Allergen sensitization and polysensitization pattern of adults and children in an urban Sub-Saharan African setting (Libreville, Gabon)

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Background: It is believed that allergic diseases are increasing in Africa. However, the health sector in Africa has yet to catch up with this paradigm shift. We looked at the number of patients referred to us for allergy testing and investigated allergen sensitization. Methods: A retrospective analysis was done on 97 serum allergen-specific IgE results collected from patients suspected of having allergies in Libreville from 2018 to 2021. Specific IgE responses to 180 allergens were investigated. The general sensitization patterns were analyzed. Also analyzed were sensitization patterns for adults and children. The difference in the IgE-binding allergen positivity rate between groups was calculated by using the chi-square $(\chi 2)$ test. **Results:** The allergens most commonly causing sensitization

were from mites (65%), barley (48%), peach (48%), dog and/or cat dander (44%), house dust (44%), peanut (39%), tomato (39%), cockroach (37%), crab (36%), garlic and/or onion (34%), rye (34%), egg white (32%), shrimp (32%), kiwi (32%), soya bean (32%), citrus mix (29%), cheese (27%), milk (27%), walnut (27%), ox-eye daisy (24%) and orchard grass (24%). Moreover, 60% of patients (36 of 60) were polysensitized to inhalant allergens, 53% (31 of 58) were polysensitized to food allergens, and 29% (14 of 48) were polysensitized to inhalant and food allergens; 65% of patients (53 of 81) were sensitized to allergens originating from mites, fungi (including Candida albicans, Alternaria alternata, Aspergillus fumigatus, Cladosporium herbarum, and Pennicillium notatum), or bacteria (staphylococcal enterotoxin B).

https://doi.org/10.1016/j.jacig.2022.10.005

Conclusions: The sensitization pattern of allergens in our setting is rich and varied, with a high prevalence of polysensitization. (J Allergy Clin Immunol Global 2023;2:23-9.)

Key words: Allergens, allergy, sensitization, IgE, Africa

Allergy was described in 1906 by yon Pirquet as an exaggerated and harmful reaction of the body to a substance called an allergen.¹⁻³ Allergy incidence has been constantly increasing in the world.⁴ Indeed, the global prevalence of allergies is about 22%.⁴ There has also been a marked increase in allergies in developing countries, particularly among children and young adults.⁵ As a result of the longtime focus on endemic infections (malaria, tuberculosis, HIV), allergies in Sub-Saharan Africa may be underdiagnosed.⁵ Studies have shown that the prevalence of allergy symptoms (asthma, rhinitis, eczema, etc) in selected African regions ranges from 3% to 27%.^{6,7} In Africa, the increase in allergic diseases had already been highlighted 20 years ago.⁸ The causes of allergies are multifactorial. However, some studies in African environments have identified factors that mainly favor the growing emergence of allergies in African environments. Thus, mites associated with allergies have been best characterized.⁹⁻¹¹ However, the factors linked to the increase in allergies do not revolve solely around house dust mites. Indeed, the incidence of food allergies in Africa is also rising.^{12,13} In Cape Town, South Africa, the prevalence of food allergies was 2.5%, with an urban sensitization rate of 11.4%.¹⁴ It was also found that the rates of asthma, eczema, and rhinitis in unselected urban South African toddlers were 9.0%, 25.6%, and 25.3%, respectively.¹²

In Central Africa and particularly in Gabon, the prevalence of allergies and their causes are little known. Phase 3 of the International Study of Asthma and Allergy in Childhood (ISAAC) study made it possible, using questionnaires, to assess the prevalence of allergies in urban areas. However, this evaluation remains inconclusive because the symptoms described by the volunteers did not give rise to a serologic search for the allergens involved.7

This work aims to investigate and provide a glimpse into allergen sensitization patterns or types of allergies that are predominant in our adults and children from an urban Gabonese setting,

METHODS

From September 2018 to March 2021, we received 97 patients suspected of having allergic diseases in the setting. All patients were tested for specific IgE

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Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication August 24, 2022; revised September 28, 2022; accepted for publication October 14, 2022.

Available online December 15, 2022.

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TABLE I. Rates and levels of inhalant allergens sensitization in patients (all)

Allergen-specific IgE level (IU/mL)		0.35-0.69	0.70-3.49	3.5-17.49	17.5-49.99	50-99.99	≥100
Class		1	2	3	4	5	6
Level		Weak	Moderate	Moderately strong	Strong	Very strong	Extremely strong
Mites $(n = 35 [65\%])$	Dermatophagoides pteronyssinus ($n = 33$), no. (%)	3 (9%)	4 (12%)	10 (30%)	6 (18%)	1 (3%)	9 (27%)
	Dermatophagoides farinae (n = 31), no. (%)	3 (10%)	5 (16%)	8 (26%)	4 (13%)	4 (13%)	8 (26%)
	Typrophgus putrescentiae (n = 22), no. (%)	4 (18%)	3 (14%)	4 (18%)	3 (14%)	1 (4%)	7 (31%)
Dog and cat danders (n = 30 [54%]), no. (%)		4 (13%)	22 (73%)	4 (13%)			
Dust mite (n = $24 [44\%]$), no. (%)		1 (4%)	5 (21%)	6 (25%)	4 (17%)	2 (8%)	6 (25%)
Cockroach (n = $20 [37\%]$), no. (%)		5 (25%)	6 (30%)	6 (30%)	1 (5%)		2 (10%)
Ox-eye daisy $(n = 13 (24\%))$, no. (%)		7 (54%)	4 (31%)	1 (8%)			1 (8%)
Orchard grass (n = $13 [24\%]$), no. (%)		3 (23%)	8 (61%)		2 (15%)		
Latex rubber (n = 8 [15%]), no. (%)		4 (50%)	2 (25%)	2 (25%)			
Penicillium notatum (n = 8 [15%]), no. (%)		3 (37.5%)	5 (62.5%)				
Alternaria alternata (n = 8 [15%]), no. (%)		4 (50%)	2 (25%)	2 (25%)			
Aspergillus fumigatus ($n = 7 [13\%]$), no. (%)		2 (29%)	5 (71%)				
Cotton wood (n = 7 [13%]), no. (%)		4 (57%)	3 (43%)				
Cladosporium herbarum (n = 6 [11%]), no. (%)		1 (17%)	3 (50%)	1 (17%)			1 (17%)
Acacia $(n = 5 [9\%])$, no. (%)		5 (100%)					
Willow $(n = 5 [9\%])$, no. (%)		2 (40%)	2(40%)	1 (20%)			
Bermuda grass (n = 5 [9%]), no. (%)			1 (20%)	4 (80%)			
Oak $(n = 5 [9\%])$, no. (%)			4 (80%)	1 (20%)			
Meadow timothy (n = 4 $[7\%]$), no. (%)			2(50%)	2 (50%)			
White pine $(n = 4 [7\%])$, no. (%)		2 (50%)	2 (50%)				
Mixed alpage B (n = 4 [7%]), no. (%)		2 (50%)	2 (50%)				
Sycamore maple leaf ($n = 4$ [(7%]), no. (%)		2 (50%)	2 (50%)				
Common reed $(n = 4 [7\%])$, no. (%)		3 (75%)	1 (25%)				
Acarus siro (n = $3 [5.5\%]$), no. (%)			1 (33%)		1 (33%)		1 (33%)
Common ragweed ($n = 3 [5.5\%]$), no. (%)		1 (33%)	2 (67%)				
Russian thistle (n = $3 [5.5\%]$), no. (%)			1 (33%)	1 (33%)			1 (33%)
⁴ Dandelion (n = 2 [4%]), no. (%)			2 (100%)				
Japanese hops (n = 1 [2%]), no. (%)							1 (100%)
Armoise $(n = 1 [2\%])$, no. (%)			1 (100%)				

antibodies against 180 individual allergens by using Portia Allergy Q tests (Proteometech, Seoul, South Korea). Briefly, the test strip, including the membrane, was completely soaked with 300 μ L of diluted wash buffer, after which the wash buffer was discarded. Next, 250 μ L of sample diluent was added, followed by 50 μ L of patient serum. All were incubated for 45 minutes on an agitator. Next, the sampled solution was removed, and the membrane was washed twice with 300 μ L of washing buffer (on an agitator for 5 minutes). After removal of the washing buffer, 250 μ L of antibody solution was added and incubated for 30 minutes at room temperature. The membrane was then washed as previously described, and 250 μ L of the enzyme was added and incubated for 30 minutes. Next, the wash steps were repeated, 250 μ L of substrate solution was added, and each test strip was incubated for 20 minutes in the dark. Following incubation, the membrane was rinsed with 250 μ L of water, dried, and then read on the Q-smart/Q-scan.

Interpretation of data

Patients who tested positive for "IgE-binding allergens" were considered sensitized. On the basis of the IgE-binding allergen titer, we defined the likelihood of having a "genuine allergy" rather than being just sensitized. The manufacturer's interpretations were as follows: (1) weak or class 1 (IgE-binding allergen titer between 0.32 and 0.69 IU/mL), (2) moderate or class 2 (IgE-binding allergen titer between 0.7 and 3.49 IU/mL), (3) moderately strong or class 3 (IgE-binding allergen titer between 3.5 and 17.49 IU/mL), (4) strong or class 4 (IgE-binding allergen titer between 17.5 and 49.9 IU/mL), (5) very strong or class 5 (IgE-binding allergen titer between 50 and 99.9 IU/mL), and (6) extremely strong or class 6 (IgE-binding allergen titer higher than 100 IU/mL).

On the basis of the test manufacturer's interpretation and in the absence of a standardized titer threshold, we defined highly sensitized patients as those

having an allergy with a moderate to extremely strong level of IgE-binding allergens.

Statistics

The sensitization rate was presented as a percentage or frequency. The intergroup difference was calculated by using the chi-square (χ^2) test and Prism, version 6.0 (GraphPad Software, San Diego, Calif). The statistical significance was defined as a *P* value less than .05.

Ethics

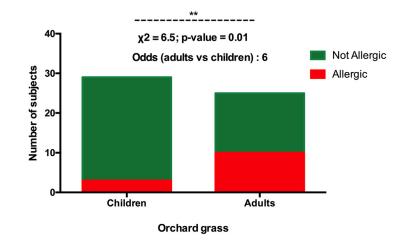
The research was done following Gabonese ethical guidelines and regulations, and the study was approved by the Mother and Child University Hospital Scientific and Ethical Board.

Availability of data and materials

Data can be accessed and made available by contacting the corresponding author by e-mail (joel.djoba@gmail.com).

RESULTS

A total of 97 patients (54% females and 46% males) were enrolled in this study. Among them, 43 (44%) were adults (aged \geq 18 years) and 54 (56%) were children (aged <18 years). Both the mean age and median age of the children were 6 years. The adults' mean age was 39 years, with a median age of 37 years.



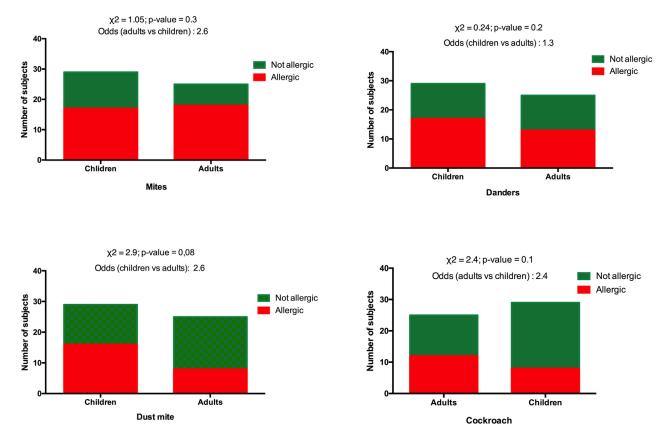


FIG 1. Inhalant allergen sensitization in children and adults. The graphs are from the contingency table analysis. The χ^2 test statistical significance was defined as P < .05. Only orchard grass allergen sensitization was significantly higher in adults than in children (odds ratio = 6; χ^2 = 6.4; P = .01).

In all, 35 patients (36.1%) were tested with the food, respiratory, and atopic allergies panels; 13 (13.4%) were tested with the food and respiratory allergies panels; 10 (10.3%) were tested with the food and atopic allergies panels; and 5 (5.1%) were tested with the respiratory and atopic allergies panels.

A total of 16 patients (16.5%) were tested with the food allergies panel only, 12 (12.4%) were tested with the respiratory

allergies panel only, and 6 (6.2%) were tested with the atopic allergies panel only. Therefore, if we look at testing based on allergy types, 74 patients (76.3%) were tested for food sensitization, 65 (67%) were tested for anti-inhalant allergen IgE, and 56 (58%) were tested for other atopic allergies.

Of the 97 patients enrolled in the study, 81 (83.5%) were sensitized (positive for IgE-binding allergens).

TABLE II. Rates and levels of food allergens sensitization in patients (all)

Allergen-specific IgE level (IU/mL)	0.35-0.69	0.7-3.49	3.5-17.49	17.5-49.99	50-99.99	≥100
Class	1	2	3	4	5	6
Level, no. (%)	Weak	Moderate	Moderately strong	Strong	Very strong	Extremely strong
Barley (n = $21 [48\%]$), no. (%)	6 (28%)	10 (48%)	4 (19%)			1 (5%)
Peach (n = $21 [48\%]$), no. (%)	5 (24%)	12 (57%)	3 (14%)	1 (5%)		
Peanut (n = $17 (39\%)$), no. (%)		16 (94%)	1 (6%)			
Tomato (n = $17 (39\%)$), no. (%)	5 (29%)	5 (29%)	6 (35%)			1 (6%)
Crab (n = $16 [36\%]$), no. (%)	2 (12.5%)	11 (69%)		1 (6%)	1 (6%)	2 (12.5%)
Garlic-onion (n = $15 [34\%]$), no. (%)	1(7%)	8 (53%)	5 (33%)			1 (7%)
Rye (n = $15 [34\%]$), no. (%)	5 (33%)	3 (20%)	5 (33%)	1 (7%)		1 (7%)
Egg white $(n = 14 [32\%])$, no. (%)		14 (100%)				
Shrimp (n = 14 [32%]), no. (%)	1 (7%)	9 (54%)	1 (7%)		1 (7%)	2 (14%)
Kiwi (n = 14 [32%]), no. (%)	3 (21%)	7 (50%)	4 (29%)			
Soya bean $(n = 14 [32\%])$	1 (7%)	12 (86%)	1 (7%)			
Citrus mix (n =13 [29%]), no. (%)		7 (54%)	5 (38%)			1 (8%)
Cheese (n =12 [27%]), no. (%)		12 (100%)				
Milk (n =12 [27%]), no. (%)	2 (17%)	9 (75%)	1 (8%)			
Walnut (n = $11[27\%]$), no. (%)	3 (27%)	7 (58%)		1 (9%)		
Rice $(n = 10 [23\%])$, no. (%)	2 (20%)	5 (50%)	2 (20%)			1(10%)
Beef $(n = 9 [20\%])$, no. (%)		9 (100%)				
Wheat $(n = 9 [20\%])$, no. (%)	1 (11%)	7 (78%)	1 (11%)			
Chestnut (n = 8 [18%]), no. (%)	1 (12.5%)	6 (75%)				1 (12.5%)
Chicken $(n = 7 [16\%])$, no. (%)	2 (29%)	71%				
Apple (n = 6 $[14\%]$), no. (%)	1 (17%)	4 (67%)		1 (17%)		
Clam (n = 5 $[11\%]$), no. (%)	1 (20%)	3 (60%)	1 (20%)			
Pork (n = 5 [11%]), no. (%)	1 (20%)	4 (80%)				
Tuna (n = 5 (11%]), no. (%)	1 (20%)	4 (80%)				
Buckwheat (n = 5 $[11\%]$), no. (%)	1 (20%)	3 (60%)			1 (20%)	
Almond (n = 4 $[9\%]$), no. (%)		4 (100%)				
Mackerel (n = 4 $[9\%]$), no. (%)		4 (100%)				
Salmon ($n = 4 [9\%]$), no. (%)	1 (25%)	2 (50%)	1 (25%)			
Potato (n = 4 $[9\%]$), no. (%)	1 (25%)	1 (25%)	2 (50%)			
Cod (n = $3 [7\%]$), no. (%)		3 (100%)				

Inhalant allergens

Sensitization. Of the patients tested for inhalant allergies, 83% (54 of 65) were sensitized. IgE sensitization to the following allergen sources was most common: mites (65%), dog or cat dander (54%), mite dust (44%), cockroach (37%), ox-eye daisy (24%), and orchard grass (24%) (Table I).

In children as in adults, the allergens eliciting the highest rates of sensitization were still those from mites (59% in children vs 72% in adults), dog or cat dander (59% in children vs 52% in adults), dust mites (55% in children vs 32% in adults), cockroach (27% in children vs 48% in adults), ox-eye daisy (31% in children vs 16% in adults) and orchard grass (10% in children vs 40% in adults [Fig 1]). The rate of sensitization to mite allergens (odds ratio = 2.6; $\chi^2 = 2.9$; P = .08) was higher in adults than in children and did not reach statistical significance. Sensitization to orchard grass allergen sensitization was significantly higher in adults than in children (odds ratio = 6; $\chi^2 = 6.4$; P = .01). Also, rates of sensitization to dust mite allergens (odds ratio = 2.6; $\chi^2 = 2.9$; P = .08) and ox-eye daisy allergen (odds 2.4; $\chi^2 = 1.7$; P = .2) were higher in children than in adults, although statistical significance was not reached (Fig 1).

High-level sensitization. IgE-binding allergen titer analysis showed that 65% of patients tested for inhalant allergies (39 of 60) were highly sensitized (ie, they were likely to have a genuine allergy). Of the 54 patients sensitized to inhalant allergens, 15 (28%) showed a weak sensitization.

Food allergens

Sensitization. Among the 74 patients tested for food allergies, 44 (59%) were sensitized (Table II). Regarding food allergens, patients were mostly sensitized to allergens from barley (48%), peach (48%), peanut (39%), tomato (39%), crab (36%), garlic and/or onion (34%), rye (34%), egg white (32%), shrimp (32%), kiwi (32%), soya bean (32%), citrus mix (29%), cheese (27%), milk (27%), and walnut (27%).

A comparison of children and adults did not reveal any significant differences in their rates of food allergen sensitization (Fig 2). Nevertheless, sensitizations to allergens from egg white (odds ratio = 2.2; $\chi^2 = 1.4$; P = .2) and cheese (odds ratio = 2.4; $\chi^2 = 1.6$; P = .2) were higher in children than in adults.

High-level sensitization. Regarding food allergies, IgEbinding allergen titer analysis showed that 51% of the patients tested for food allergies (38 of 74) were highly sensitized (likely to have a genuine allergy). Of the 44 patients sensitized to food allergens, 6 (14%) showed weak sensitization.

Polysensitization

Polysensitization was defined as sensitization to 2 or more allergens.¹⁶ We determined that 60% of patients (36 of 60) were polysensitized to inhalant allergens, 53% (31 of 58) were polysensitized to food allergens, and 29% (14 of 48) were polysensitized to inhalants and food allergens.

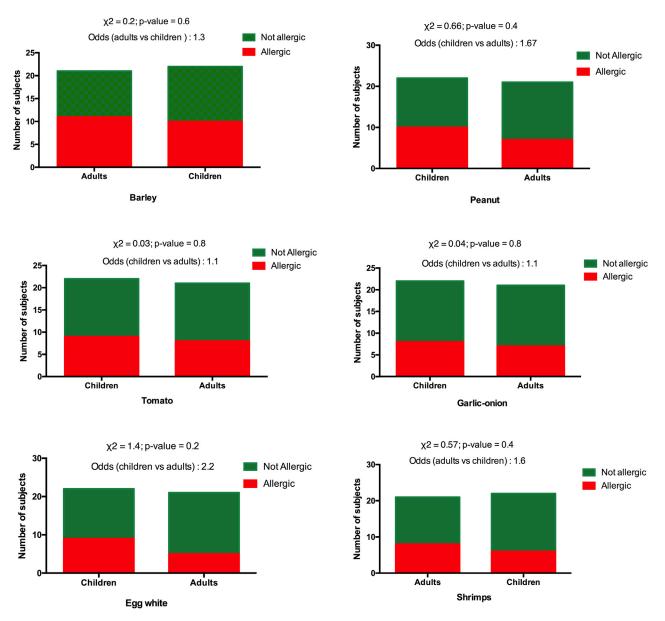


FIG 2. Food allergen sensitization in children and adults. The graphs are from the contingency table analysis. The χ^2 test statistical significance was defined as *P* <.05. No significant differences were observed in the rate of food allergen sensitization.

Role of parasites (mites), fungi, and bacteria in the burden of allergies

The testing also showed that 65% of patients (53 of 81) were sensitized to allergens originating from parasites (mites [Dermatophagoides pteronyssinus, Dermatophagoides farinae, and Tyrophagus putrescentiae]), and fungi (Candida albicans, Alternaria alternata, Aspergillus fumigatus, Cladosporium herbarum, and Pennicillium notatum), and bacteria (Staphylococcal enterotoxin B).

DISCUSSION

In 2.5 years, only about 100 patients were referred to our laboratory (the only laboratory in the country providing diagnostics for specific IgE antibodies against individual allergens)

for allergy testing or investigation. This indicates that referral for allergy testing is very low in Libreville, Gabon, which is probably due to the lack of information on test availability and the limited access to testing. As a result, allergies are most certainly undiagnosed in our setting.

With 83% of patients being sensitized by inhalant allergens and 59% by food allergens, respiratory allergies seem to be the more prevalent type of allergies. Our data showed that the 5 most common allergens to which patients were sensitized are mites (65%), barley (48%), peach (48%), dog and/or cat dander (44%), and house dust (44%). Similar to what is observed in all parts of the world, mites and house dust were major sensitizing allergens.^{9,10,17-20} The presence of the food allergen (barley and peanut) in the top 3 most common sensitized allergens and the fact that about one-third of patients were sensitized to peanut, tomato,

crab, garlic and/or onion, rye, egg white, shrimp, kiwi, and soya bean shows and confirms that food allergies are a growing problem in Africa.^{12,21} A study carried out on children in South Africa also showed that although sensitization to allergens from mites (or dust mites) and animal sources predominates, sensitization to food allergens is not to be neglected.²²

A comparison of adults and children revealed that adults were 6 times (odds ratio = 6) more likely to be sensitized by orchard grass and 6 times (odds ratio = 2.6) more likely to be sensitized by mites. Children were more than 2 times more likely to be sensitized to house dust, ox-eye daisy, egg white, and cheese. It is essential to relativize these observations, as the difference in sensitization against orchard grass was statistically significant and the sample size was relatively small.

Polysensitization was high in our patients, with 60%, 53%, and 29% of patients being polysensitized to inhalants, food, and both types of allergens, respectively. Reports have shown that polysensitization could be high in patients with allergy (often >60%).^{16,23-26} As polysensitization has been shown to exacerbate the severity of symptoms^{23,27} and increase the risk for allergic multimorbidity,²⁸⁻³⁰ identifying polysensitized patients and quantifying the levels of allergen-specific IgE may be clinically relevant in the management of patients.³¹

Indeed, an important fact to consider is that many people who are sensitized may not develop a hypersensibility reaction (and symptoms) when reexposed to the allergens to which they are sensitized.³² In our setting, IgE-binding allergen titer analysis showed that 28% and 14% of patients were weakly sensitized to inhalants and food, respectively. Because sensitization does not always translate to clinical allergy, interpretation in the context of clinical history is critical.³²

Interestingly, 65% of patients were sensitized to allergens originating from parasites (mites), fungi, or bacteria. Therefore, it would not be a senseless assertion to say that like the pattern of infectious diseases, the pattern of allergies in Africa is, to a certain extent, linked to the continent's entomologic, bacterial, and fungal ecosystem. African tropical climates may provide favorable conditions for parasites (mites), fungi, and bacteria to grow, which, in turn would increase Africans' exposure to these parasites, fungi, and bacteria-associated allergens. Recently, van Rooyen et al showed that fungi allergens, including allergens from A alternata, A fumigatus, and C herbarum, were among the top 10 allergens sensitizing individuals in South Africa.²² Interestingly, the sensitizing allergens' ranking varied according to geography.²² Moreover, as pointed out by Pfavayi et al, there is a wide spectrum of immune-mediated fungal diseases, such as allergic rhinitis, allergic conjunctivitis, and allergic fungal sinusitis, as well as asthma and atopic dermatitis.³³

The underreporting of allergic disorders in Africa has relegated allergies to the level of low-priority diseases. To really grasp the extent of the allergic disease burden in Africa, it would probably be wise to estimate that burden and characterize allergies in African settings both etiologically and phenotypically.

The relatively small number of patients, which might put our findings into perspective, also reveals limited access to allergy laboratory diagnostics in our country. We must increase the capability to diagnose allergy in a setting such as ours not only to provide better care to patients with allergy but also to assess the true extent of allergies in low-income countries.

Conclusion

In conclusion, if sensitizations to inhalant allergens (including mites, dog and/or cat dander, and dust mites) are more prevalent among patients with allergy in Libreville, sensitizations to food allergens (including peach, peanut, tomato, crab, garlic and/or onion, rye, egg white, shrimp, and so forth) appear to not be negligible. Moreover, polysensitization must be taken into account when caring for patients with allergies.

We thank all the patients for consenting to participate.

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