri Lanka	2.38 (1.35–4.18)	0.0035	2.76 (1.41–5.41)	0.0046
Females				
Egypt	0.33 (0.12–0.89)	0.03	0.52 (0.19–1.42)	NS
Morocco	0.46 (0.17–1.24)	NS	0.53 (0.17–1.7)	NS
Brazil	2.37 (1.24–4.52)	0.01	3.00 (1.44–6.22)	0.005
El Salvador	1.17 (0.43–3.17)	NS	1.84 (0.67–5.04)	NS
Ecuador	2.87 (1.4–5.88)	0.006	3.98 (1.83–8.65)	0.0006
Peru	2.02 (1.33–3.09)	0.001	1.42 (0.79–2.57)	NS
China	0.68 (0.33–1.39)	NS	0.52 (0.19–1.42)	NS
Philippines	0.46 (0.27–0.79)	0.0057	0.59 (0.32–1.09)	NS
Sri Lanka	0.61 (0.22–1.67)	NS	0.72 (0.22–2.29)	NS

CI = confidence interval; NS = not significant.

**Fig. 3.** Percentage distribution of patients according to the period of allergy/asthma onset: relationship with immigration to Italy.

222 (84.5%) declared that allergic/asthmatic symptoms had appeared after their arrival in Italy, as before leaving the country of origin they had been symptom-free. The mean period of residence in Italy before allergy/asthma onset was 4 years and 7 months (data ranging from 3 months to over 21 years) (Fig. 3).

Discussion

The findings of this study indicate that most of the extra-European immigrants to Milan (84.3%) were symptom-free before leaving the country of origin, and that allergic/asthmatic symptoms appeared after their arrival in Italy. The average time interval between immigration to Italy and allergy/asthma onset was 4 years and 7 months. Several epidemiological studies have shown a higher prevalence of allergy/asthma in industrialized

countries than in developing countries [5, 6, 9]. It seems indeed that some environmental factors in industrialized countries favour the appearance of allergy/asthma. One reasonable hypothesis is that exposure to allergens, in combination with a polluted atmosphere, favours sensitization and appearance of allergy/asthma symptoms in predisposed subjects [18, 19]. Milan is a heavily polluted city. This is due to its geographical location in the centre of the Padan Valley, with no or scarce wind throughout the year. The main sources of air pollutants are vehicle exhaust, industry and heating systems. A dramatic increase in automobile use has occurred in the past 30 years. Furthermore, the number of diesel vehicles has increased as well. Several studies have shown that exposure to diesel exhaust particles favours allergen-specific IgE synthesis and Th2 cytokine production in mice [20–23]; therefore, allergen exposure in the presence of diesel exhaust particles could have contributed

to allergen sensitization in extra-European immigrants. The demonstration of a positive association between traffic density on street of residence and allergy/asthma development reinforces the possible role of environmental pollution [24, 25]. In addition, it was observed that traffic limitations during the summer Olympic Games held in 1996 in Atlanta (GA, USA) resulted in air quality improvement and a significant decrease in childhood asthma events [26].

Another hypothesis lies in the improved hygienic life conditions that might contribute to the appearance of allergy/asthma symptoms in extra-European immigrants in Milan. In 1989 Strachan observed an inverse relation between allergic rhinitis and the number of children in the household [27]. He proposed that the declining family size led to a reduced rate of infection among children, thus favouring allergic sensitization. This hypothesis, which is known under the name of the 'hygiene hypothesis', has been reinforced in the last few years by several studies showing an inverse relation between the rate of infections, mainly transmitted by the orofaecal route, and prevalence of allergic disorders [28–31]. According to this theory, the lack of exposure to infectious agents during childhood and adolescence, as well as changes in intestinal microflora and frequent use of antibiotics, could hamper a correct development of the immune system and could favour immune responses against innocent antigens, like allergens.

This theory has been suggested to explain the rising trend of allergies in the new generations of populations living in industrialized countries. This suggestion could be also valid for immigrants to a western industrialized city. Although the immigrants of our study were generally young adults, the reduced exposure to infectious agents could in fact facilitate Th2-mediated immune responses towards allergens [32]. Prevalence of infections transmitted by the orofaecal route in the north of Italy is much lower than in most developing countries and this might have contributed to the development of allergic disorders in extra-European immigrants.

In line with this hypothesis stands the observation of a high prevalence of asthma symptoms in Ethiopian immigrants to Israel [33]. This phenomenon could reasonably be ascribed to the improved hygienic conditions, with reduced exposure to infectious agents transmitted by the orofaecal route and eradication of parasitoses [34]. A recent study by Scrivener et al. [35], performed in an Ethiopian population, showed that high degrees of parasite infection seem to prevent asthma symptoms in atopic individuals. Therefore, it is conceivable that treatment of parasitic infections in atopic individuals increases the risk of appearance of allergy/asthma symptoms [36]. It is demonstrated that most parasites greatly stimulate IgE synthesis and so these IgE may compete with allergen-specific IgE for binding and activating mast cells and basophils [37].

Another factor influencing allergy development may be the environmental exposure to endotoxins. Some recent studies have demonstrated an inverse relation between endotoxin exposure, which is high in rural areas and low in urban environment, and allergic sensitization [38, 39]. Therefore, it may be argued that it is not the immigration to a western country carrying the risk of allergy but, in particular, the immigration to an industrialized city where few animals and very few endotoxins are to be found.

The spectrum of allergic sensitization in extra-European immigrants living in Milan was similar to the one noted in the

Italian population living in the north of Italy [17] and in line with the observations of Kalioncu et al. on extra-European immigrants to Sweden [40]: grass pollens were the most important allergens followed, in ranking order, by house dust mites, birch pollen and parietaria. Exposure to epidermal derivatives of domestic animals resulted in an increased risk of sensitization to these allergens.

Another interesting finding of our study is that the proportion of men attending the clinic was lower than the proportion of men in the extra-European immigrant population. This indicates that in adults, asthma is more common in women than in men, and is in line with other observations regarding hospital admission rate and asthma severity in European and North American populations [41, 42]. In contrast, childhood asthma is more frequent in boys than in girls [43], suggesting a possible contribution of sex hormones to the pathogenesis and clinical presentation of asthma. Another finding of our study is that the risk of allergy/asthma development varies according to the country of origin. There was an over-representation of Central-South American patients attending the clinic, which persisted also after adjustment for sex and was not due to a longer stay in Italy, as the mean time spent in Italy was similar to that of other patient populations. Furthermore, the city district close to the hospital was not preferentially inhabited by Central-South American people, and so over-representation of Central-South American patients could not be ascribed to geographical factors. It seems indeed that Central-South American immigrants carry an increased risk of allergy/asthma development because of a genetic predisposition.

In conclusion, our retrospective study conducted on extra-European immigrants suggests that lifestyle and environmental factors in a western industrialized city favour the development of allergy and asthma symptoms in extra-European immigrants, with a variable risk according to the ethnic group. Probably, major contributing factors are the 'hygienic' lifestyle and allergen exposure in the presence of a polluted atmosphere [44].

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