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The Most Common Inhalation Allergens of Animals Epithelia, Pollens and Fungi in Male and Female Pediatric Patients with Allergic Renitis in Iraq

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ABSTRACT

Background: Allergic rhinitis (AR) is considered as an abnormal immune response to harmless environmental stimuli usually inhalant allergens. The most prevalent allergic disease in pediatric is AR, the prevalence of AR has gradually increased. Moreover, Inhalation allergens especially pollens are the main cause of AR.

Objective: This study aimed to determine differences between sexes to the most common inhaled allergen (Animals Epithelia, Pollens and Fungi) in Pediatric Patients with allergic rhinitis in Iraq.

Methods: A cross-sectional observational study was conducted during the period from January 2023 to February 2025. Allergic children age ranged from 1 to 14 years old. They were collected from many clinics in City of Iraq. The pediatric inhalation panel kit Polycheck® – Diagnostics was used to reveal to the sensitivity of 20 different allergens.

Results: There were significant disparity between males and females in the positive rates regarding inhalation Allergens of pollens, males exhibited significantly higher sensitivity compared to females for 7 out of 8 pollen allergens; alder pollen (p=0.010), brich pollen (p=0.013), oka pollen (p=0.016), mugwort pollen (p=0.016), plantaine pollen (p=0.021) and timothy grass pollen (p=0.027). Rye pollen (p=0.109) was not significant, but trended towards higher male sensitivity and Hazel pollen showed no significant difference (p=0.171). Regarding to Fungal Allergens, males showed significantly higher sensitivity to *Dermatophagoides pteronyssinus* (p=0.032), while no significant gender differences were found for the other fungal and animal epitlelia allergens.

Conclusion: Male pediatric patients with allergic rhinitis in this Iraqi sample are significantly more likely to be sensitive to common environmental pollens (Birch, Alder, Oak, Timothy Grass, Mugwort, Plantain) and fungus (*Dermatophagoides Pteronyssinus*) compared to females.

Keywords: Allergic rhinitis (AR), Pediatric, Inhalantion allergens, Animals Epithelia, Pollens, Fungi.

Introduction

Allergic rhinitis (AR) is a prevalent allergic disease, characterized as a chronic, non-infectious inflammation of the nasal mucosa, mediated by immunoglobulin E (IgE) in response to allergen exposure[1,2]. Allergic rhinitis is an important disease with a global footprint and increasing prevalence, affecting both children and adults. Despite its under diagnosis and under treatment, it affects more than 500 million people worldwide[3,4]. In the pediatric population, AR has significant social and economic consequences; it reduced quality of life and sleep, poor academic performance[5-7], and AR is a main risk factor for the development of comorbid situations (like asthma, rhino sinusitis, and otitis media with effusion)[6]. The most prevalant allergic disease in pediatric population is AR[8], and the occurrence of AR has gradually increased, especially in early childhood[9,10]. Moreover, Inhalation allergens are the key determinants of AR[8,11]

The pathogenesis of AR involves a complex interaction between genetic predisposition and environmental exposure[6,12]. Upon sensitization, re-exposure to allergens like pollens, fungal spores, or animal-derived proteins initiates a type 2 inflammatory response, leading to classic symptoms of rhinorrhea, nasal congestion, sneezing, and pruritus, that influences the lungs and leads to difficulties in breathing[12]. The specific culprit allergens exhibit dramatic geographical variation, influenced by climate, flora, fauna, cultural habits (e.g., pet ownership), and urbanization levels. Therefore, creating a regional and national profile of sensitization patterns is not an academic exercise but a critical prerequisite for effective diagnosis, management, and development of targeted public health strategies[13].

Additionally, several types of allergen are found around us, the most common inhalation allergens that account for most allergic rhinitis in children, are fungi (*Dermatophagoides Pteronyssinus*), animal epithelia[14-16], pollen[15,17]. The three major categories of aeroallergens central to this study are:

- Animal Epithelia and Proteins: Allergens derived from cats, dogs, and other domestic animals are potent triggers. These small, sticky proteins can remain airborne for long periods and permeate environments, including those without pets, making them a significant indoor allergen[18].

- Pollens: Pollen grains (2.5–10 mm), male reproductive structures of plants, are a major causal agent of respiratory allergy[19,20]. Pollen is one of the common triggers of AR, and pollen-induced allergic rhinitis imposes a considerable burden on public health. High-risk atopic individual exposure to pollen leads the upper respiratory tract to release allergic mediators such as histamine and then triggers allergic reactions[21]

- Fungi (Molds): Fungi are ubiquitous in indoor and outdoor environments and can manifest health effects via IgE sensitization to specific genera. A comprehensive understanding of fungal sensitization prevalence and risk factors is currently limited to a handful of common environmental fungi (eg, *Alternari*, *Aspergillus*)[22]. Sensitivity to fungi, has been strongly associated with persistent and severe asthma and AR[23]. One of independent risk factors for fungal sensitization is male sex and differed for some fungi by ecoregion[24].

In Iraq, the unique environmental profile-characterized by a hot, arid climate, distinct seasonal patterns, specific vegetation along the Tigris and Euphrates rivers, and increasing dust storm activity-creates a distinctive aeroallergen milieu. Recent studies have begun to shed light on the Iraqi sensitization landscape. For instance, a 2020 study in Baghdad screening the sera for eight allergen types (animal dander, grasses, house dust, insects, mites, molds, trees and weeds) identified that molds as major allergens in AR and AS patients[25], while another in Al-Najaf concluded that approximately 93% of the children in Iraq were allergic to at least one inhalant[26]. On the other hand, one study showed that females outnumber males in AR patients[15,27].

Furthermore, the potential influence of sex (male vs. female) on allergic sensitization is an emerging area of interest. Epidemiological studies have shown that the prevalence and severity of allergic

diseases can fluctuate with age and sex, often attributed to hormonal influences, genetic factors, and differences in environmental exposure or immune response[28]. Investigating whether such differences exist in the Iraqi pediatric cohort is crucial for personalized medicine approaches. For doctors and scientists, it is becoming more and more important to understand the influencing factors, pathogenesis, and treatment progress of allergic diseases[29]. Identifying the factors influencing sensitization profiles are necessary for improving public health, and determining the distribution of allergens is important to understanding these afflictions[30,31]

In an individual, Inhalation allergen sensitization refers to allergen-specific immunoglobulin E (IgE) production and it is confirmed by measuring allergen specific IgE levels, total IgE in serum, or by positive responses to skin prick test (SPT)[32,33]

This study aimed to determine differences between sexes to the most common inhaled allergens (Animals Epithelia, Pollens and Fungi) Pediatric Patients with allergic rhinitis in Iraq. The results of this study provide a cornerstone for diagnosis, management, treatment, epidemiology, prevention/control, scientific research of pediatric allergic rhinitis in population.

Patients and Method

SUBJECTS IN THE STUDY

A cross-sectional observational study was performed during period from January 2023 to February 2025. Sixty four pediatric patients 32 male and 32 female with allergic renitis were referred to the lab for detection of the inhalation allergens responsible for their allergy, allergic children age range 1 to 14 years old from many clinics in City of Iraq.

INHALATION ALLERGENS DETECTION

Serum samples were collected from each patient and stored at 2–8°C for 4 weeks or frozen at -20°C for longer periods until analysis. Specific IgE antibodies against 20 inhalation allergens[34], including common inhalants: animal epithelia (dog, cat, horse, guinea big, hamaster, rabbit), various pollens (brich, alder, hazel, oka, timothy grass, rye, mugwort, plantaine) and fungi allergens (*Dermatophagoides Pteronyssinus*, *Dermatophagoides Farinae*, *Aspergillus Fumigatus*, *Cladosporium herbarum*, *Penicillium notatum*, *Alternaria alternata*), were detected using the quantitative enzyme immunoassay (EIA). Allergen-specific IgE testing was performed using the Polycheck® allergic Diagnostics kit (Germany), according to the manufacturer's instructions. In brief, serum samples were incubated in the cassette for 60 minutes. After washing, anti-IgE antibody was then added. following incubation, the precipitate was developed using a substrate. The color intensity of each line proportional to the respective allergen specific-IgE concentration was quantified using Biocheck Imaging Software (BIS). Results were interpreted according to the colors' intensity, categorized into classes ranging from 0 to 6, where class 0 represents non specific IgE antibody detection, class 3 clear antibody concentration and classes 4 to 6 indicate increasing concentrations of specific IgE antibody (lower limit of IgE concentration detection: 0.15 kU/L). Results are reported in kU/L (International Units per liter). For each patient, a result of class 3 or higher was representing a positive result for the corresponding allergen.

ETHICAL CONSIDERATIONS

The study concept for human studies was approved from College of Medicine, Jabir Ibn Hayyan university for medical and pharmaceutical sciences, Iraq by The Institutional Ethics Committee. Additionally, before taking part in the study, each individual gave written informed consent. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

The data have been analyzed by the use of Microsoft excel 2024 and SPSS version 26. These results are based on F-tests (likely ANOVA comparing male/female means). The "Mean"

values represent the average level of sensitivity (measured in kU/L) within each group.

Results

The different inhaled allergens have been viewed by tables (1), (2) and (3), in which p-value = < 0.05 is considered as significant. No statistically significant differences were found between males and females for any animal epithelium allergen tested (Dog, Cat, Horse, Guinea Pig, Hamster, Rabbit), all p-values Sig. are > 0.05 (range: 0.115-0.927). While mean values sometimes differed (e.g., Dog: Male 2.07 vs Female 3.93), (Table 1).

Table (1): The Most prevalent inhalation Allergens of animals epithelia in males and females Pediatric Patients with allergic renitis in Iraq

Type of allergen/epithelia		N	Mean	Std. Error	F test	Sig.
Dog	Male	32	2.0684	1.52619	0.553	0.460
	Female	32	3.9344	1.99242		
	Total	64	3.0014	1.25043		
Cat	Male	32	1.5766	1.21308	0.008	0.927
	Female	32	1.4194	1.21273		
	Total	64	1.4980	.85088		
Horse	Male	32	.4972	.14836	2.339	0.131
	Female	32	.2559	.05357		
	Total	64	.3766	.07970		
Guinea pig	Male	32	.1500	.00000	2.556	0.115
	Female	32	.1672	.01075		
	Total	64	.1586	.00544		
Hamaster	Male	32	.1553	.00402	0.013	0.908
	Female	32	.1559	.00362		
	Total	64	.1556	.00268		
Rabbit	Male	32	.1759	.01258	0.012	0.912
	Female	32	.1738	.01514		
	Total	64	.1748	.00976		

There were significant differences between sexes in the positive rates regarding inhalation Allergens of pollens, males exhibited significantly higher sensitivity compared to females for 7 out of 8 pollen allergens; alder pollen (p=0.010), brichpolline (p=0.013), okapolline (p=0.016), mugwort pollen (p=0.016), plantain epollen (p=0.021) and timothy grass pollen (p=0.027). Note Rye pollen (p=0.109) was not significant, but trended towards higher male sensitivity and Hazel pollen showed no significant difference (p=0.171) (Table 2).

Table (2): The most prevalent inhalation allergens of pollens in male and female pediatric patients with allergic renitis in Iraq.

Type of allergen/pollen		N	Mean	Std. Error	F test	Sig.
Brich	Male	32	6.0391	2.00222	6.575	0.013
	Female	32	.8456	.30505		
	Total	64	3.4423	1.05652		
Alder	Male	32	14.8009	5.50111	7.093	0.010
	Female	32	.1500	.00000		
	Total	64	7.4755	2.88049		
Hazel	Male	32	.4950	.24923	1.916	0.171
	Female	32	.1500	.00000		
	Total	64	.3225	.12552		
Oka	Male	32	15.0347	5.21407	6.172	0.016
	Female	32	1.9687	.68711		
	Total	64	8.5017	2.73539		
Timothy Grass	Male	32	2.1141	.68998	5.128	0.027
	Female	32	.4772	.21546		
	Total	64	1.2956	.37307		
Rye	Male	32	6.9341	2.92563	2.644	0.109
	Female	32	1.8869	1.03757		
	Total	64	4.4105	1.57220		
Mugwort	Male	32	4.0991	1.40653	6.108	0.016
	Female	32	.5887	.19733		
	Total	64	2.3439	.73838		
Plantain	Male	32	10.9747	3.67974	5.609	0.021
	Female	32	1.9706	.95590		
	Total	64	6.4727	1.96924		

Regarding to Fungal Allergens, males showed significantly higher sensitivity to D. pteronyssinus (p=0.032), while no significant differences according to sexes were found for the other fungal allergens (Table 3).

Table (3): The Most prevalent inhalation Allergens of fungi in male and female Pediatric Patients with allergic renitis in Iraq

Type of allergen		N	Mean	Std. Error	F test	Sig.
D. pteronyssinus	Male	32	.5428	.17141	4.840	0.032
	Female	32	.1650	.01043		
	Total	64	.3539	.08844		
D. farinae	Male	32	.2331	.02411	1.156	0.286
	Female	32	.1991	.02055		
	Total	64	.2161	.01586		
Aspergillus Fumigatus	Male	32	.2413	.06400	1.511	0.224
	Female	32	.1622	.00646		
	Total	64	.2017	.03229		
Cladosporium herbarum	Male	32	.2125	.03976	2.007	0.162
	Female	32	.1559	.00359		
	Total	64	.1842	.02012		
Penicillium notatum	Male	32	.2125	.03976	2.007	0.162
	Female	32	.1559	.00359		
	Total	64	.1842	.02012		
Alternaria alternata	Male	32	.1763	.00849	0.265	0.609
	Female	32	.2016	.04844		
	Total	64	.1889	.02444		

Discussion

Allergic rhinitis (AR) is one of the most common chronic inflammatory diseases in the pediatric population and up to 40% of children are affected globally[4]. The occurrence of allergic diseases in pediatric population not only has persistent adverse effects on qualiy of life, such as poor sleep quality and academic consequences, but also increases the risk of sleep disordered breathing, and is a major risk factor for the development of comorbid conditions such as asthma, rhinosinusitis, eczema, and otitis media with effusion[35]. Sensitization to inhalation allergens precedes the development of AR and is a strong risk factor for onset of clinical disease[36-38]

Allergic rhinitis is caused by seasonal or perennial exposure to outdoor pollens and fungi as well as indoor allergic triggers[39]. Children with pollen-AR are at high risk of persistent disease for at least 20 years. Childhood up to adolescence seems to be the most dynamic period of AR progression, and there are close cross-sectional and longitudinal association between sensitization, AR and asthma[40]. Common aeroallergens in RA pediatric patients include *D. pteronyssinus* (House dust mites), cats, alternaria, and animal allergens[15].

Atopic disease incidence is characterized by sex differences[41] and our study was conducted with the aim of specifically targeting the pediatric population, and to our knowledge, this may be the first study aimed solely at identifying gender differences in relation to the most common inhalation allergens (animal epithelium, pollen, and fungi) in pediatric patients with allergic rhinitis under the age of 14 years in Iraq.

Regarding to Dog Epithelium, females showed significantly higher mean sensitization levels compared to males (3.9344 vs 2.0684), although the difference was not statistically significant (p=0.4, >0.05). This result compatible with a case control study in Iraq (Baghdad), It was also observed that the percentage of female patients was significantly higher than the corresponding percentage in AR male patients but IgE level in sensetization to animal dander did not have statistically significant differences in both genders[42] The significant differences of allergens sensitization between females and males may be gradually appeared by age[43,44]. This trend warrants further investigation into potential sex-specific exposure patterns or immune response differences to dog allergens.

On the other hand, other animal epithelia (cat, horse, guinea big, hamaster, rabbit), no statistically significant differences were observed for these inhalation allergens according to genders. Means were generally low, suggesting these are less prominent inhalation allergens or that sensitization levels are similar between males and females in this population. Similar studies in Shenzhen and Guangdong, States of China were showed similar results, where sensitization to animals epithelia (especially dogs and cats) was not significant diferences among genders[45,46].

This study demonstrates that Pollen allergy the strongest and most consistent sex disparity, with males being significantly more sensitive across multiple types (Alder, Birch, Oak, Mugwort, Plantain and Timothy Grass with p-value: 0.010, 0.013, 0.016, 0.016, 0.021 and 0.027 respectively). A retrospective cross-sectional study in China included a total of 4,279 children (<1-18y) diagnosed with AR, Mugwort reported the higher sexes disparity than other inhaled polen allergens, male patients showed a significant increased risk[45].

The observed differences likely result from a complex interplay of: 1.behavioral factors; males often engage in more outdoor activities leading to greater cumulative pollen exposure, potentially increasing sensitization risk[11], while females spent most of their time at home 2.biological factors; sex hormone is major determinant of sex-related difference, playing a crucial role in regulating growth and development during puberty. It also exert broad range modulation of immune cell functions, and a dichotomy exists in the immune responses between the sexes[47]. 3. lifestyle such as hormonal medications and sports habits[48-50] 4. Regional Flora[51]; The specific pollens showing strong male predominance are likely major inhalation allergens in the study region, and males appear disproportionately affected.

On the other hand, A multicenter study in other regions It was also observed that the percentage of AR male pediatric patients was significantly higher than the percentage in AR female patients but did not have statistically significant differences of all pollen allergens (eg, Grass, Tree, Weed) except *Chenopodium album* and *Artemisia vulgaris* allergens (were quite similar between females and males). The sensitizations to pollen allergens varied widely among geographical areas[52]. It might be related to the difference in sexual hormones and lifestyle such as hormonal medications and sports habits[48,52]. While Hazel and Rye pollens showed higher male means but did not reach statistical significance (p value= >0.05), possibly due to smaller effect size or sample size limitations.

Although males showed significantly higher sensitization to *D. pteronyssinus* compared to females. Two studies in China in two different regions, A 2022 study in Guangdong, that involved 2,316 pediatric patients with age 1-14 years suggesting a higher prevalence of D. pteronyssinus

sensitization in males than females (p=0.003), and 2025 study in Shenzhen, revealed that the most common inhalation allergen is house dust, and such high frequency confined to male AR patients only (p=<0.001)[45]. On the other hand, a cohort study in United States observed a higher rate of fungal sensitization for male versus female allergic patients for each fungus (like *Aspergillus* and *Alternaria*) across all age ranges tested, this US study concluded that male was one of independent risk factors for fungal sensitization. This Male predisposition potentially linked to hormonal influences on IgE response[47] Differences in results may be related to genetic, environmental, geographic/climatic factors, or even lifestyles[53].

Whereas other Fungi (*D. farinae*, *A. fumigatus*, *C. herbarum*, *P. notatum*, *A. Alternata*, *Cladosp. Herbarum* and *Pennotatum*), no statistically significant differences were found for these allergens according to sex. Means were generally low, suggesting these are less prominent triggers or that sensitization levels are similar between genders in this population. In contrast, a few smaller investigations reported higher prevalence among female patients. For example, *A. alternata* sensitization rate was higher in children and in adolescent girls in Northern Greece[54].

A recent case control study in Iraq (Baghdad) was maesured the IgE antibody level against four allergen types (animal dander, grasses, mites, and molds) observed a tendency for males to have a higher level of IgE than females in AR, but the differences did not attend a significant level, and the level of IgE may not be affected by sex.[42]. In an Italian study, there was an equal rate of prevalence to several fungi for both sexes[55]. This differences due to geographic differences with regard to sex-specific prevalence, the distribution and pattern of allergy varied widely from one country to another and from area to another[15,24,52].

In our study females was observed less susceptible to most inhalation allergens, this may be due to females exhibit stronger innate and adaptive immune responses than males even though the immune system protection similarly in males and females[56], this making females less susceptible to most inhalation allergens and enables them to fight foreign bodies more efficiently, this is the reason why females were exposed to certain types of inhalation allergens less than males.

The small sample size (N=32 per gender per allergen group) limits generalizability but provides clear preliminary evidence of significant pollen-related gender differences. Further study needed to be carried out.

Conclusions

Male pediatric patients with allergic rhinitis in this Iraqi sample are significantly more likely to be sensitive to common environmental pollens (Alder, Birch, Oak, Mugwort, Plantain, Timothy Grass) and one key fungal allergen (*D. Pteronyssinus*) compared to females.

Conflict of Interest Statement:

None declared.

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