

IMMUNOALLERGIC DISORDERS IN THE ELDERLY

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ABSTRACT

Although allergic diseases have become increasingly prevalent in the elderly, there are few data on this population. Through a retrospective analysis of the electronic medical records of patients aged 65 years and above followed in our Immunoallergy Unit, we aimed to characterize the immunoallergic diseases of the elderly. The most common disorders were respiratory diseases (n=185; 50%), mucocutaneous diseases (n=113; 31%), drug allergy (n=31; 8%), food allergy (n=9; 2%), and anaphylaxis (n=9; 2%). Use of specific immunotherapy was residual (n=1; 1%). There was an association between anaphylaxis and both, drug ($p=0.004$) and food ($p=0.013$) allergies. Non-allergic rhinitis and bronchial asthma were more frequent in females, and ACE inhibitors/ARB induced-angioedema in males. Recognizing the characteristics of immunoallergic diseases in the elderly and the specificities of this age group is paramount in providing these patients with the best possible care.

Key words: elderly, old-aged, allergy, immunoallergic, prevalence

LIST OF ABBREVIATIONS

ACE - Angiotensin-converting-enzyme

ACO - Asthma-COPD overlap

ARB – Angiotensin II receptor blockers

CHULC - *Centro Hospitalar Universitário de Lisboa Central*

CI – Confidence interval

COPD - Chronic obstructive pulmonary disease

DRESS - Drug reaction with eosinophilia and systemic symptoms

IAL - Immunoallergology

IgE - Immunoglobulin E

NSAID – Nonsteroidal anti-inflammatory drug

INTRODUCTION

In recent years, the average life expectancy of the population has been increasing, particularly in developed countries. The World Health Organization considers elderly people those over the age of 65 in developed countries, and those over the age of 60 living in developing countries¹. Thus, the elderly population has increased over the past few years. In Portugal, 20.1% of the population is 65 or older², 19.4% is the percentage in Europe³. The diseases of this age group have become more frequent and complex, and allergic disorders (such as respiratory and mucocutaneous diseases, drug hypersensitivity, and food allergy) are no exception^{4,5}. Although allergic conditions are often thought of as childhood disorders, they often persist into older age and can occasionally make its initial appearance in the elderly⁶. Besides, clinical manifestations may be less straightforward than in younger age groups, hampering the recognition of the disease, and resulting in a more complicated differential diagnosis⁶. As most studies regarding immunoallergic disorders do not include the elderly population, only limited data is available^{6,7} on its frequency and characteristics, making their management even more difficult.

OBJECTIVE

We aimed to characterize the elderly population followed in our outpatient Immunoallergology (IAL) Unit regarding their immunoallergic diseases. With this study, we intended to focus our attention on this particular group of patients, with the ultimate goal of improving the care that is provided to them. Thus, we hope to contribute to a better understanding of the allergic diseases and their management in this age group with numerous specificities.

METHODS

Patient selection

We performed a retrospective analysis of patients aged 65 years and older followed between 2009 and 2019 in the IAL outpatient Clinic at *Centro Hospitalar Universitário de Lisboa Central* (CHULC), in Portugal. Referral to our IAL Unit is done through the national Immunology network. A total of 31,758 patients attended our Unit between 2009 and 2019, of which 1,721 (5.4%) were elderly. Based on an estimated rhinitis prevalence of 50%, in our population, with 5% error margin and a CI of 97%, we obtained a sample size of 370 patients. Randomization was performed through the Microsoft Excel® RAND function. Based on our previous experience, we estimated to lose 25-30% of patients because some of the clinical records from the period between 2009 and 2014 were not accessible in electronic format, as this represents the transition period from manual to electronic medical records in our Unit. Thereby, we included a total of 480 patients. Patients with incomplete (n=1) or without filled electronic clinical records (n=109) were excluded and thus, a total of 370 patients were analysed.

Data collection

Data was collected through the manual review of the electronic medical records.

Definitions

For the analysis of the immunoallergic diseases, we obtained the diagnosis registered by the assistant physician in the clinical files. Respiratory diseases, mucocutaneous diseases, drug allergy, food allergy, and other less frequent immunoallergic diseases were considered. Rhinitis, bronchial asthma, asthma-chronic obstructive pulmonary disease overlap (ACO), and Churg-Strauss syndrome were included in the respiratory diseases subgroup. In the mucocutaneous diseases subgroup we included angioedema without urticaria, urticaria with or without angioedema, contact dermatitis, and atopic dermatitis. The diagnosis of food allergy was made through the medical history, tests for sensitization, and in cases of doubt, oral food challenges. The diagnosis of drug hypersensitivity was based on the clinical history and, when appropriate, skin prick tests, intradermal tests, and drug provocation tests. All patients whose drug allergy was excluded underwent drug provocation tests.

Statistical analysis

The statistical analysis was made with IBM SPSS Statistics version 26 for Windows. The variables gender, age immunoallergic diseases, and sensitization profile were analysed.

The normal distribution of continuous variables was tested using the Kolmogorov-Smirnov test and by visual analysis of the histogram. The non-parametric variables assessed were expressed as median and interquartile range. A comparison between the categorical variables was made using

the chi-squared test or the Fisher's exact test with Bonferroni corrections, as appropriate. All statistical tests were bilateral and with a 5% significance level.

Data protection

The study protocol was reviewed and approved by the local ethics committees.

RESULTS

Characterization of population

The median (P25-P75) age of the patients in our sample was 75 (71-81) years. There was a predominance of the female gender (n=261; 71%). For most immunoallergic diseases, there was no statistically significant difference in gender distribution; there were, however, some exceptions, namely non-allergic rhinitis and bronchial asthma, more frequent among females, and ACE inhibitors/ARB induced-angioedema, more common in males (Table I).

The frequency of different groups of immunoallergic disorders is shown in figure 1. The most common diseases were respiratory diseases (n=185; 50%), mucocutaneous diseases (n=113; 31%), drug allergy (n=31; 8%), food allergy (n=9; 2%), and anaphylaxis (n=9; 2%). Immunoallergic diseases were excluded in 16% (n=61) of patients.

Respiratory diseases

Respiratory diseases were the most common disorders affecting these elderly patients (n=185; 50%), with rhinitis (n=169; 46%), and bronchial asthma (n=73; 20%) being the most frequent diagnoses. The concomitant diagnosis of rhinitis and bronchial asthma was present in 31% (n=58) of these individuals. The sensitization profile for aeroallergens was assessed in 162 patients (88%), through skin prick test and/or specific serum IgE: 57% (n=92) were sensitized to aeroallergens, as shown in Table II. Sensitization to a single aeroallergen group was found in 68% (n=63): either house dust mite, (n=32; 51%) or pollen (n=31; 49%). All sensitized patients to pet or mold allergens, were also sensitized to other allergen groups.

Specific immunotherapy to inhalant allergens was being administered to only one patient in our sample. This patient had allergic rhinitis and was taking subcutaneous immunotherapy for grass pollen.

Considering the patients with rhinitis, the sensitization profile was obtained in 93 % (n=157), with 58% (n=91) classified as allergic rhinitis. Among the 66 patients with non-allergic rhinitis (42%), senile rhinitis was diagnosed in 15% (n=10). Concomitant diagnosis of sinusitis was found in 7% (n=11) of rhinitis patients, of which 64% (n=7) also had nasal polyposis. Nasal surgery was

performed in 57% (n=4) of the patients with rhinosinusitis and nasal polyposis, and the remaining (n=3; 43%) were managed with medical therapy, namely topical nasal glucocorticoids.

In what concerns asthma, most of the patients in our sample had disease onset after the age of 40 (76%; n=39). Asthma onset before the age of 40 was recorded in 12 cases (24%). Information on the age of asthma onset was missing from the electronic medical records of the remaining 22 patients. The sensitization profile of the patients with bronchial asthma was evaluated in 82% (n=60), and sensitization to aeroallergens was found in 63% of them (n=38).

Allergic asthma was more common among patients with disease onset before the age of 40 (80%; n=8 of 10 patients with skin prick tests or specific serum IgE) than among patients with asthma onset after the age of 40 (52%; n=16 of 31 patients with skin prick tests or specific serum IgE). ACO was diagnosed in 8% (n=6).

None of these patients were managed with biological therapies.

Other respiratory diseases were rare. Churg-Strauss syndrome was diagnosed in one patient (0.3%), well controlled with daily oral 5 mg of equivalent prednisolone; another one (0.3%) had nonsteroidal anti-inflammatory drugs (NSAID)-exacerbated respiratory disease.

Mucocutaneous diseases

Mucocutaneous disorders were the second most frequent subgroup of diseases (n=113; 31%), with the most common being angioedema without urticaria (n=55; 15%), urticaria (n=46; 12%), and contact dermatitis (n=12; 3%).

The aetiology of angioedema without urticaria, could not be identified in 53% (n=29) of the affected patients, thus classified as having idiopathic angioedema. In 42% (n=23), it was attributed to angiotensin-converting-enzyme (ACE) inhibitors and in 2% (n=1) to angiotensin II receptor blockers (ARB). From the subgroup of patients with ACE inhibitors-induced angioedema, an ARB was tried as alternative in 59% (n=9), all with tolerance. C1 inhibitor deficiency was found in 4% (n=2) of the patients with angioedema; a haematological neoplasm was diagnosed in one of them (acquired deficiency) and the other one did not complete the investigation.

Urticaria was diagnosed in 46 patients, most of them with chronic urticaria (74%; n=34). Chronic urticaria was classified as spontaneous in 82% (n=28) of the cases and as inducible in the remaining (18%; n=6). Patients with chronic spontaneous urticaria were mostly managed with oral H1 antihistamine agents, taken once a day (n=18; 64%), twice a day (n=8; 29%), or four times a day (n=2; 7%). Because of lack of response to antihistamines, one patient received treatment with cyclosporin, which had to be stopped after one year due to haematological toxicity. This patient was then treated with oral H1 antihistamine agents taken four times a day and mirtazapine, with a good response and no adverse effects. Treatment with omalizumab had not been started in any

patient in our sample. Among the patients with inducible urticaria, dermographism was diagnosed in 83% (n=5), and cold-induced urticaria in 17% (n=1); all of them were well controlled with oral H1 antihistamine agents taken twice a day (n=3; 50%), three times a day (n=1; 17%), or as needed (n=2; 33%). Acute urticaria was diagnosed in 26% (n=12) of urticaria patients, being idiopathic and self-limited in all cases.

Twelve patients (3%) had a diagnosis of contact dermatitis. During the etiological investigation, epicutaneous tests were carried out. Several agents were identified, with nickel (n=4; 33%) and caines (n=4; 33%) being the most common ones.

In our sample no patient was diagnosed with atopic dermatitis.

Drug allergy

Investigation of suspected drug hypersensitivity was carried out in 21% (n=78) of patients (Table III). The diagnosis was excluded in 50% (n=39), 14% (n=11) did not complete the investigation, and the remaining 40% (n=31) were diagnosed with drug allergy. Three patients (4%) were studied for more than one drug allergy.

Mild mucocutaneous symptoms were the most frequent clinical manifestation in patients with confirmed drug allergy (n=24; 77%). In 16% of patients (n=5), anaphylaxis was the clinical presentation (local anaesthetic, iodinated contrast agent, inhaled budesonide, NSAID, and gliptin) and one patient (3%) had a severe cutaneous adverse reaction, namely drug reaction with eosinophilia and systemic symptoms (DRESS) due to allopurinol.

In the patients who did not complete the investigation (n=11; 14%) and in those in whom drug allergy was excluded (n=39; 50%), mild mucocutaneous symptoms were the most frequent manifestation (n=8; 73% and n=26; 67%, respectively). In both groups, unspecific symptoms were the second most frequent clinical presentation (n=3; 27% and n=10; 26%, respectively) and no severe reactions were registered.

Food allergy

Food allergy was diagnosed in 2% (n=9) of the patients (Table IV). The most implicated food group was the crustaceans (n=6; 67%); a concomitant sensitization to house dust mite was found in four of these patients. The two patients with allergy to fresh fruits also had allergy to nuts, with sensitization to lipid transfer protein, both with a concomitant sensitization to pollens. There was no diagnosis of milk, eggs, cereals, or profilins allergy. Most patients presented mild mucocutaneous reactions (n=6; 67%). However, there were 3 cases of anaphylaxis (33%), all due to nuts.

Other less frequent immunoallergic diseases

Hymenoptera venom allergy was confirmed in 2 patients (1%). Both presented with anaphylactic reaction, one after a bee sting and the other one after a wasp sting. Specific immunotherapy was administered only to the former since the latter refused it. Hymenoptera venom allergy was excluded in another patient whose symptoms were attributed to a toxic reaction after being stung by a swarm of about 200 bees.

Common variable immunodeficiency was diagnosed in one patient (0.3%), controlled with regular administration of subcutaneous immunoglobulin.

There was no record of latex allergy in this sample.

Associations between immunoallergic diseases

Allergic rhinitis had a statistically significant association with allergic bronchial asthma ($p < 0.001$) and food allergy ($p = 0.012$).

Non-allergic rhinitis had a statistically significant association with non-allergic bronchial asthma ($p < 0.001$).

Confirmed drug allergy ($p = 0.004$) and food allergy ($p = 0.013$) were significantly associated with anaphylaxis.

No additional statistically significant associations were found between the other analysed disorders.

DISCUSSION

In our outpatient Unit, the elderly population accounted for a minority of the patients observed. However, we expect that an increasing number of older people will be referred to allergy clinics as the current younger allergic cohorts age and are joined by those developing allergies in later life⁷. More targeted studies are needed to understand if this expected increase is only due to the ageing of the general population, or if immunoallergic diseases are also becoming more prevalent and recognized in the elderly.

Respiratory diseases were the most common immunoallergic disorders affecting our sample, with rhinitis and bronchial asthma being the most frequent. In line with previously published data, we found sensitization to aeroallergens in 57% of these patients, with a clear predominance of house dust mite and pollen allergens^{4,8-10}. Pollen sensitization varies worldwide depending on species prevalence in each region. In our sample, similarly to the available data in our country in younger ages, the most commonly involved pollen allergens were wall pellitory, grass, and olive tree¹⁰. However, while grass pollen represents the most common pollen sensitization in the general population¹⁰, sensitization to wall pellitory and grass pollen were equally common in our elderly

sample. Most patients were sensitized only to a single group of aeroallergens – either house dust mites or pollens – and less common sensitizations, like pet epithelia or molds, were only found in polysensitized patients.

Bronchial asthma was one of the more common disorders, alerting to the importance of learning strategies to deal with the particular problems presented by these patients: difficulty with therapy administration due to their less dexterity, reduced self-management capability associated with less disease awareness, and frequent cognitive impairment¹¹. In congruence with previous studies^{12,13}, while asthma diagnosed before the age of 40 was more often allergic, late onset asthma was more often non-allergic. Moreover, whereas atopic disease usually begins in childhood and early adulthood, non-allergic asthma may be related to cumulative exposure to irritants such as occupational exposures and smoking and thereby becomes evident only later in life¹³.

In our sample, some patients were diagnosed with ACO in concordance with its greater prevalence in older patients¹⁴. A substantial percentage of elderly patients had a simultaneous diagnosis of allergic rhinitis and allergic bronchial asthma, with a statistically significant association between these diseases, similarly to what is found in younger patients⁵. Non-allergic rhinitis was also a common diagnosis, a result we could expect since it is a frequent condition in this age⁴. We have also found a significant association between non-allergic rhinitis and non-allergic asthma, in line with previously published data¹⁶. The diagnosis of local allergic rhinitis was not taken into account because nasal provocation tests were not implemented in the routine diagnostic approach. Thus, we admit that some patients may have been wrongly diagnosed with non-allergic rhinitis, which is one of the limitations of our study.

Angioedema without urticaria was the most common mucocutaneous disorder. The majority of patients was diagnosed with idiopathic angioedema, which is in line with published data in younger cohorts¹⁷. ACE inhibitors/ARB-induced angioedema represented the second most common cause of angioedema without urticaria in our sample, with a higher frequency compared to other published studies^{17,18}. Most patients had this clinical presentation in response to an ACE inhibitor, and a considerable percentage tolerated an ARB as an alternative drug. This is a relevant finding given the well-established benefits of this drug class in cardiovascular and renal diseases, when compared to the available alternatives, namely calcium channel blockers. More studies are needed to support our results.

Similarly to other published studies⁶, urticaria, especially chronic spontaneous urticaria, was quite common and well managed with oral H1 antihistamine agents. The patient who remained uncontrolled despite treatment with oral H1 antihistamine agents taken four times a day, and thus treated with cyclosporin, was diagnosed in 2014. By that time, the available guidelines advocated the treatment either with cyclosporin or omalizumab in patients who did not respond to oral antihistamines¹⁹. In this patient, the choice of mirtazapine after cyclosporin discontinuation was based on the presence of depressive manifestations and on published reports of its efficacy in several skin disorders, including chronic urticaria^{20,21}. It had a good efficacy and tolerance showing

that, in some cases, alternative drugs for the treatment of urticaria failing to respond to H1 antihistamine agents might be useful and more cost-effective than the therapy advocated by the guidelines. This fact can be especially relevant in the context of limited financial resources for health care. As for idiopathic angioedema, it is particularly important in the elderly to exclude other disorders that may be the cause of chronic urticaria, before assuming a diagnosis of chronic spontaneous urticaria^{6,22}.

Contact dermatitis was not very frequent in our sample and, in line with another published study in elderly patients, the most implicated allergens were nickel and caine.²³ No patient was diagnosed with atopic dermatitis, as expected from its lower prevalence compared to younger patients⁶.

Drug allergy is particularly important in this age group considering its polypharmacy and, therefore, the higher probability of developing a drug allergy²⁴. On the other hand, polypharmacy may make the identification of the culprit drug more difficult and complex, especially when it is an essential drug which cannot be easily withdrawn. In our study, the most implicated drugs were NSAIDs, beta-lactam antibiotics, and allopurinol, in agreement with other published data^{6,24}. Although mild mucocutaneous symptoms were the most common presentation, anaphylaxis had a considerable frequency in our sample. Moreover, we found a statistically significant association between confirmed drug allergy and anaphylaxis. It is crucial to perform an early diagnosis and a correct approach to anaphylaxis cases, minimizing new episodes that could have drastic consequences in a high-risk population for a fatal outcome^{25,26}.

It is important to underline that we were able to exclude drug allergy in half of the patients with suspected drug hypersensitivity. The most often suspected and excluded drugs were beta-lactam and macrolide antibiotics, local anaesthetics, and iodinated contrast agents. Exclusion of drug allergy has a huge importance as it allows these elderly patients to receive the most effective and less toxic drug and, in the case of antibiotic agents, contributes to improve the resistance profile of many bacterial microorganisms²⁷.

Food allergy had a relatively low frequency in this aged population, mimicking other published studies⁶. The most implicated allergens were crustaceans and nuts. Although mild mucocutaneous symptoms were the most common clinical presentation, we found a statistically significant association between food allergy and anaphylaxis, which underlines the critical importance of making a correct diagnosis to avoid a second episode that could be fatal in such a fragile population⁹. A significant association between food allergy and allergic rhinitis was also found. This association may be due to cross-reactivity between house dust mites and crustaceans (house-dust mite crustaceans syndrome) or pollens and vegetable foods (pollen-food allergy syndrome)²⁸. As expected, there were no cases of allergy to milk or egg, the most common food allergies in paediatric patients and with a natural tendency for resolution^{29,30}.

Only two patients were receiving specific immunotherapy (one to grass pollen and one to bee venom), in agreement with the previously published data referring to low use of this resource in

the elderly for reasons of efficacy and safety^{31,32}. However, recent studies³¹ support the use of specific immunotherapy in this population. We expect that its application in the elderly may increase in the near future, with beneficial effects on symptom control and quality of life.

For most immunoallergic disorders, we did not find any statistically significant differences between genders. However, the frequency of non-allergic rhinitis and bronchial asthma was higher in females, as previously published³³. ACE inhibitors/ARB-induced angioedema was more common in males, in line with previously reported data¹⁸ and against what was found in younger ages^{17,34}.

Limitations

Some limitations can be identified in our study. Because this constitutes a single-centre study, the results should not be generalized. Being a retrospective study, the established associations between disorders could not be definitive since many confounding factors could not be controlled. Moreover, the analysed data were obtained from electronic medical records, and possibly resulted from subjective interpretation from each patient's assistant physician. As mentioned earlier, the diagnosis of local allergic rhinitis was not considered and, therefore, some misdiagnosis of non-allergic rhinitis was possibly made. Hypersensitivity to chemotherapy drugs was not observed in our series because the approach to those patients is usually performed at the Chemotherapy Day Unit and not at the Outpatient Unit.

CONCLUSION

The most frequent immunoallergic disorders of the elderly patients evaluated in our IAL outpatient Unit are respiratory diseases, namely allergic and non-allergic rhinitis and bronchial asthma. Patients with respiratory allergies are mainly sensitized to house dust mites or pollen. Mucocutaneous diseases are also common, especially angioedema, both idiopathic and ACE inhibitors/ARB induced, and chronic spontaneous urticaria. Drug allergy represents an important diagnosis in a polymedicated population. We were able to exclude it, however, in half of the cases. Food allergy is less common. We found an association between anaphylaxis and both drug and food allergies.

In summary, it is crucial to consider the specificities of this population, whose referral to the IAL consultation will likely increase in the upcoming years. Particular attention is required if we are to provide them with the best quality care and, ultimately, improve their quality of life. More tailored studies targeting this population group are needed to support our results.

CONFLICTS OF INTEREST

The authors declare the absence of economic or other types of conflicts of interest.

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TABLES

Table I: Gender distribution of the main immunoallergic disorders (n=370). ACE - angiotensin-converting-enzyme; ARB - angiotensin II receptor blockers.

DISORDER	FEMALE n (%)	MALE n (%)	<i>p</i> value [*]
Rhinitis	131 (50)	38 (35)	0.007
Allergic	68 (26)	23 (21)	0.313
Non-allergic	54 (21)	12 (11)	0.027
Sensitization not assessed	9 (3)	3 (3)	
Bronchial asthma	61 (23)	12 (11)	0.006
Allergic	32 (12)	6 (5)	0.051
Non-allergic	17 (7)	5 (5)	0.475
Sensitization not assessed	12 (5)	1 (1)	
Acute urticaria	9 (3)	3 (3)	1.000
Chronic urticaria	26 (10)	8 (7)	0.426
Spontaneous	20 (8)	8 (7)	0.915
Inducible	6 (2)	0 (0)	0.186
Contact dermatitis	11 (4)	1 (1)	0.193
Angioedema	57 (21)	25 (23)	0.005
Idiopathic	13 (7)	11 (10)	0.297
ACE/ARB	11 (4)	13 (12)	0.006
C1 deficiency	1 (0)	1 (1)	0.503
Drug allergy	55 (22)#	23 (21)	0.995
Confirmed	22 (8)	9 (8)	0.816
Excluded	27 (10)	12 (11)	0.889
Evaluation not completed	9 (3)	2 (2)	0.519
Food allergy	4 (2)	5 (5)	0.131
Hymenoptera venom allergy	1 (0)	1 (1)	0.503
Anaphylaxis	7 (3)	2 (2)	1.000
Total of patients	261 (71)	109 (29)	

* level of significance <0.05

In three female patients, a hypersensitivity reaction was confirmed to one drug and excluded to another one

Table II: Characterization of the sensitization profile of aeroallergens in patients with respiratory disorders (n=162). Weed mix extract contains: plantago, artemisia, salsola, and chenopodium.

AEROALLERGEN SENSITIZATION	TOTAL n (%)
House dust mite	59 (36)
Pollen	55 (34)
Wall pellitory	27 (17)
Grass	26 (16)
Olive tree	21 (13)
Weed mix	19 (12)
Plane tree	14 (9)
Birch tree	1 (.)
Pet epithelium	12 (8)
Cat dander	11 (7)
Dog dander	7 (4)
Fungi	3 (2)
Negative	70 (43)
Total of patients	162

Table III: Characterization of the patients with a completed drug allergy evaluation (n=70). Note: Only two patients with suspected ACE inhibitors/ARB hypersensitivity were included in this table, both with a maculopapular rash, since bradykinin-mediated symptoms were not considered hereby. Some patients were evaluated for more than one suspected drug hypersensitivity. ACE - angiotensin-converting-enzyme; ARB - angiotensin II receptor blockers; NSAIDs - nonsteroidal anti-inflammatory drugs

DRUG	SUSPECTED n (%)	EXCLUDED n (%)	CONFIRMED n (%)
Analgesics	17 (24)	3 (8)	14 (45)
NSAIDs	11 (65)	0 (0)	11 (79)
Metamizole	2 (12)	0 (0)	2 (14)
Paracetamol	4 (24)	3 (100)	1 (7)
Antibiotics	33 (47)	25 (64)	8 (26)
Beta-lactam	26 (79)	20 (80)	6 (75)
Macrolides	5 (15)	4 (16)	1 (13)
Sulphonamides	1 (3)	0 (0)	1 (13)
Metronidazole	1 (3)	1 (4)	0 (0)
Cardiovascular	7 (10)	5 (13)	2 (6)
Antiplatelet agents	1 (14)	0 (0)	1 (50)
Gliptins	1 (14)	0 (0)	1 (50)
ACE inhibitors/ARB	2 (29)	2 (40)	0 (0)
Beta-blockers	1 (14)	1 (20)	0 (0)
Calcium channel blockers	1 (14)	1 (20)	0 (0)
Amiodarone	1 (14)	1 (20)	0 (0)
Anaesthetics	5 (7)	5 (13)	1 (3)
Local	4 (83)	4 (80)	1 (100)
General	1 (17)	1 (20)	0 (0%)
Others	16 (23)	8 (21)	8 (26)
Allopurinol	6 (38)	1 (13)	5 (63)
Iodinated contrast agents	5 (31)	4 (50)	1 (13)
Inhaled budesonide	1 (6)	0 (0)	1 (13)
Mydriatic ocular drug	1 (6)	0 (0)	1 (13)
B12 vitamin	1 (6)	1 (13)	0 (0)
Prednisolone	1 (6)	1 (13)	0 (0)
Iodopovidone	1 (6)	1 (13)	0 (0)
Total of patients	70 (100)	39 (56)	31 (44)

Table IV: Characterization of the sensitization profile of patients with food allergy (n=9).

FOOD ALLERGEN SENSITIZATION	TOTAL n (%)
Crustaceans	6 (67%)
Nuts	3 (33%)
Fresh fruits	2 (22%)
Fish	2 (22%)
Molluscs	2 (22%)
Legumes	1 (11%)
Total of patients	9

FIGURES

Figure 1: Most common immunoallergic disorders (n=370)