

URBAN VERSUS RURAL ENVIRONMENT – ANY DIFFERENCES IN AEROALLERGENS SENSITIZATION IN AN ALLERGIC POPULATION OF COVA DA BEIRA, PORTUGAL?*

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SUMMARY: Cova da Beira is an interior central region of Portugal, with a population of 93 000 inhabitants divided in urban and rural living areas. The aim of this study was to access the prevalence of aeroallergens sensitisation in an allergic population, according to the urban and the rural environmental exposure and according to age. 1096 patients observed for suspected allergic symptoms, for a five-year period (1995-2000) were submitted to skin prick tests and were included in this study. They were divided in two environmental exposure groups (A: urban; B: rural) and in to four age subgroups (subgroup I: ≤ 10 yr; subgroup II: 11-20yr; subgroup III: 21-40yr; subgroup IV: >40 yr). The total population included 444 male (40.5%) and 652 female (59.4%) with an average age of 26.5 ± 17.2 yr. 83% of the 1096 performed SPT were positive. The frequency of aeroallergens sensitisation, comparing the urban versus the rural environment, was respectively: *D. pteronyssinus* 32% and 34.7%, *D. farinae* 28.5% and 30.7%, moulds mixture 15.3% and 12%, cat dander 17.1% and 15.2%, dog dander 11% and 10%, grasses mixture 51.3% and 36.4%, *Parietaria judaica* 29.4% and 14%, *Olea europea* 30.2% and 23.3%.

The sensitisation to indoor aeroallergens, was similar in all the age subgroups and it was lower than that to pollens. There were important differences concerning the pollen sensitisation, when comparing the urban and the rural environmental exposure. We admit that pollution could enhance the sensitisation to pollens in the urban environment.

Key-words: Aeroallergens - Allergic sensitisation - House dust mite - Pollen - Moulds - Urban environment - Rural environment.

INTRODUCTION

Cova da Beira is a inland central region of Portugal, located in the latitude $40^{\circ} 16'$, the longitude $7^{\circ} 30'$ and the altitude of 600m above the sea level, and has a continental climate.

The local flora includes *Castanea*, *Olea*, *Pinus*, *Ficus*, *Eriobotrya*, *Acacia*, *Prunus*, *Platanus*, *Pseudotsuga*, *Tilia*, *Rubus*, *Ailanthus*, *Cytisus*, *Umbilicus*, *Rumex*, *Parietaria*, *Mercurialis*, *Polypodium* and *Sedum*. The gardens in this city include *Vitis*, *Arundo* and *Anagallis*, *Brassicaceae*, *Labiatae*, *Compositae*, *Tilaceae* and *Platanaceae*. In the valley of this region there are cultivated fruit trees.

In the first polinic map carried out throughout the whole country (March 1999 - March 2000), this area had the highest pollen counts in Portugal (SPAIC/Schering-Plough) (1). The genera more frequently identified were *Olea* (31%), *Castanea sativa* (21%), grasses (7%), *Urtica* type B (5%), *Urtica* type A (5%),

Platanus (5%), *Ailanthus* (2%), *Rumex acetosella* (1%), *Cupressacea* (1%), *Quercus deciduous* (1%), *Quercus coccifera* (1%) and other pollens (16%).

The 93 000 inhabitants of this region constitutes a homogeneous population (without any external interferences, namely migration) that is distributed in both urban and rural living areas.

The skin prick tests (SPT) are an easy method to determine the aeroallergens sensitisation in epidemiologic studies (2).

The aeroallergen sensitisation prevalence in general population is related to different factors. In each region, the sensitisation reflects the allergens exposure and the influence of other environmental factors such as the pollution (2-5).

Nowadays the national aerobiology networks in Europe, using the same methodology, integrate the European Pollen Information Network, and made available data concerning the pollen concentration of different species (6).

The different clinical studies available on literature are difficult to compare, because of the heterogeneity

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* MEETING of GAILL Alcacer-Portugal 23-25 April 2005.

of the design, the very discrepant samples, and the different aeroallergens tested. The Position Paper published in 1998 is a relevant document that extensively analyses all the studies concerning pollen sensitisation in Europe (3). The EFA study, performed in 2000 (7), showed the impact of the allergic diseases in 10 countries, and this information was consistent with the European Allergy White Paper contents (8).

There are a highly heterogeneity of sensitisation throughout Europe. The genetics, the climate, the geography, the local flora (changes related to the forest fires, agricultural methods and cultivation, importation of non-native species), the pollution and the demography are responsible for these different patterns.

The pollen sensitisation is higher in urban than in rural areas. This issue depends on several factors, mainly the pollution, particularly vehicle emissions, and the increased concentration of ozone in the air (9). The risk is also increased in people living in high buildings, and in urban areas with wide greenland zones (10).

The components of air pollution interact with inhalant allergens carried out by pollen grains and may enhance the risk of both atopic sensitization and exacerbation of symptoms in sensitized subjects (11, 12), since urban air pollution affects both airborne allergenic pollen and the airways of exposed subjects.

The aeroallergens sensitisation in this region has never been studied before.

The aim of this study was to analyse the aeroallergens cutaneous reactivity in an allergic population of Cova da Beira, as well as its prevalence according to the environmental exposure influence and according to the age groups.

METHODS

During a five-year period (from May 1995 to May 2000) 1790 consecutive outpatients were observed for suspected allergic symptoms. The 1096 patients that underwent skin prick tests (SPT) to aeroallergens were included in this study. The aeroallergens extracts tested (ALK-Abelló, Spain), included at least 20 local flora species: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Acarus siro*, *Blattella* mixture, moulds mixture, *Candida albicans*, cat and dog dander, grasses mixture, *Parietaria judaica*, *Artemisia vulgaris*, *Plantago lanceolata*, *Chaenopodium album*, *Olea europea*, *Robinia pseudoacacia*, *Platanus aceri-*

folia, *Tilia cordata*, *Pinus radiata* and *Betula pubescens*. According to the clinical history there were performed SPT with other aeroallergens such as storage mites and another pollen allergens including: *Dactylis glomerata*, *Festuca pratensis*, *Lolium perenne*, *Phleum pratense*, *Secale cereale*, *Triticum aestivum*, *Avena sativa*, *Poa pratensis*, *Holcus lanatus*, *Crisanthemum leucanthemum*, *Taraxacum officinalis*, *Ambrosia tryphida*, *Urtica dioica*, *Alnus glutinosa*, *Eucalyptus globus*, *Fraxinus excelsior*, *Quercus robur*, *Amygdalus communis*, *Mallus pumilla*, *Pyrus communis*, *Prunus cerasus* and *Prunus persica*. SPT were performed according to the international guidelines (2). It was considered positive for a wheal 3 mm above the negative control.

The patients were divided according to the environmental exposure in two groups (Group A urban and Group B rural) and according to age into four age subgroups (Subgroup I: ≤ 10 years old; Subgroup II: 11-20 years old; Subgroup III: 21-40 years old; Subgroup IV: ≥ 41 years old). We analysed the prevalence of the aeroallergens sensitization of the total population and according both to environmental exposure and to age.

RESULTS

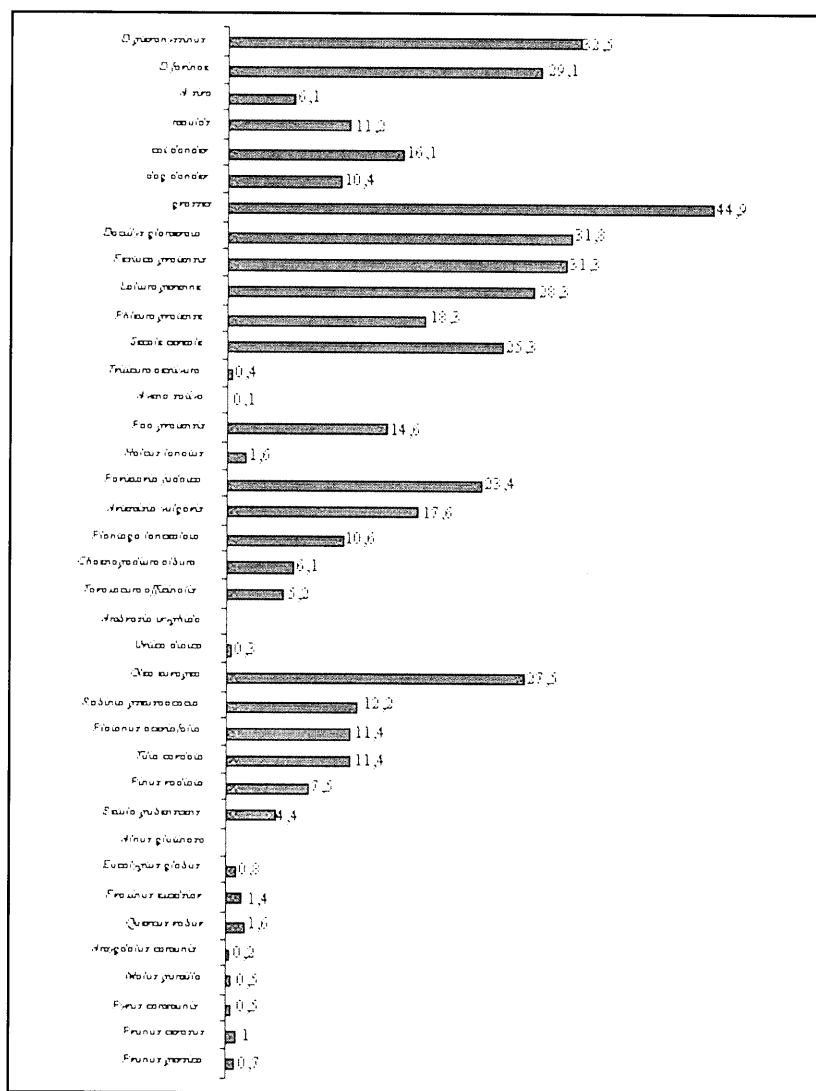
The demographic data of the 1790 consecutive outpatients observed are represented in table 1. We included in this study 1096 patients submitted to SPT (table 2). This total population included 444 male (40.5%) and 652 female (59.4%) with an average age of 26.5 ± 17.2 yr. These patients were divided in 690 urban living patients and 406 rural living patients. In each environmental exposure group, the patients were divided in four age subgroups (table 2). The Graphic 1 represents the aeroallergens sensitisation prevalence in the total population. The Graphic 2 (2A-2D) shows the aeroallergens sensitisation prevalence concerning environmental exposure. The aeroallergens sensitisation prevalence concerning the age subgroups is represented in Graphic 3A for the urban environmental exposure group and in Graphic 3B, for the rural environmental exposure group B.

	Total	Group A	Group B
n	1790	1138	652
M:F	0.7:1	0.74:1	0.68:1
Age(years)	30.5 ± 20.9	29.8 ± 20.3	31.6 ± 22.0

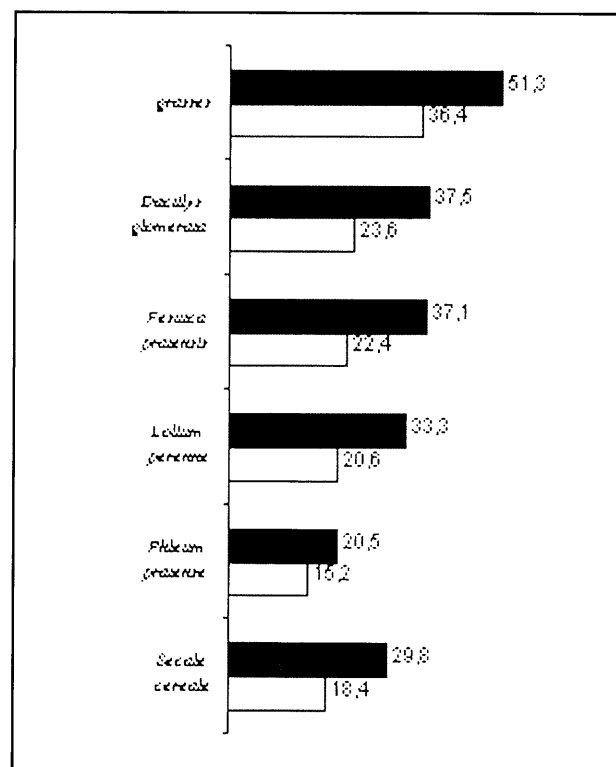
Table 1: Demographic data: total population and environmental exposure groups (A = urban; B = rural).

		n	M:F	Age(years)	SPT	
					positive	negative
Total		1096	0.68:1	26.5 ± 17.2	910 (83%)	186 (17%)
Group A (urban)	Total	690	0.7:1	22.2±16.8	592 (86%)	98 (14%)
	I	152	1.6:1	6.5±2.3	131 (86.1%)	21 (13.9%)
	II	139	0.9:1	15.2±2.8	131 (94.2%)	8 (5.8%)
	III	247	0.5:1	29.9±5.6	219 (88.6%)	28 (11.4%)
	IV	152	0.4:1	51.6±7.9	111 (73%)	41 (27 %)
Group B (rural)	Total	406	0.61:1	26.5±17.8	319 (78.5%)	87 (21.5%)
	I	98	0.9:1	6.6±2.4	79(80%)	19 (20%)
	II	83	1:1	15.1±2.7	73 (88%)	10 (12%)
	III	131	0.5:1	29.8±5.6	104 (79%)	27 (21%)
	IV	94	0.3:1	52.8±8.8	63 (67%)	31 (33%)

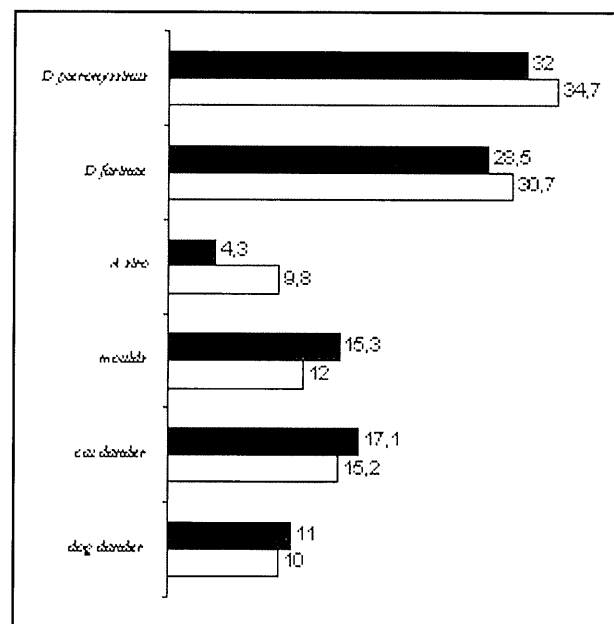
Table 2: Demographic data of patients submitted to SPT, concerning the total population, the environmental exposure groups (A = urban; B = rural) and the age subgroups (I: ≤ 10 years; II: 11-20 years; III: 21-40 years; IV: ≥ 41 years).



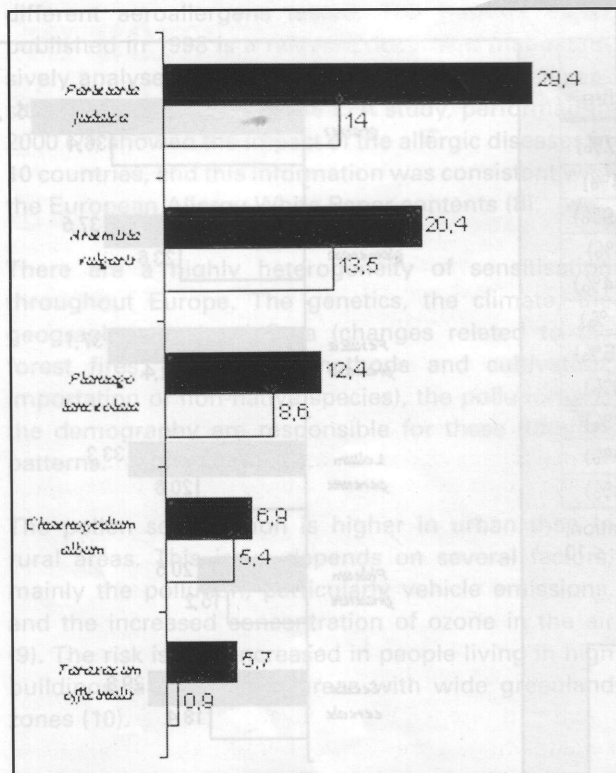
Graphic 1: Aeroallergens sensitisation prevalence in the total population (%).



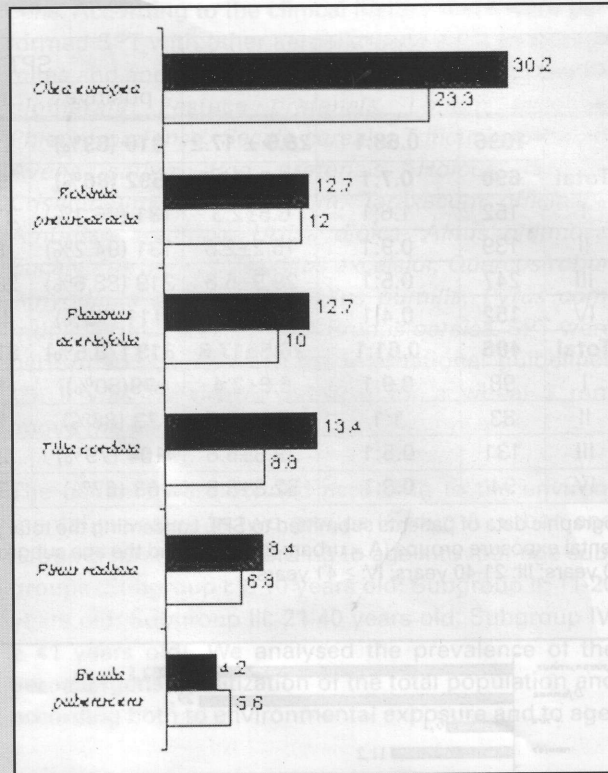
Graphic 2b: Grasses sensitisation prevalence (%) concerning to the environmental exposure groups: ■ urban exposure and ■ rural exposure.



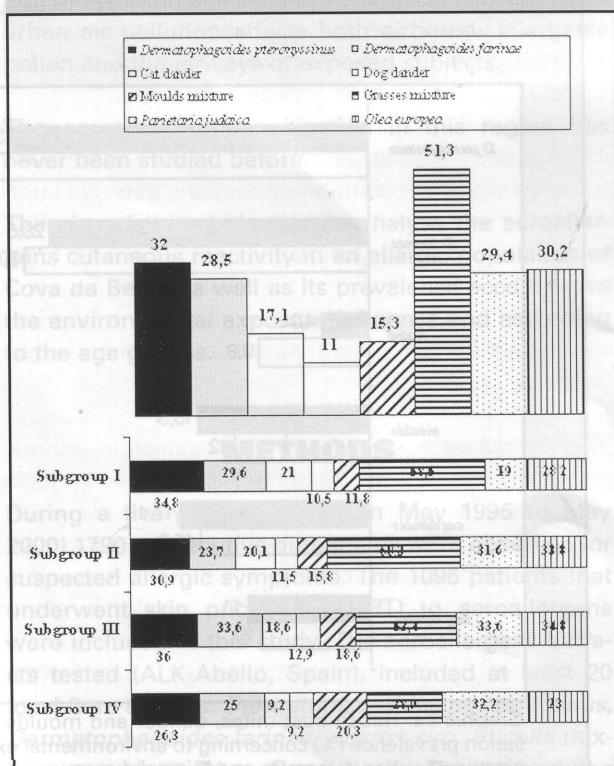
Graphic 2a: House dust mites, dander and moulds sensitisation prevalence (%) concerning to environmental exposure groups: ■ urban exposure and ■ rural exposure.



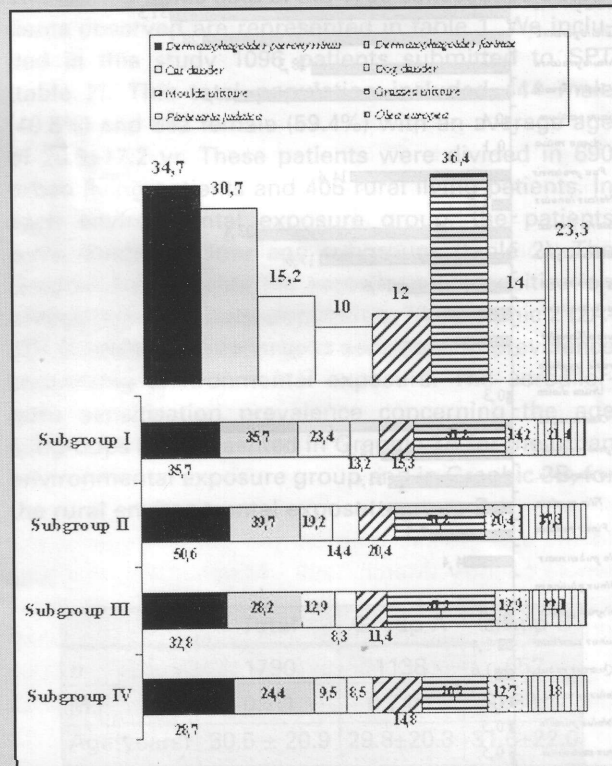
Graphic 2c: Weeds sensitisation prevalence (%) concerning the environmental exposure groups: ■ urban exposure and ■ rural exposure.



Graphic 2d: Trees sensitisation prevalence (%) concerning the environmental exposure groups: ■ urban exposure and ■ rural exposure.



Graphic 3a: The most representative aeroallergens sensitisation prevalence (%) in the urban exposure group (A), concerning the total population and the age subgroups.



Graphic 3b: The most representative aeroallergens sensitisation prevalence (%) in the rural exposure group (B), concerning the total population and the age subgroups.

DISCUSSION

The population studied showed a high aeroallergens sensitisation (83%) with the urban exposed population presenting the highest frequency of aeroallergens sensitisation (86%) compared to the rural exposed population (78.5%).

The cutaneous reactivity to the tested aeroallergens revealed a sensitisation prevalence in the general population: grasses mixture (44.9%), *D. pteronyssinus* (32.5%), *D. farinae* (29.1%), *Olea europea* (27.5%), *Parietaria judaica* (23.4%), cat dander (16.1%), *Artemisia vulgaris* (17.6%), *Robinia pseudoacacia* (12.2%), *Platanus acerifolia* (11.4%), *Tilia cordata* (11.4%) moulds mixture (11.2%), *Plantago lanceolata* (10.6%), dog dander (10.4%), and *Pinus radiata* (7.5%).

Grasses sensitisation prevalence was the highest in the general population. The most relevant grasses species were *Dactylis glomerata* (31.8%), *Festuca pratensis* (31.3%), *Lolium perenne* (28.3%), *Secale cereale* (25.3%), *Phleum pratense* (18.3%) and *Poa pratensis* (14.6%). Grasses aeroallergens are important all over Europe (3,4). They are the most relevant polinic aeroallergens in Portugal (13-21), with a sensitisation prevalence ranging from 12.6% to 36%.

Sensitisation to house dust mites (HDM) was the second most important in this population. In other regions of Portugal (16-20, 22-24), HDM sensitisation prevalence ranges from 14.3% to 97% (16-20, 22-28), being the highest followed by grasses sensitisation.

The sensitisation prevalence to *Olea europea* was the third most relevant (27.5%). It was higher than in other portuguese studies (16, 17), but similar to studies performed in Southern european areas (3,29,30). *Olea europea* has been recognized as one of the most important causes of seasonal respiratory allergy in the Mediterranean areas (31).

The sensitisation to *Parietaria judaica* was 23.4%, a value higher than in other portuguese (16-18) and spanish (4, 29) studies, but lower than in italian studies (4, 30). *Parietaria* is a widespread plant in the south of Europe, mainly in the coastal areas, reaching the highest ratios of allergic sensitisation, and inducing severe pollinosis in adolescent and young adult patients in these areas. However, there has been an obvious increase in children in the last years (32).

Sensitisation to moulds showed lower values compared to pollens, HDM and dander. Moulds sensitisation prevalence was 11.2% and it was similar to values founded by other authors (23, 33). However, this

result is very discrepant from other portuguese studies (17-19, 34) showing lower values (3%). International studies refer to very discrepant sensitisation prevalence values (35).

There are much data available concerning pollen concentration of different species with a methodology that permit to compare the distinct national networks in Europe (6). But it is very difficult to compare the different clinical studies available on literature, because of the heterogeneity of the design, the very discrepant samples, and the different aeroallergens tested. An interesting study in Liguria, Italy, evaluated during 10 years the airborne pollen concentration and the skin sensitisation to aeroallergens (30). *Parietaria*, grass and *Olea* pollen allergy were the most prevalent in the sensitised patients, but there were no differences between the individuals living in the coastal areas and those living in the inland areas.

Cova da Beira is an inland region of Portugal. The urban area is an industrialised town surrounded by cultivated areas. We analysed the aeroallergens sensitisation in the different environmental exposure groups. We observed that HDM, dander and moulds sensitisation prevalence was similar in both groups (graphic 2A). However, the pollen sensitisation prevalence was different comparing the urban and the rural living groups. Grasses, weeds and *Olea europea* sensitisation prevalence was greater in the urban group (graphic 2B-2D). This difference was not so relevant for the other tree sensitisation prevalences (graphic 2D). In the urban environmental exposed group, pollen sensitisation prevalence was more relevant than HDM, dander and moulds sensitisation prevalence. In the rural environmental exposed group, grasses sensitisation prevalence was similar to the HDM sensitisation prevalence. Even the younger groups (subgroup I and subgroup II) presented this aeroallergens sensitisation pattern. Comparing to the rural living group, the urban living children and adolescent were more frequently sensitised to pollen, namely Grasses, *Parietaria judaica* and *Olea europea* (graphic 3A and 3B). Grasses sensitisation occurred very early in both environmental exposure groups, without differences concerning the age subgroups. However, it was higher in the urban living group.

Parietaria judaica sensitisation was also higher in all the urban exposed age subgroups, comparing to the rural living age subgroups. However, it was not constant in the age subgroups. Indeed, it increased in the urban living groups according to age and it was similar in all the age rural living subgroups.

The *Olea europea* sensitisation was higher in all the age urban living subgroups, comparing to the age rural living subgroups. The younger subgroups presented a similar sensitisation to the older subgroups.

In the studied population, grasses allergens were the most relevant concerning the pollen sensitisation in this population, in the total population and in all the environmental exposure groups and in all the age subgroups. All the other tested pollens induced important cutaneous reactivity sensitisation prevalence, but with more relevance in the urban environmental exposed group, even in younger subgroups.

The aeroallergen sensitisation prevalence in the general population is related to different factors. In each region, the sensitisation reflects the allergens exposure and the influence of other environmental factors such as the pollution (2-5).

Indeed, the interaction between urban air pollution and pollen allergy has been studied by several authors. Among the components of air pollution there are frequently high concentrations of ozone favoured by sunny days and ultraviolet radiations. The diesel exhaust particles (DEP) are the major contribute to particulate pollution. In sunny cities, the DEP and ozone reach high levels during periods of high pressure in the summer, known as "summer smogs". Several reports correlated these summer smogs with asthma exacerbations. Reports from Japan refers that a higher prevalence of allergy to cedar pollen has been observed in people living close to motorways, as compared with people living in a more rural environment close to a cedar forest and being exposed to the same number of cedar pollens (36).

Indeed, it has been explained that the components of air pollution interact with inhalant allergens carried by pollen grains and may enhance the risk of both atopic sensitization and exacerbation of symptoms in sensitized subjects (11, 12, 37), since urban air pollution affects both airborne allergenic pollen and the airways of exposed subjects. The air pollution (particulate matter, ozone) causes airway mucosal damage and impaired mucociliary clearance. This may facilitate the access of inhaled allergens to the cells of the immune system. In addition, vegetation reacts with air pollution and environmental conditions and influences the plant allergenicity. Several factors influence this interaction, including the type of air pollutants, plant species, nutrient balance, climatic factors, degree of airway sensitization and hyperresponsiveness of exposed subjects.

DEP may promote inflammation and the allergic state through three mechanisms: may act as a carrier for

the transport of allergens into the airways by adsorbing allergenic proteins onto their surface; may act as an adjuvant in promoting the switching of B cells to produce allergen-specific IgE; may affect a number of downstream immunological mechanisms, leading to increased prevalence or increased severity of allergic and asthmatic disorders

By acting as a carrier of allergens, DEP might deliver allergenic material to the airways. Some allergens, such as the major rye grass pollen allergen Lol p1, bind specifically to DEP (37). In an in vitro study of allergen adsorption to indoor-suspended particulate matter (ISPM) and DEP Fel d1, Can f1 and Bet v1 were all found on the surface of ISPM whereas Der p1 was not. However, all four allergens were found to be absorbed to DEP (38).

In urban areas pollen grains can become coated with fuel residues and combustion products. The binding of pollen or other inhaled allergens to DEP may modulate the allergenic epitopes and thereby increase their allergenicity (39).

DEP have been shown to have a direct enhancing effect on IgE production (40). In humans, diesel particles have been shown to potentiate nasal IgE production four days after challenge with DEP (41). There was also an increase in the number of IgE-secreting cells in lavage but no increase in IgA-secreting cells. Similarly, nasal challenge with a combination of DEP and allergen has been shown to induce higher ragweed-specific IgE and IgG4 responses compared with DEP or ragweed alone but with similar total IgE levels (42).

In addition to these allergen-specific effects, exposure to DEP alone causes an inflammatory response in the airways, which may then prime the airways and increase the magnitude of the response to allergen challenge. Inhalation of DEP damages the bronchial epithelium and cilia, thereby impairing their ability to act as a biological barrier against inhaled substances (43). Allergens may therefore remain on the epithelial surface for longer periods of time, and increase penetration of allergen across the respiratory mucosa (44).

In vitro, DEP induce eosinophil degranulation and adhesiveness to epithelial cells without changing the eosinophil survival rate. These results indicate that DEPs may play a significant role in the promotion of airway hypersensitivity induced by enhanced eosinophil infiltration and degranulation (45).

In conclusion, Cova da Beira is an inland region of Portugal with a very high pollen sensitisation prevalence, comparing to the other regions of the country and even with the available European studies. The high pollen

counts for long periods of time, could explain these results, even in very young patients. However other factors, such as environmental exposure, are obviously relevant. This study observed that urban living patients presented the higher rates of pollen sensitisation. HDM, dander and moulds sensitisation was similar in both groups. Our results enhance the environmental exposure as an important factor contributing to these differences.

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