

## **Airborne food and aeroallergens levels in healthcare settings. An unaccounted but potentially relevant source of exposure?**

**Short title:** Food and aeroallergens in healthcare

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## Abstract

**Background:** Exposure to airborne allergens of biological origin associates with the development and exacerbation of allergic asthma and rhinitis. Assessment of allergens exposure in healthcare facilities may contribute to monitor hygiene and survey specific allergens which may cause symptoms in sensitized subjects.

**Objective:** To assess concentration of indoor and airborne food allergens across different healthcare settings.

**Methods:** Dust was vacuumed from primary health care centers in Lisbon; and emergency unit, day hospital, internal medicine ward, operating room and the outpatient clinic of a university central hospital in Porto. Samples were sieved, weighed, extracted and concentrations of Nbos d 5, Cor a 9, Gal d 2, Ara h 3, Ara h 6, Der p 1, Fel d 1, Can f 1, Bla g 2, Alt a 1 and Phl p 5 were determined using a multiplex array for allergens (MARIA™).

**Results:** All airborne food and aeroallergens were found at least in one sampled area, except for Alt a 1. Levels of Der p 1 and Fel d 1 ranged from 13.0  $\mu g/g$  to 971.0  $\mu g/g$  and from 7.0  $\mu g/g$  to 4618.8  $\mu g/g$ , respectively. The emergency unit revealed the higher levels of food allergens, namely Nbos d 5 (16034.0  $\mu g/g$ ) and Cor a 9 (10649.5  $\mu g/g$ ).

**Conclusions:** With the exception of the operating room, exposure levels of dust mite, cat and dog allergens in healthcare facilities were above the values associated with sensitization and occurrence of allergic asthma or rhinitis symptoms in sensitized subjects.

**Key words:** Airborne food allergens. Allergic disease. Healthcare centers. Aeroallergens. Indoor exposure

## Resumen

**Antecedentes:** La exposición a alérgenos en el aire de origen biológico se asocia con el desarrollo y exacerbación del asma alérgica y la rinitis. La evaluación de la exposición a los alérgenos en los centros sanitarios puede contribuir a controlar la higiene y examinar los alérgenos específicos que pueden causar síntomas en sujetos sensibilizados.

**Objetivo:** Evaluar la concentración de alérgenos alimentarios en interiores y en el aire en diferentes entornos de atención médica.

**Métodos:** Se aspiró el polvo de centros de atención primaria de salud en Lisboa, de la unidad de urgencias, hospital de día, sala de medicina interna, sala de operaciones y la clínica ambulatoria de un hospital central de la universidad de Oporto. Las muestras fueron tamizadas, pesadas, extraídas y se determinó las concentraciones de Nbos d 5, Cor a 9, Gal d 2, Ara h 3, Ara h 6, Der p 1, Fel d 1, Can f 1, Bla g 2, Alt a 1 y Phl p 5 utilizando una matriz múltiple para alérgenos (MARIA™).

**Resultados:** Todos los alimentos en el aire y los aeroalérgenos se encontraron al menos en un área muestreada, excepto Alt a 1. Los niveles de Der p 1 y Fel d 1 variaron de 13.0 a 971.0 µg/g y de 7.0 a 4618.8 µg/g, respectivamente. La unidad de emergencia reveló los niveles más altos de alérgenos alimentarios, a saber, Nbos d 5 (16034.0 µg/g) y Cor a 9 (10649.5 µg/g).

**Conclusiones:** Con la excepción de la sala de operaciones, los niveles de exposición a los ácaros del polvo y a los alérgenos de gato y perro en los centros de salud fueron superiores a los valores asociados con la sensibilización y la aparición de asma alérgica o síntomas de rinitis en sujetos sensibilizados.

**Palabras clave:** Alérgenos de alimentos en el aire. Enfermedad alérgica. Centros de salud. Aeroalérgenos. Exposición interior.

## Introduction

Allergic diseases are one of major concern in developed western countries and the prevalence continues to increase worldwide [1-4]. The time spent indoors has been one of the most prominent changes in our lifestyle over the past decades. This raises concerns on the impact of indoor air pollutants on allergic symptoms not only at homes, but also at day-care buildings, nurseries, schools and other public places has emerged [5-7]. Although several studies reported the health effects of both chemical and biological agents [8, 9], indoor and airborne food allergens have been poorly studied.

Allergen exposure has been associated with the development and exacerbation of allergic asthma and rhinitis [10, 11]. The World Health Organization (WHO) has proposed a Der p 1 threshold for acute asthma symptoms of 10.0  $\mu\text{g/g}$  [12]. Recently, other thresholds have been defined for Fel d 1 sensitization and asthma symptoms (1.0  $\mu\text{g/g}$  and 8.0  $\mu\text{g/g}$ , respectively), Bla g 2 (1.6  $\mu\text{g/g}$ ) and for Can f 1 (10.0  $\mu\text{g/g}$ ) [13]. Most of these thresholds have been used as the minimal exposure required for the induction of sensitization and allergic symptoms and to assess exposure-response relationship between allergens and symptoms or exacerbations [13-17].

Residential exposure to several allergens is common and, in many homes, high levels of allergens have been found [18]. A large study in the United States showed that more than 90% of bedrooms had 3 or more detectable allergens and over two thirds had at least one allergen highly elevated [19]. Assessment of allergen exposure in the workplace has also increased, especially in environments with dominant exposures to particular allergens, such as bakeries, animal facilities, seafood-processing environments and healthcare facilities [20-22]. Furthermore, in healthcare facilities, the purposes of allergen levels monitoring in the environment surrounding a patient can be three-fold: to monitor hygiene standards, examine the presence of specific allergens, which may be the source of allergic symptoms, and also to use such information to establish thresholds for several allergens. Therefore, we aimed to assess indoor and airborne food allergens levels in different healthcare settings.

## Methods

### Setting and study design

Dust samples were collected from primary health care centers (PHCCs) and from a university central hospital as part of ExPOSE study in July and December 2018, respectively [23]. ExPOSE is a cross-sectional study assembled in ten PHCCs in Lisbon and in five different areas of a university central hospital in Porto, Portugal.

At the PHCCs, samples were collected from medical offices, vaccination rooms, treatment rooms, corridors and warehouse/cleaning rooms. At the university central hospital, dust samples were

collected from the yellow ward emergency unit, day hospital, internal medicine ward, one room of the operating room (OR), and from the outpatient clinic (Table S1). These areas have been selected from those with similar conditions, representative of each building and that represented a greater exposure for health workers and patients identified by the walkthrough survey [24]. Medical offices, treatment and vaccination rooms were cleaned at least once a day after working hours, at the PHCCs. Treatment and vaccination rooms were also cleaned several times a day, namely if a procedure involving organic fluids or waste was performed [24]. At the university central hospital, the operating room was cleaned frequently between surgeries and procedures, while the yellow ward emergency unit had its own cleaning routines throughout the day. Every time a procedure is done, surfaces and floor were promptly cleaned, and waste was collected. Regarding the day hospital, internal medicine ward and the outpatient clinic surfaces and floors were cleaned after working hours, during the evening. Every area had its own hygiene plan and all cleaning actions were operated by an external company according to standardized and approved protocols.

The study was conducted according to the Declaration of Helsinki. The project was approved by the University and Hospital Health Ethics Committee and by the Regional Health Administration Ethics Committee.

### **Sample collection and processing**

Settled dust was collected using a vacuum cleaner (HOOVER Brave BV71\_BV10 A2, USA) with a DUSTREAM® collector (Indoor Biotechnologies, USA) placed on the distal end of the vacuum's extension wand containing a 40 micron nylon collection filter. All sampling areas were vacuumed for a period of 10 minutes (Table S2) during working hours. One settled dust sample was collected in each primary health care center and each university central hospital area (n=15) from floor, chairs, desks and other upholstered furniture. After each sampling, collection filter was removed from the collector, sealed in a polyethylene bag and frozen at - 80 °C until analysis.

### **Measurement of indoor and airborne food allergens**

Before analysis, vacuumed dust samples were sieved through 355 µm mesh to remove unwanted particles and weighed to a maximum of 100 mg and a minimum of 20 mg (Table S3), according to the manufacturer's instructions (Indoor Biotechnologies, Inc., Charlottesville, VA).

Samples were extracted in PBS-T solution (0.05% Tween 20 in phosphate buffered saline, pH 7.4), considering the proportion of 1 mg of dust to 0.02 mL of extraction solution. For samples between 20 and 100 mg, an adjusted proportional volume of PBS-T was added. Samples were resuspended using a vortex mixer and were mixed for two hours, using a lab rocker.

MARIA™ 8-plex and 3-plex analysis (Indoor Biotechnologies, Inc., Charlottesville, VA) was performed to determine the concentration of airborne food and common indoor allergens, including milk (*Bos domesticus* β-lactoglobulin - Nbos d 5), hazelnut (*Corylus avellane* - Cor a 9), egg (*Gallus*

*domesticus* - Gal d 2), peanuts (*Arachis hypogaea* - Ara h 3, Ara h 6), mites (*Dermatophagoides pteronissinus* – Der p 1), cat (*Felis domesticus* - Fel d 1), dog (*Canis familiaris* - Can f 1), cockroach (*Blattella germanica* - Bla g 2), molds (*Alternaria alternata* - Alt a 1) and grass (*Phelum pretense* - Phl p 5), respectively. For MARIA™ 8-plex, dust extract samples were diluted in a factor of 1/10, 1/100 and 1/10000 and for MARIA™ 3-plex dust extract samples were diluted at 1/1, 1/5, 1/20 and 1/100. Measurements were performed in Luminex® 200™ in a multiplex array for allergens according to the manufacturer's instructions. The array uses fluorescently labeled beads conjugated to monoclonal antibodies specific for purified allergen molecules. A 12-point standard curve was executed in duplicates to quantify the allergen levels. Additionally, quality controls provided with the test kit were applied. Results were expressed in nanogram per milliliter ( $\eta g/ml$ ) and then converted to microgram per gram ( $\mu g/g$ ) (Table 1).

Lower limits of detection (LLOD) were calculated based on the lowest usable point of the standard curve for each allergen and multiplied the expected allergen concentration of this point by the lowest dilution factor in the assay (10 for indoor allergens and 1 for airborne food allergens). The LLOD were 12.0  $\mu g/g$  for Ara h 3, Bla g 2, Can f 1 and Der p 1, 4.0  $\mu g/g$  for Alt a 1, Ara h 6 and Fel d 1, 10.0  $\mu g/g$  for Phl p 5 and 0.4  $\mu g/g$  for Nbos d 5, Cor a 9 and Gal d 2.

The concentration of allergens was determined based on the result of median fluorescent intensities (MFI) for each allergen and sampling area, considering the usable MFI range of the standard curve. If more than one value was within usable MFI range: the geometric mean was considered if the test results were within 30% coefficient of variability; or the result corresponding to the lowest dilution was considered if the test result increased with the increasing dilution factor.

## Results

Levels of milk (Nbos d 5), hazelnut (Cor a 9) and peanut (Ara h 3 and Ara h 6) where the highest within the emergency unit of the university central hospital, respectively 16034.0  $\mu g/g$ , 789.3  $\mu g/g$ , 276.4  $\mu g/g$  and 80.5  $\mu g/g$ . As for egg (Gal d 2), the highest levels were observed in a primary care health center and in the emergency unit of the university central hospital, respectively 136612.9  $\mu g/g$  and 10649.5  $\mu g/g$  (Table 1, Figure 1).

In relation to indoor allergens, dust mite (Der p 1) concentrations were higher in one of the primary care centers (971.0  $\mu g/g$ ) whilst, among hospital areas, higher levels were observed in the outpatient clinic (394.1  $\mu g/g$ ). Regarding cat (Fel d 1) and dog (Can f 1) allergens, the maximum concentrations were also found in the primary care health centers, respectively 4618.8  $\mu g/g$  and 2111.4  $\mu g/g$  whereas in the hospital outpatient clinic Fel d 1 concentration reached 1320.4  $\mu g/g$ . Cockroach (Bla g 2) allergen concentrations were only observed in two primary health care centers (98.2  $\mu g/g$  and 133.9  $\mu g/g$ ). Levels of Phl p 5 were detected only in six primary health care centers, and all the levels corresponding to hospital areas were below the LLOD (Table 1, Figure 1).

## Discussion

Our observational study has relevant findings. Surprisingly, with the exception of the operating room, exposure levels of dust mite, cat and dog allergens in healthcare facilities were above the values associated with sensitization and occurrence of allergic asthma or rhinitis symptoms in sensitized subjects [12, 13]. Measurable concentrations of indoor and airborne food allergens in the settled dust were found among healthcare areas, where allergic patients are frequently observed and evaluated, as in the emergency unit and in the outpatient clinic. Although exposure to airborne food allergens does not typically result in anaphylaxis, these levels may cause allergic symptoms, such as itchy eyes, runny nose, cough, nasal congestion and respiratory distress [25].

Our observations have a few limitations. The cross-sectional nature of our study does not allow us to establish causal relationships. Furthermore, for operational reasons, dust samples were collected during the summer at the primary health care centers, and in the wintertime at the university central hospital, which may have influenced the concentration of pollen aeroallergens indoors, either by infiltration or through ventilation [26]. In fact, differences in pollen levels between facilities (only measurable in PHCCs) may reflect these diverse times of collection. In addition, we did not evaluate the effect of these allergen concentrations on health workers and patients' health, given by symptoms or IgE measurements. Also, collected dust weight in the operating room was below the minimum defined by the manufacturer for the analysis, being possible that the detected levels may be underestimated. Still, our study has important strengths. This is the first study measuring the levels of airborne food and indoor allergens in different healthcare settings, including several primary health care centers as well as diverse milieus within a tertiary hospital. Additionally, dust samples have been collected from floors, chairs, desks and other upholstered furniture, considered a proxy of exposure [10]. In these reservoirs, particles have a large diameter and deposit instead of remaining airborne, improving the certainty of measuring allergen exposure in healthcare areas [10]. Recent studies have shown evidence of adverse associations between indoor allergen exposure and health outcomes, even though most of these have quantified levels of aeroallergens in allergic patients' homes [19, 27, 28]. A correlation between exposure and sensitization has been suggested [15, 29-31] and it is well known that sensitization to dust mite is associated with asthma, wheeze and bronchial hyperresponsiveness [32-34]. One study from Malaysia reported that even lower concentrations of Der p 1 (median=0.5562  $\mu\text{g/g}$ ) were associated with wheeze, rhinoconjunctivitis, and airway symptoms in allergic subjects [35]. Considering that healthcare facilities are heavily occupied by both patients and health workers, the high levels of indoor allergens may be a source for symptomatic exacerbations in susceptible subjects attending the hospital or a primary health care center.

In previous studies conducted in hospitals, concentrations of dust mite allergen have also been reported [21, 22]. One study conducted in the UK found lower allergens concentrations than ours (<

10.0  $\mu\text{g/g}$ ) [22]. In North West of England, Der p 1, Fel d 1, Can f 1 and Bla g 2 were measured in dust samples collected by vacuuming upholstered chairs, carpets and mattresses in fourteen hospitals. Levels of Bla g 2 and Der p 1 were below the limits of detection, but higher concentrations of Can f 1 and Fel d 1 were found in upholstered chairs, suggesting they may serve as a reservoir for indoor allergens [22]. However, a reduction in dog and cat allergens concentration in upholstered chairs has been observed with a more frequent vacuum-cleaning [22]. In fact, our observed dust mite allergen concentrations were higher than those reported in Portuguese homes (median = 9.2  $\mu\text{g/g}$ ) [26]. Allergen levels may vary according to building characteristics and indoor activities, type of ventilation, temperature and humidity, furniture and cleaning routines. Most of the previous studies have been performed in allergic subjects' homes, and these differences may be explained by selection bias due to the often cleaning of allergic subjects' homes [27] and the high occupancy rate of healthcare settings. Indeed, occupants' behaviors have been associated to higher concentrations of aeroallergens, as pet ownership [36, 37]. For instance, Berge, Munir [38] and De Lucca, O'Meara [39] found that cat, dog and mite allergens are brought to public areas by their owners, who may carry allergens from one place to another. Clothing dispersal of allergens and the lack of uniform wearing may also explain the high concentrations of cat allergen found in our sampled areas. Iraola, Carrillo-Diaz [40] also reported hair and scalp as a source of mite allergens being potentially transferred from individuals to the clinical setting. In addition, measurable levels of Bla g 2, Fel d 1, Can f 1 and Der p 1 found in health care centers may suggest that different cleaning procedures could be implemented to reduce these concentrations, taking into account the symptoms' threshold. However, comparisons between our results, previous studies and the proposed thresholds are limited by the distinct methodologies used for allergen quantification [41].

The role of non-ingesting route of food allergens in asthma and other diseases has been recognized [25, 42]. Exposure can occur by inhalation or just by being in the vicinity of the food [25], inducing airway reactions [43, 44]. In our study, cow's milk (Nbos d 5), hazelnut (Cor a 9) and egg (Gal d 2) allergens were detected in all assessed areas, except in one primary health care center. Others have found that eating in bed was linked to the presence of cow's milk allergen in mattresses dust [45]. Also, a significant increase in hen's egg protein has been detected both in house and children's bed dust after its cooking or consumption [46]. We were not expecting to find cow's milk, hazelnut and egg allergens inside healthcare facilities, since none of the vacuumed areas included eating spaces. Eating habits within workplaces, as medical offices or nurseries, could explain these findings. Egg allergen distribution and spreading through other routes, such as saliva or hands, may be important to understand these unexpected high concentrations among healthcare spaces, which are not physically and architecturally related to eating areas, as dining halls or coffee shops.

Considering our findings, it would be important to assess the health effects of indoor and airborne food allergens in healthcare settings, especially in places occupied by high risk patients such as those from the allergy clinic, and review the sensitization and symptoms thresholds. In addition,

sampling and analysis methodologies should be standardized, providing an identification and management of environmental exposures and assessment of health effects. As a matter of fact, the topic of aerosolized allergic reactions has stirred enough controversy among food-allergic travelers that some airline companies have stopped serving peanuts on flights. This not only reflects the impact of exposure may have on human health, but also the need of further research on this topic. Taken together, our findings suggest that high levels of indoor and airborne food allergens can be found in very dissimilar healthcare settings. Therefore, further studies are needed to identify possible sources and procedures that led to the levels obtained, ascertain the clinical significance of allergen exposure on patients and health workers' health and to implement concrete actions to reduce these concentrations.

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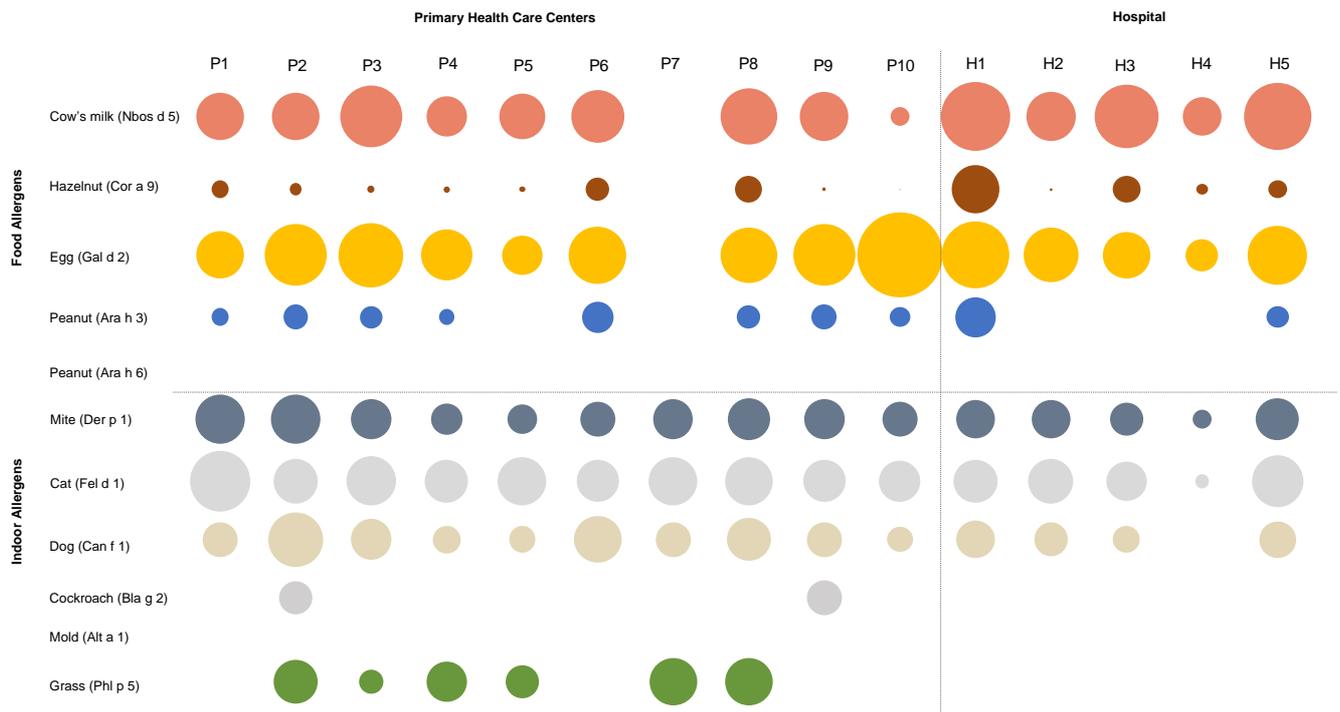
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**Table 1.** Concentration of airborne food and indoor allergens measured in each primary health care center and university central hospital areas (n=15).

	Food Allergens					Indoor Allergens					
	Milk	Hazelnut	Egg	Peanut	Peanut	Mite	Cat	Dog	Cockroach	Mold	Grass
	Nbos d 5	Cor a 9	Gal d 2	Ara h 3	Ara h 6	Der p 1	Fel d 1	Can f 1	Bla g 2	Alt a 1	Phl p 5
P1	661.5	11.3	693.3	11.5	23.4	971.0	4618.8	122.0	<12.0	<4.0	<10.0
P2	733.5	5.3	5719.3	30.1	33.7	888.2	482.9	2111.4	98.2	<4.0	456.9
P3	5155.1	2.7	7815.7	22.3	26.4	277.9	968.1	296.4	<12.0	<4.0	31.7
P4	283.5	2.4	1310.3	9.0	<4.0	73.0	395.1	48.9	<12.0	<4.0	266.5
P5	528.9	2.3	246.7	<12.0	34.8	67.1	832.7	39.6	<12.0	<4.0	105.2
P6	1720.1	25.3	2911.0	77.5	30.9	140.6	352.3	673.6	<12.0	<4.0	<10.0
P7	<0.4	<0.4	<0.4	< 12.0	9.5	243.6	845.5	126.9	<12.0	<4.0	800.1
P8	2831.9	42.3	2350.1	25.7	31.8	374.0	771.5	411.9	<12.0	<4.0	817.8
P9	843.7	1.6	5699.8	32.3	67.3	301.4	352.2	135.3	133.9	<4.0	<10.0
P10	15.0	1.2	136612.9	16.4	8.4	119.1	305.4	34.9	<12.0	<4.0	<10.0
H1	16034.0	789.3	10649.5	276.4	80.5	226.6	424.1	193.6	<12.0	<4.0	<10.0
H2	939.1	1.5	1911.8	<12.0	<4.0	211.1	510.7	107.6	<12.0	<4.0	<10.0
H3	7274.9	43.2	6784.0	<12.0	15.6	107.7	248.0	41.4	<12.0	<4.0	<10.0
H4	230.4	4.6	86.9	<12.0	<4.0	13.0	7.0	<12.0	<12.0	<4.0	<10.0
H5	10983.0	13.0	3663.1	21.1	33.5	394.1	1320.4	155.9	<12.0	<4.0	<10.0

P: primary health care centers; H: university central hospital; H1: yellow ward emergency unit; H2: day hospital; H3: internal medicine ward; H4: operating room; H5: outpatient clinic; Nbos d 5: *Bos domesticus*  $\beta$ -lactoglobulin; Cor a 9: *Corylus avellane*; Gal d 2: *Gallus domestics*; Ara h 3, Ara h 6: *Arachis hypogaea*; Der p 1: *Dermatophagoides pteronissinus*; Fel d 1: *Felis domesticus*; Can f 1: *Canis familiaris*; Bla g 2: *Blattella germanica*; Alt a 1: *Alternaria alternata*; Phl p 5: *Phelium pretense*. Values expressed in  $\mu\text{g/g}$ ;

**Figure 1.** Geometric representation of the concentration of airborne food and indoor allergens measured in each healthcare setting (n=15).



P: primary health care centers; H: university central hospital; H1: yellow ward emergency unit; H2: day hospital; H3: internal medicine ward; H4: operating room; H5: outpatient clinic; Nbos d 5: *Bos domesticus*  $\beta$ -lactoglobulin; Cor a 9: *Corylus avellane*; Gal d 2: *Gallus domesticus*; Ara h 3, Ara h 6: *Arachis hypogaea*; Der p 1: *Dermatophagoides pteronissinus*; Fel d 1: *Felis domesticus*; Can f 1: *Canis familiaris*; Bla g 2: *Blattella germanica*; Alt a 1: *Alternaria alternata*; Phl p 5: *Phelum pretense*.

Concentrations of food and indoor allergens (in  $\mu\text{g}/\text{g}$ ) were logarithmic transformed.