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ORIGINAL ARTICLE

EAST in Children with Allergic rhinitis: Experience from Indian Tertiary Centre

P. Naina[1] · Susmitha Karunasree Perumalla[2] · Megha Krishnan[1] · Mary John[1] · Ajoy Mathew Varghese[1] · John Antony Jude Prakash[2]

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Abstract Allergic rhinitis (AR) is recognized as a growing global health disease with considerable importance among children and adolescents. This study aims to study the clinical and sensitization profile of children with allergic rhinitis using EAST. All children presenting to pediatric ENT outpatient with a clinical diagnosis of AR were prospectively recruited. Detailed demographic and clinical history including self-reported allergens, predominant symptoms and associated comorbid conditions were obtained. Severity of symptoms was graded on a visual analogue scale. Specific Ig E antibodies to 20 inhalant allergens was measured using EAST (EUROIMMUN, Germany).The pattern of sensitization was analyzed with respect to age, symptoms, associated comorbid conditions and urbanization. We recruited 328 children with a clinical diagnosis of AR (Mean age 10.3 year, IQR 8–13 years) Nasal block was the predominant symptom across all age groups, sneezing became more troublesome during adolescence. In 191 children sera were tested for allergen specific IgE, 119 (62.3%) showed positive sensitization. The most common sensitization noted was for cockroach, followed by dust mite and pollens. Majority had polysensitization (73%). Those who were predominantly sneezers were more likely to be sensitized with indoor allergens ($p < 0.05$). Among the comorbid conditions, asthma and atopic dermatitis accounted for maximum non ENT physician visits. The pattern of sensitization did not vary with age, urbanization or comorbid condition. This study highlights the clinical and sensitization profile of children with AR in South East India. Various peculiarities of this community has been presented which needs further attention.

Keywords Allergic rhinitis · Pediatric · India · Enzyme allegro sorbent assay · Sensitization · Clinical profile · Blockers · Sneezers · Comorbid conditions · Dust mites

Introduction

Allergic rhinitis (AR) is a common global health concern with a worldwide prevalence reported to be between 10 and 30% [1–3]. It is characterized by nasal mucosal inflammation with four cardinal symptoms of nasal congestion, pruritus, rhinorrhea and sneezing. A recent meta-analysis has reported the overall prevalence of AR in children to be around 12.6%, causing significant impairment of quality of life [4, 5]. Phase 3 of the International study of asthma and allergy in children (ISSAC) study reported the prevalence of AR to be 11.3% in children aged 6–7 years and 24.4% in children aged 13–14 years in India [3]. Although there are plenty of reports on AR they are mostly reported from high income countries in the western hemisphere with limited data from low and middle income countries especially South East Asia [6].

AR is increasing in prevalence due to genetic predisposition and increased environmental exposure to allergens. Sensitization to an allergen is an important risk factor for development of allergic disease. Tests to detect sensitization help to confirm an allergic trigger suspected on clinical history. This knowledge can help to formulate

✉ P. Naina
drp.naina@hotmail.com

[1] Department of ENT, Christian Medical College, Vellore, Tamil Nadu, India

[2] Department of Microbiology, Christian Medical College, Vellore, Tamil Nadu, India

environmental control measures focusing on prevention of sensitization and progression of disease. Sensitization can be assessed by skin tests or in vitro assays [4, 7]. The most common method continues to be skin prick test (SPT) as they are more easily available and less expensive. However, it is limited by the compliance of multiple skin pricks in children, potential for anaphylaxis and interference with skin conditions. In vitro tests such as Radioallergosorbent test (RAST), Multiple allergen simultaneous test (MAST), Fluorescence allergosorbent test (FAST), and Enzyme linked allegro sorbent test (EAST) do not have those limitations [8]. They are far less invasive and safer but can be costlier with delayed results. Our study aims to study the clinical and sensitization profile of children with allergic rhinitis using EAST.

Methodology

A prospective study was performed between 2016 and 2019 after obtaining institutional review board approval (IRB No 10140/16). All consecutive children with a clinical diagnosis of AR presenting to a pediatric ENT outpatient were recruited. The diagnosis was made by a pediatric otolaryngologist and was defined as a child with history of one or more of the symptoms including nasal bock, rhinorrhea, sneezing, and pruritus consistent with an allergic cause and examination showing but not limited to pale boggy mucosa, clear rhinorrhea [9, 10]. A detailed history taking and examination was done. History included demographic details, type and severity, family history, residence, and self-reported specific or nonspecific allergen that they were aware of. Children were asked to report their predominant nasal symptom, if it was sneezing and watery discharge they were classified as "sneezers", and if it was nasal blockade they were described as "blockers [10, 11]. In addition they had to grade the severity of their four cardinal symptoms on a visual analogue scale (VAS) scale ranging from 0 to 10. Intermittent AR was characterized by symptoms for less than 4 days per week or less than 4 consecutive weeks. Persistent AR was defined by symptoms occurring more than 4 days per week for at least 4 consecutive weeks [10, 12]. The severity was assessed as mild or severe based on ARIA guidelines [10]. Furthermore, other coexisting conditions were also noted and its relation with the different allergens was noted.

In recruited children, five ml sera were tested to determine allergies to inhalant allergens using the Euroline Pediatric IgE test kit EAST (EUROIMMUN, Germany) according to the directions of the manufacturer. EAST is an ELISA test measuring total and specific IgE antibodies in serum or plasma against food and inhalant-allergens. It contains test strips coated with parallel lines of twenty different allergen extracts. The intensity of bands was calculated with the EURO Line scan digital evaluation system and any score above 1 was taken as positive.

Statistics- The children were stratified across different age groups. The pattern of inhalant allergens determined by EAST was described and analyzed with respect to age, symptoms, urbanization, and comorbid conditions.

Results

We recruited 328 children with a clinical diagnosis of AR. The mean age was 10.3 years (IQR 8–13 years). The demographic and clinical characteristics of the study group are presented in Table 1. More than three-quarters (76.2%) had mild symptoms. Nasal block was noted as the predominant symptom in 67% of children. Table 2 depicts the mean ±SD of the VAS score across the different age groups. While nasal block consistently remained a troublesome symptom across all age groups, sneezing became more troublesome during adolescence. The pattern of allergens was analyzed between those 'predominantly blockers' and 'predominantly sneezers' (Fig. 1). Those who were predominantly sneezers were more likely to be sensitized with indoor allergens such as house dust mite mix ($p = 0.014$), *D. farinae* ($p = 0.02$), and molds such as Trichophyton ($p = 0.00$).

Among the 328 children with AR, 191 were tested with EAST and only 119 (62.3%) showed positive sensitization. The pattern of sensitization on EAST is shown in Fig. 2. The most common sensitization noted was for cockroach, dust mite mix, and D farina followed by pollens such as corn, rye, sunflower, and timothy grass. Majority had polysensitization (87/119). No significant correlation of polysensitization with age was noted. In addition, when we looked at individual allergens there was no difference in the pattern of allergens across age groups (Fig. 3). Most of our study population were from urban (58.2%) or suburban (18.9%) background, only 20% were from rural background. There was no significant correlation between the pattern of allergens and the place of residence in our population (Table 3).

Table 1 also enlists the common coexisting conditions in our study group. Of this asthma and atopic dermatitis accounted for maximum non-ENT physician visits in our study group. The pattern of sensitization did not vary between those with AR and those with AR and those with coexisting asthma or atopic dermatitis (Table 4).

Table 1 Clinical and demographic characteristics of children with AR

Age	Mean ± SD	10. ± 3.4 years
	Median (IQR)	11.0 (8–13)
Gender	Males	226 (68.9%)
	Females	102 (31.1%)
Type and severity	Mild intermittent	138 (42%)
	Severe intermittent	41 (12.5%)
	Mild persistent	112 (34.1%)
	Severe persistent	37 (11.2%)
Predominantly Blockers	219	67%
Predominantly Sneezers	109	33%
Residence	Urban	191 (58.2%)
	Rural	75 (22.9%)
	Suburban	62 (18.9%)
Pattern of self-reported allergens	Specific-	Nonspecific-
	Dust-254 (77.4%)	Weather change-253 (77.1%)
	Dampness-212 (64.2%)	Exposure to cold-239 (72.9%)
	Indoors-216 (65.9%)	Increased humidity-68 (20.7%)
	Smoke-88 (26.8%)	After exercise-61 (18.6%)
	Pollen-97 (29.7%)	
	Traffic fumes-79 (24.1%)	
	Pets-44 (13.4%)	
	Food related-60 (18.3%)	
Common comorbid conditions	Chronic hawking cough	114 (34.8%)
	Atopic dermatitis	112 (34.1%)
	Allergic conjunctivitis	105 (32.0)
	Adenoid hypertrophy	94 (28.7%)
	Asthma	80 (24.4%)
	GERD	52 (15.9%)
	Tubal block	46 (14.0%)
	Sleep disturbed breathing	38 (11.6%)
Most reasons for Non ENT physician visits	Pediatrician-Asthma	96 children (29.2%)
	Dermatologist-Atopic dermatitis	112 children (34.1%)
	Opthalmologist-Allergic conjunctivitis	43 children (13.1%)
Family history of AR in any one parent		221 (67.4%)
History of AR in siblings		47 (14.3%)
History of asthma in family		104 (37.7%)

Discussion

This was a cross-sectional study to describe the clinical presentation and evaluate the pattern of allergen-specific sensitization in children in our population using EAST. The peak prevalence was in 10–14 years, similar results have been observed by others [4, 13, 14]. Similarly, male preponderance observed in this study has also been reported in the literature [14]. Majority (76%) had mild disease and there was almost equal distribution between intermittent and persistent type (1.2:1). Positive family history of allergy, an important risk factor [15], was present in 67.4% of our patients. Less than 20% of our study population was living in rural areas and this in agreement with the protective influence of a rural environment reported by other authors [16, 17]. However, analysis of our data could not implicate any specific allergen in the urban population. Among the self-reported allergens in our population non-allergic triggers such as weather change, dampness, and exercise were more commonly reported than specific triggers like indoor dust mites, pollen, or pets. Poor awareness of the disease and the types of allergens could be the reason

Table 2 Mean and SD of Visual analogue score of four symptoms of AR across various age groups

Age group	Nose block	Discharge	Sneezing	Itching
2–4	5.50 ± 2.24	3.69 ± 1.80	3.75 ± 2.30	2.00 ± 1.41
4–6	5.98 ± 2.20	3.80 ± 2.23	3.26 ± 2.32	3.48 ± 2.83
6–8	5.54 ± 2.14	3.30 ± 2.13	4.38 ± 2.34	2.91 ± 1.68
8–10	5.89 ± 2.38	4.26 ± 2.55	4.14 ± 2.72	3.45 ± 2.73
10–12	6.20 ± 2.28	4.74 ± 2.60	4.74 ± 2.44	3.33 ± 2.38
12–14	6.28 ± 2.09	4.29 ± 2.39	5.23 ± 2.93	3.32 ± 2.63
14–16	6.90 ± 1.99	4.93 ± 2.84	5.62 ± 2.90	3.08 ± 2.26
16–18	6.40 ± 2.07	4.40 ± 2.51	7.00 ± 3.67	2.00 ± 0.00

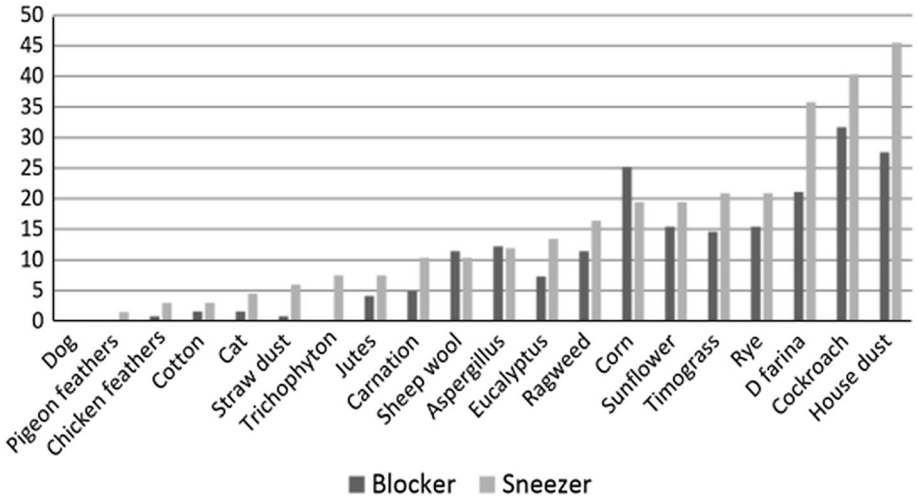

Fig. 1 Pattern of sensitization between nasal blockers and sneezers. The allergens house dust mite mix (p = 0.014), *D. farinae* (p = 0.02), Trichophyton (p = 0.00) and straw dust (p = 0.034 were significantly more in sneezers

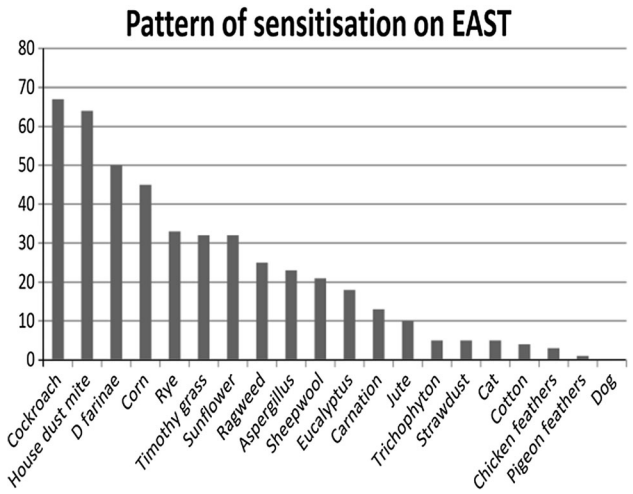

Fig. 2 Pattern of sensitization with EAST. Indoor allergens (Dust mites, cockroach) were more common than pollen allergens

for poor reporting of specific allergens [6]. This pattern of nonspecific triggers was seen in a study from Nigeria and can confuse with vasomotor rhinitis [18]. One accepted explanation of the predominance of nonspecific triggers in tropical countries is suggested by Caraballo et al. [19]. They state that in tropical regions change in weather or onset of rains, can change the humidity and temperature predisposing to a higher allergen mite and mold content, change in the aerobiology, and prejudicing to viral infections [19].

Most (67.7%) of the children in our study were predominantly 'nasal blockers'. The symptom of nasal block had consistently the highest VAS score across all age groups except in the adolescence age when sneezing was more troublesome. Different populations have reported contradictory results on the predominant symptoms [5, 14, 18, 20]. This is a reflection of the different genetic constitutions, epigenetic events, and environmental influences in different regions and highlights the need for each region to have its own data. In our analysis, those with indoor allergens were more likely to be 'predominantly sneezers' ($p < 0.05$), this is in contrast to earlier studies from India which reported blockers to be more sensitized to polyvalent house dust, dust mites and fungi and sneezers to pollen [11, 20].

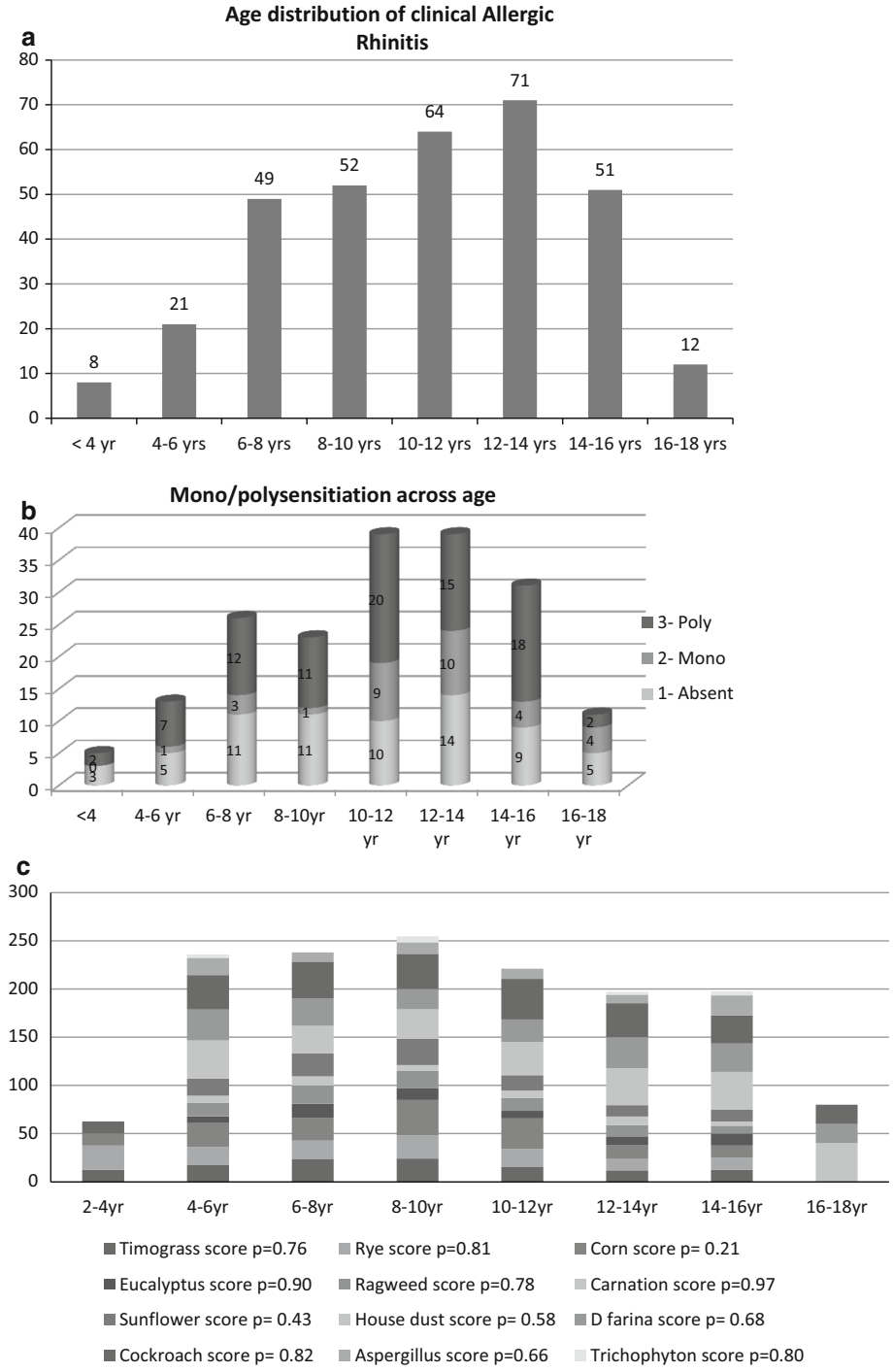

Fig. 3 **a** Age distribution of children with Allergic rhinitis. **b** Pattern of poly and mono sensitization across different age groups. **c** Pattern of different allergens across different age groups

Allergen sensitization pattern revealed that indoor allergens such as house dust mite mix, *D. farina*, and cockroach were the most common followed by pollen allergen. Although the allergen panel specially designed for India was used, only 62.3% showed positive sensitization despite all having symptomatic allergic rhinitis. The low rate of positivity has been noted by other authors and is a cause for concern [21]. This could be because some allergens causing AR in our population may not have been picked up as they were not included in the panel [22]. This highlights the need to relook at the commercial allergen panels for tropical countries especially those made for India.

Among those showing a positive response poly sensitization was more common than mono sensitization. Within our study population, the rate and diversity of polysensitisation showed a rising trend after the age of 4 years, peaking at ten years then decreasing by adolescence.

Table 3 Pattern of inhalant allergens across urban, rural and suburban backgrounds

Allergen	Area			P value
	Urban	Rural	Sub-Urban	
Timothy grass	17 (81)	2 (9.5)	2 (9.5)	0.072
Rye	14 (73.7)	3 (15.8)	2 (10.5)	0.308
Corn	18 (69.2)	6 (23.1)	2 (7.7)	0.195
Eucalyptus	6 (75)	1 (12.5)	1 (12.5)	0.596
Ragweed	8 (72.7)	2 (18.2)	1 (9.1)	0.521
Carnation	4 (66.7)	1 (16.7)	1 (16.7)	0.901
Sunflower	15 (78.9)	2 (10.5)	2 (10.5)	0.139
House dust mix	31 (75.6)	6 (14.6)	4 (9.8)	0.025
D. farina	28 (77.8)	5 (13.9)	3 (8.3)	0.021
Cockroach	21 (65.6)	8 (25)	3 (9.4)	0.211
Cat	2 (66.7)	1 (33.3)	0 (0)	0.643
Chicken feathers	0 (0)	0 (0)	1 (100)	0.150
Aspergillus	3 (30)	4 (40)	3 (30)	0.174
Trichophyton	1 (100)	0 (0)	0 (0)	0.691
Cotton	0 (0)	0 (0)	0 (0)	
Straw dust	1 (50)	1 (50)	0 (0)	0.546
Jutes	0 (0)	1 (50)	1 (50)	0.253
Sheep wools	4 (44.4)	2 (22.2)	3 (33.3)	0.613

Previous studies have also found the prevalence and range of polysensitisation to increase with age [14, 23]. We noted the peak in sensitization and clinical allergy to be almost parallel. Usually, two or three seasons of pollen exposure and subsequent sensitization are needed for clinical allergy, while in perennial indoor allergens this can occur after few months of exposure.

House dust mite allergy was predominant in our study and is similar to that seen in other studies [11, 19, 21, 24]. Tropical countries such as Singapore, Taiwan, and Malaysia especially have shown a high prevalence of sensitization to mites due to the warm and humid climate [19, 21, 25]. The next common allergen was cockroach as reported in other studies from urban tropical regions [26]. The role of dust mite being a primary sensitizer and facilitator for cockroach sensitization has been studied by cross inhibition studies [19]. Pollen (Timothy grass, ragweed, rye, and corn, sunflower) sensitization was the next commonly seen allergen after dust mites and cockroach. A similar pattern of sensitization has been reported from Indonesia and Thailand [22, 26]. Pollen sensitization rates are much lower than those reported from similar populations in temperate countries [13, 19]. This could be due to the different aerobiology of different geographical areas. A different pattern of pollen sensitization such as oil palm pollen and resam fern spores has been reported from tropical countries [21]. This highlights the need for more information on the sensitization potentials of tropical pollen and molds.

AR is a local nose specific manifestation of allergic disease. The coexistence of AR with other allergic conditions such as asthma, allergic conjunctivitis, and atopic dermatitis as seen in this study is well known [6, 10, 11, 19]. Atopic dermatitis is a common association with AR and is thought to be associated with a two-fold increase in AR when compared to those without AD [19, 27]. AD is generally considered to be the first manifestation of the allergic march progressing to asthma and AR, although this typical phenomenon is seen in less than 7% of children [28]. Cough in AR could be due to a variety of causes which include rhino bronchial reflex and post-nasal drip [4]. However, in chronic cough, asthma should always be considered as a possible etiology. Pediatric asthma is seen in 3–38% of children with AR while Allergic conjunctivitis is seen in 35% to 74% of patients with AR [4, 5, 19, 23, 29]. A higher prevalence of adenoid hypertrophy, similar to ours has been noted in children with AR [30]. Increased sensitization to inhalant allergens is believed to alter the immunology of the adenoid tissue and predispose to adenoid hypertrophy.

Our study found that the children with symptomatic AR, with or without comorbidities such as atopic dermatitis and asthma were more likely to show poly sensitization even though this was not statistically significant. However, when

Table 4 Pattern of number and type of allergen in children with only AR, AR with Asthma and AR with atopic dermatitis

Allergen	AR, N = 191		AR with Asthma, N = 48		AR with Atopic dermatitis N = 56		P value
	N	%	N	%	N	%	
Number of allergens							
Absent	72	37.7	16	33.3	22	39.3	0.671
Mono	32	16.7	6	12.5	3	5.4	0.346
Poly	87	45.5	26	54.2	31	55.4	1.000
Type of allergen							
Timothy grass	32	16.8	13	27.1	12	21.4	0.241
Rye	33	17.3	12	25	13	23.2	0.2
Corn	45	23.6	16	33.3	16	28.6	0.245
Eucalyptus	18	9.4	9	18.8	5	8.9	0.251
Ragweed	25	13.1	13	27.1	12	21.4	0.241
Carnation	13	6.8	5	10.4	4	7.1	0.162
Sunflower	32	16.8	11	22.9	11	19.6	0.21
House dust mite mix	64	33.7	16	33.3	21	37.5	0.162
D farina	50	26.2	14	29.2	16	28.6	0.187
Cockroach	67	35.1	23	47.9	21	37.5	0.313
Cat	5	2.6	0	0	2	3.6	0.032
Dog	0	0	0	0	0	0	–
Pigeon feathers	1	0.5	0	0	0	0	–
Chicken feathers	3	1.6	2	4.2	2	3.6	0.086
Aspergillus	23	12	8	16.7	3	5.4	0.253
Trichophyton	5	2.6	1	2.1	0	0	0.08
Cotton	4	2.1	0	0	1	1.8	0.034
Straw dust	5	2.6	1	2.1	3	5.4	0.058
Jute	10	5.2	1	2.1	3	5.4	0.058
Sheep wool	21	11	4	8.3	7	12.5	0.094

we looked at individual allergens, none had any significant association with asthma or atopic dermatitis. This is in contrast to other studies which has shown that sensitization to indoor aeroallergens such as dust mites and cockroach is significantly associated with childhood asthma [19, 21, 23, 24, 26].

To summarize the age distribution and male preponderance of AR has universally similar presentations. Most children presented with mild disease which is why AR is still considered a nuisance disease and not given its due. Nasal block was the most troublesome symptom although with age sneezing also caused increased misery. Indoor allergens were the most common allergens in our children and sneezers were most likely to have sensitization to them. A significant number of children with AR had coexisting conditions such as asthma, adenoid hypertrophy, dermatitis, and conjunctivitis. There is a role to further outline these associations and see how the management of one can affect the other.

The major limitation of our study was that we studied only patients who visited our hospital. Therefore, there was a possibility of selection bias because patients with severe symptoms were overrepresented in the study. A community-based study with a larger sample size will help us understand and define the epidemiological trends and risk factors that will help in better management of children in this geographical location.

Conclusion

To conclude this is the first study from this geographical location highlighting the clinical and sensitization profile of children with AR. The profile of allergy and sensitization in this community has certain peculiarities that need further attention. The fact that indoor allergens are the most common allergens in AR and its associated comorbidities needs further detailed investigation. The need for a specific panel for this geographic location is highlighted. The results of this study will help to increase our knowledge of AR in children in this geographical area and formulate specific avoidance measures.

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Data availability All authors had access to the data and a role in writing the manuscript.

Code availability Not applicable.

Compliance with ethical standards

Conflicts of interest The authors have no benefits, financial interests, or conflicts of interests to disclose.

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