

Original article

Allergy, asthma and markers of infections among Albanian migrants to Southern Italy

Background: Studies of immigrants represent an useful tool to determine the relative relevance of environmental vs genetic factors in causing the reported rapid increase of the prevalence of sensitization and allergic diseases.

Methods: A total of 152 Albanian migrants to Southern Italy responded to a questionnaire based on the European Community Respiratory Health Survey (ECRHS) and 139 of them underwent skin prick test, and 61 serological assays for total IgE and IgG antibodies against *Toxoplasma gondii* (TG), herpes simplex virus 1 (HSV-1), hepatitis A virus (HAV) and *Helicobacter pylori* (HP).

Results: Reported asthma was rare (2/152; 1.3%) and reported nasal allergies rather frequent (24/152; 15.8%). Sensitization to common inhalant allergens occurred in 27/139 (19.4%) subjects. The frequency of skin sensitization to pollen ($P = 0.003$) and that of hay fever ($P = 0.004$) increased with the time spent in Apulia. All the 61 sera had antibodies against HAV, 59/61 (96.7%) against HSV-1, 48/61 (78.7%) against HP and 34/61 (55.7%) against TG. The prevalence of skin sensitization and hay fever symptoms were correlated to the duration of residence in Southern Italy.

Conclusions: Data presented indicate that Albanian migrants to Italy, in spite of the low prevalence of allergic diseases and sensitization in their country of origin, manifest with time an increasing prevalence of sensitization to local allergens and nasal symptoms after immigration to Italy. This would suggest a permanent role of allergen exposure and lifestyle factors in influencing the appearance of sensitization and symptoms of allergic diseases.

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Allergic diseases (asthma, rhinitis, conjunctivitis) have nowadays a high, increasing prevalence worldwide (1). As changes in prevalence have been observed even over a short period of time (2, 3), environmental rather than genetic factors are better candidates as causes of these epidemics.

Surveys have shown that the prevalence of allergic diseases is higher in westernized than in developing countries (2), in West than in East Germany before the fall of the Berlin wall (4), in the general population than among farmers (5) and antroposophic communities (6). Therefore, several lifestyle factors may explain the increasing prevalence of allergy and asthma (7).

According to the hygiene hypothesis, a higher exposure to some infectious agents may protect from

the development of allergic diseases (8–9). In fact, both in Europe (10–12) and in US (13) the presence of antibodies to hepatitis A virus (HAV), and *Toxoplasma gondii* (TG) are associated with a lower prevalence of allergic diseases. Exposure to infections during the very first period of life has been considered to be sufficient to provide lifetime protection from the development of allergic diseases (9). However, it has been also speculated that 'removal of protection' during adulthood (e.g. by a reduced exposure to microbes) might favour the appearance of allergy in genetically predisposed subjects (10).

Migrants from developing countries to countries with a westernized lifestyle offer a useful model to evaluate the contribution of lifestyle to the increase of allergy and asthma (14). According to the International Study of

Asthma and Allergies in Childhood (ISAAC) (2) and the European Community Respiratory Health Survey (ECRHS) (15), Albania has one of the lowest prevalence of allergic diseases, significantly lower than that of several westernized countries including Italy (2, 7) which has similar climatic and aerobiological conditions but a more westernized lifestyle.

This study aims at investigating the prevalence of allergic diseases and asthma in Albanian migrants to Southern Italy in relation to the age of immigration and number of years lived in the hosting country as well as to serology for HAV, TG, HP and HSV-1.

Materials and methods

Study population

The target population included all the Albanian migrants aged 20–44 living in Toritto and in Monopoli and registered in the administrative lists of these two towns of the Apulia region. We could examine 24 subjects (16 males) in Toritto and 128 subjects (81 males) in Monopoli, corresponding to 100% of those registered in Toritto and 74.4% of those registered in Monopoli. The mean age of the men and women examined was 30.4 (95% CI 29.1–31.8) and 32.0 (95% CI 30.4–33.6), respectively. The most common occupation was agriculture (50%), while 19% of participants had non-manual occupations, 5% were students and 25% were unemployed or house-workers. School was attended by 58% of participants until 14 years of age, by 36% until 15–20 years and by only 6% over 20 years. All the participants provided their written informed consent. The study protocol was approved by the Ethical Committee of the Policlinico Hospital, University of Bari, Italy. This study was part of the International Project of Cooperation between Italy and Albany, Interreg II.

Questionnaire

All subjects answered a questionnaire based on the ECRHS (7) during their stay in Apulia (February–December 2001). The Albanian version of the questionnaire had been already validated and used in a previous study (15).

Skin prick test

A total of 139 of the 152 subjects (91.4%) accepted to undergo skin prick tests (SPT). The following common airborne allergens (Merck s.p.a., Milan, Italy) were used: house dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), cat, grass pollen, *Alternaria alternata*, *Parietaria officinalis*, olive, *Artemisia vulgaris*, Cypress; positive (histamine 1%) and negative control were also tested according to the procedures described by the ECRHS. The length and the width of the wheal reactions were measured after 15 min. A positive reaction was defined if the mean wheal diameter was 3 mm or larger after subtraction of the mean wheal diameter of the negative control.

Serological assays

Sixty-one of the 152 subjects (40%) accepted to undergo a blood drawing. There was no statistically significant difference in major socio-demographic characteristics (age, gender, occupation)

between those who accepted and those who did not accept to undergo blood sampling (data not shown).

Peripheral blood was obtained by venipuncture and the sera frozen at –70 °C until tested. Total IgE (CAP IgE FEIA; Pharmacia, Uppsala, Sweden) and specific IgE (CAP-RAST IgE FEIA; Pharmacia) against *Dermatophagoides pteronyssinus* (d1), timothy grass (g6), cat (e1), *Parietaria officinalis* (w19), olive (t9) were tested according to standard procedures. To compare the prevalence of previously acquired infections among participants with that from historical data in Italian populations, sera were tested also for the presence of IgG against *Toxoplasma gondii* (Nuclear Laser Medicine, Milan, Italy), herpes simplex virus 1 (HSV-1) (Nuclear Laser Medicine), HAV (Abbott, Rome, Italy), *Helicobacter pylori* (HP) (Nuclear Laser Medicine).

Definitions

‘Asthma’ was defined as a positive answer to the question ‘Have you ever had asthma?’. ‘Current asthma’ was defined as a positive answer to the question ‘Have you had an attack of asthma in the last 12 months?’. ‘Allergic rhinitis’ was defined as a positive answer to the question ‘Do you have any nasal allergies including hay fever?’. ‘Current treatment for asthma’ was defined as a positive answer to the question ‘Are you currently taking any medicines, including inhalers, aerosols or tablets for asthma?’.

We also used a more restricted and specific operative definition of seasonal allergic rhinoconjunctivitis (hay fever). This was defined by both, a positive answer to the question ‘Do you have any nasal allergies including hay fever?’ and a positive SPT and/or RAST to one or more of the pollen extracts tested. The time spent in Apulia (years in Apulia) was defined as the answer to the question ‘How many years have you lived in this area?’.

Statistical methods

Linear trend of proportion was performed by chi-square for trend. Models with categorical variables permitted estimation of adjusted odd ratio for each exposure category (years in Apulia). Models, suitable for order categories, permitted estimation of linear component relating to years in Apulia. *P*-value ≥ 0.05 was considered not statistically significant. Stata software (Intercooled Stata 7.0; Stata Corporation, College Station, TX, USA) was used for analyses.

Results

Reported asthma was rare (2/152; 1.3%, 95% CI: 0.0–4.7%) while reported nasal allergies rather frequent (24/152; 15.8%, 95% CI: 10.4–22.6%) (Table 1). The prevalence of skin sensitization increased with the time in Apulia ($P = 0.004$) (Table 1). Interestingly, the prevalence of hay fever was also positively associated with the time spent in Apulia, as its prevalence increased from 2.5% in the 42 subjects with duration of residence < 3 years to 20.4% in the 49 subjects with a duration of residence longer than 7 years. Similarly, the prevalence of sensitization to pollens – as revealed by positive skin test – increased from 5.0% in those living in Apulia for < 3 years to 28.6% in those living in Apulia for more than 7 years. This association persisted after adjusting for

Table 1. Respiratory allergy and skin sensitization to inhalant allergens in Albanian immigrants by years spent in Apulia

	Years in Apulia								<i>P</i> for trend
	All		1–3		4–6		≥7		
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Questionnaire*	152		42		60		49		
Asthma ever (13)	2	1.3	0	0.0	2	3.3	0	0.0	NS
Current asthma (13.5.1)	0	0.0	–		0		–		–
Current treatment for asthma (13.6)	0	0.0	–		0		–		–
Rhinitis–nasal allergy (14)	24	15.8	5	11.9	6	10.0	13	26.5	0.049
Skin prick test (wheal ≥3 mm)	139		40		50		49		
Cat	3	2.2	0	0.0	1	2.0	2	4.1	NS
Mite	10	7.2	3	7.5	2	4.0	5	10.2	NS
Alternaria	1	0.7	0	0.0	0	0.0	1	2.0	NS
Cypress pollen	6	4.3	0	0.0	1	2.0	5	10.2	0.016
<i>Artemisia</i> pollen	0	0.0	0	0.0	0	0.0	0	0.0	–
Olive pollen	10	7.2	2	5.0	4	8.0	4	8.2	NS
<i>Parietaria</i> pollen	2	1.4	0	0.0	1	2.0	1	2.0	NS
Grass pollen	5	3.6	0	0.0	1	2.0	4	8.2	0.036
Any allergen	27	19.4	5	12.5	8	16.0	14	28.6	0.052
Any pollen	18	12.9	2	5.0	6	12.0	10	20.4	0.031
Two or more allergens	7	5.0	0	0.0	2	4.0	5	10.2	0.028
Hay fever†	14	10.1	1	2.5	3	6.0	10	20.4	0.004

* Question number in ECRHS questionnaire shown in brackets. The sum does not add up to the total because of one missing value.

† Rhinitis and nasal allergy during season and a positive SPT to one or more pollens.

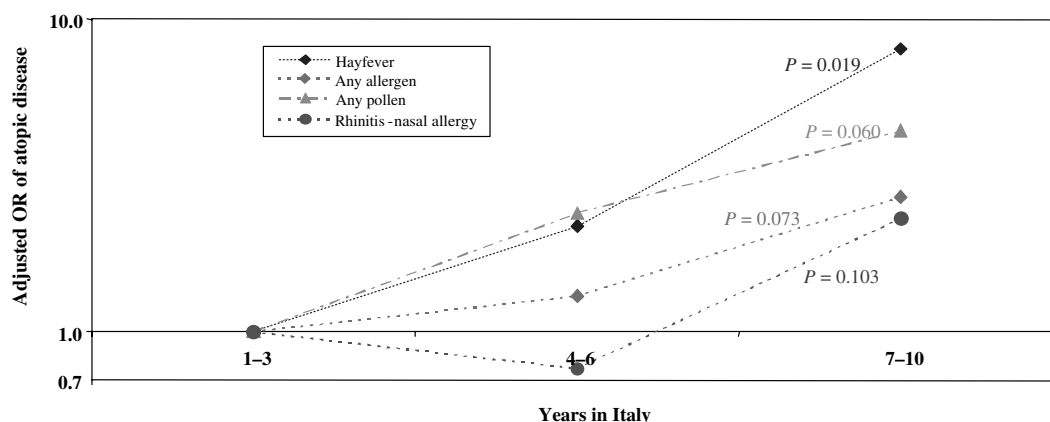


Figure 1. Odds ratio adjusted for sex and age of having hay fever, symptoms of rhinitis–nasal allergy and atopic sensitization according to years in Italy among Albanian migrants.

sex and age (Fig. 1; Table 1). Both subjects with reported asthma were negative to skin tests.

The geometric mean value of total serum IgE was 56.23 kU/l in women and 86.35 in men (71.93 kU/l overall). Only two of the 61 subjects tested (3.3%) had relatively high concentration of specific IgE (>17.5 kU/l); both of them for *Dermatophagoides pteronyssinus*. Only five subjects of the 61 examined had a RAST of class 3 or higher against at least one of the five common airborne allergens examined.

All the 61 sera examined contained IgG antibodies against HAV (100%, 95% CI: 94.0–100%) and 59/61

(96.7%, 95% CI: 88.6–99.6%) contained IgG antibodies against HSV-1. Forty-eight of the 61 sera (78.7%, 95% CI: 66.3–88.1%) were seropositive for IgG against HP and 31 (55.7%, 95% CI: 36.8–64.8%) contained IgG antibodies against TG.

Discussion

Asthma and allergy have been reported to have a very low prevalence in Albania (15). The different lifestyle, the lower number of families with pets, the less common

habit of smoking in women, the housing conditions and particularly the higher incidence of childhood infections might be advocated to explain the lower prevalence of asthma and allergy in Albania vs other countries with a similar Mediterranean climate (15). An additional reason, however, might be a higher incidence of infections, as previously proposed (15). Accordingly, we found a significantly higher prevalence of antibodies to HAV, HSV-1, HP and TG ($\times 95\%$ lower confidence limits: 94.0, 88.6, 66.3 and 36.8%, respectively) than among young Italian adults living in Central-Southern Italy (95% upper confidence limits: 28.9, 76.8, 19.9 and 25.7%, respectively) (11–12).

In Albanian migrants to Apulia the prevalence of asthma was similar to that observed in Albania, but lower than that reported for three similar Italian populations [1.3% vs 3.3%, 4.2%, 4.5% (16)] and never associated with positive skin tests. However, the prevalence of rhinitis symptoms in Albanian migrants (15.8%) was higher than that reported in Albania and similar in the Italian populations [12.5, 16.0, 16.9% (16)].

Moreover, the pattern of sensitization to inhalant allergens resembled that typical of Southern Italy, including a relatively high prevalence of sensitization to Olive (which is diffusely cultivated in Apulia and particularly in the area around Monopoli). This would suggest that changes in lifestyle may be responsible for novel sensitization to newly encountered pollens and of the onset of symptoms even in population samples with a low prevalence of allergic diseases in the country of origin. Similar observations were made by Ormerod et al. (14) in Asiatic migrants to England, by Rosenberg et al. (17) in

Ethiopic immigrants to Israel, and by Kalyoncu and Stalenheim (18) in migrants to Sweden (19).

Interestingly, we found that the prevalence of hay fever in Albania migrants was related to the length of residence in Apulia and in all rhinitic subjects in whom it was possible to obtain clear-cut information regarding the period when the allergic symptoms appeared (75% of cases), symptoms had started following immigration (data not shown). A positive association between respiratory symptoms and duration of residence in immigration countries has also been reported by Ormerod et al. (14) and by Powell et al. (20).

Data from our cross-sectional study suggest that the prevalence of food-borne orofecal infection is very high in Albania and that Albanian migrants to Italy, in spite of the low prevalence of allergic diseases and sensitization in their country of origin, manifest with time an increasing prevalence of sensitization to local allergens and nasal symptoms after migration to South of Italy. Longitudinal studies are necessary to evaluate whether this trend can be explained by a reduced exposure to infections or by other lifestyle or environmental factors differing between Albania and Southern Italy.

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References

1. WOOLCOCK AJ, PEAT JK, TREVILLON LM. Changing prevalence of allergies worldwide. *Progr Allergy Clin Immunol* 1995;**3**:167–171.
2. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998;**351**: 1225–1232.
3. STRACHAN DP. Hay fever, hygiene and household size. *Br Med J* 1989;**299**: 1259–1260.
4. VON MUTIUS E, MARTINEZ FD, FRITZSCH C, NICOLAI T, ROELL G, THIEMANN HH. Prevalence of asthma and atopy in two areas of West and East Germany. *Am J Respir Crit Care Med* 1994;**149**:358–364.
5. BRAUN-FAHRLANDER C, GASSNER M, GRIZE L, NEU U, SENNAUSER FH, VARONIER HS et al. Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. SCARPOL team. *Clin Exp Allergy* 1999;**29**:28–34.
6. ALM JS, SWARTZ J, LILJA G, SCHEYNIUS A, PERSHAGEN G. Atopy in children with an anthroposophic lifestyle. *Lancet* 1999;**353**:1485–1488.
7. BURNEY PG, LUCZYNSKA C, CHINN S, JARVIS D. The European Community Respiratory Health Survey. *Eur Respir J* 1994;**7**:954–960.
8. STRACHAN DP. Family size, infection and atopy: the first decade of the 'hygiene hypothesis'. *Thorax* 2000;**55**: S2–S10.
9. HOLT PG. Environmental factors and primary T-cell sensitisation to inhalant allergens in infancy: reappraisal of the role of infections and air pollution. *Pediatr Allergy Immunol* 1995;**6**:1–10.
10. MATRICARDI PM. Infections preventing atopy: facts and new questions. *Allergy* 1997;**52**:879–882.
11. MATRICARDI PM, ROSMINI F, FERRIGNO L, NISINI R, RAPICETTA M, CHIONNE P et al. Cross-sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus. *Br Med J* 1997;**314**:999–1003.
12. MATRICARDI PM, ROSMINI F, RIONDINO S, FORTINI M, FERRIGNO L, RAPICETTA M et al. Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study. *Br Med J* 2000;**320**:412–417.
13. MATRICARDI PM, ROSMINI F, PANETTA V, FERRIGNO L, BONINI S. Hay fever and Asthma in relation to markers of infection in the United States. *J Allergy Clin Immunol* 2002;**110**:381–387.

14. ORMEROD LP, MYERS P, PRESCOTT RJ. Prevalence of asthma and 'probable' asthma in the Asian population in Blackburn. *UK Respir Med* 1999;**93**: 16–20.
15. PRIFTANJI AV, QIRKO E, LAZZELL JC, BURR ML, FIFIELD R. Asthma and allergy in Albania. *Allergy* 1999;**54**: 1042–1047.
16. European Community Health Survey. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1996;**9**:687–695.
17. ROSENBERG R, VINKER S, ZAKUT H, KIZNER F, NAKAR S, KITAI E. An unusually high prevalence of asthma in Ethiopian migrants to Israel. *Fam Med* 1999;**31**:276–279.
18. KALYONCU AF, STALENHEIM G. Serum IgE levels and allergic spectra in migrants to Sweden. *Allergy* 1992;**47**: 277–280.
19. JOGI R, JANSON C, BJORNSSON E, BOMAN G, BJORKSTÉN B. Atopy and allergic disorders among adults in Tartu, Estonia compared with Uppsala, Sweden. *Clin Exp Allergy* 1998;**28**:1072–1080.
20. POWELL CVE, NOLAN TM, CARLIN JB, BENNETT CM, JOHNSON PDR. Respiratory symptoms and duration of residence in migrants teenagers living in Melbourne, Australia. *Arch Dis Child* 1999;**81**:159–162.