# Identification of aero-allergen sensitization in children seeking treatment for bronchial asthma at a tertiary care hospital for children in Sri Lanka

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## Abstract

*Objectives* Despite a significant rise in asthma globally as well as in Sri Lanka, data regarding allergen sensitization patterns and other risk factors for asthma are not available. Therefore, we set out to determine the allergen sensitization patterns in children with asthma in Sri Lanka.

*Methods* Skin prick testing for common indoor aeroallergens (cockroach, cat, dog, house dust mite, moulds) were carried out in 156 children with bronchial asthma at Lady Ridgeway Hospital for Children.

*Results* 49.1% of the patients were sensitized to at least one allergen and 6.4% were sensitized to three or more allergens. Of the children 37.8% tested positive to house dust mite, 23.7% to cockroach, 5.8% to indoor moulds, 12.2% to cats and 8.9% to dogs. Allergen sensitization was significantly less in children aged four years or younger than in older children ($p$<0.0001). A family history of asthma or allergic rhinitis (AR) was a significant risk factor ($p$<0.0001) for allergen sensitization (OR 10.9, 95% CI 3.9 to 30.1). Frequency of symptoms was significantly higher in those who used firewood alone compared to those who used other fuels (OR 2.5, 95% CI 1.1 to 5.8).

*Conclusions* Sensitization to aero-allergens was seen in a majority of children with asthma. Sensitization was significantly more in children above 4 years of age. Patients with more frequent symptoms and with AR were more likely to be sensitized to allergens.

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## Introduction

Asthma, atopic dermatitis (AD), allergic rhinitis (AR), allergic conjunctivitis and food allergies are a significant cause of morbidity and mortality. Such diseases, which are regarded as IgE antibody mediated diseases, occur due to sensitization to common environmental allergens [1]. These disorders are unfortunately on the rise.

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Guidelines from the US National Asthma Education and Prevention Programme recommends that the role of potential indoor allergen sensitization should be evaluated in at least those with persistent asthma [2]. Guidelines from Australian Government Department of Health and Aging recommend evaluation of those with asthma for allergen sensitization as 80% of individuals with asthma have allergen sensitization [3]. These guidelines state that allergen sensitization should be evaluated by skin prick testing, which is considered the gold standard in allergy testing [4]. The European Asthma Paediatric Group has also recommended allergen testing in those who are likely to have allergen induced asthma, because identifying the asthma phenotype is important in patient management [5]. All these guidelines state that aeroallergens should be identified and avoided wherever possible.

The International Study of Asthma and Allergies in Childhood (ISAAC) epidemiological research programme established in 1991 aimed at determining the scale of the problem worldwide and the factors affecting its prevalence because asthma and allergies were increasing in prevalence and severity [1]. The ISAAC study, first conducted in 1972 and repeated in 2002 showed a dramatic increase in overall prevalence of AD, asthma and allergic rhinitis [1]. Although the rise in allergic diseases is highest in developed countries, especially in the temperate climates, several epidemiological studies from Asia also show that asthma and other allergy related diseases are on the rise [6]. The prevalence rates of asthma in several South East Asian countries have significantly increased and in 2002 the prevalence rates were shown to be between 6.3-27.4% [7]. Data from the ISSAC study for the South Asian region shows a prevalence of asthma of 6.4% among children [1].

Although many studies have been carried out to determine patterns of allergen sensitization in US and European countries, such data are not available for Sri Lanka. Due to differences in the environment, patients with allergic diseases in South Asian countries may have allergen sensitization patterns different to those in temperate climates. Identification of the allergen/s responsible help patients avoid them, resulting in significant improvement of symptoms [8]. Apart from allergen avoidance, desensitization has been successfully achieved in many patients, with dramatic effect on the patient's symptoms. Sublingual and subcutaneous immunotherapy are as effective as inhaled budesonide in controlling asthma and offer additional benefits such as treating rhinitis symptoms and bronchial hyper responsiveness [9].

Skin prick tests or the measurement of specific IgE antibodies in blood are some of the tests that identify allergens [10]. Of these, the skin prick test is considered the gold standard in diagnosis of allergies [11]. The skin prick test is more specific and sensitive in the diagnosis of allergies and correlates well with the severity of allergy [12]. Therefore, we set out to determine the indoor aeroallergen sensitization patterns in a cohort of paediatric patients attending an asthma clinic at the Lady Ridgeway Hospital for Children in Sri Lanka.

## Methods

One hundred fifty six patients who were referred to the asthma clinic at the Professorial Unit Lady Ridgeway Hospital for Children were included in the study after obtaining informed written consent from parents. Approval was obtained from the Ethics Review Committees of the Faculty of Medicine, University of Colombo and the Medical Research Institute, Colombo. An interviewer administered questionnaire recorded clinical details of the patients including severity, co-morbid factors and environmental factors. Asthma was diagnosed according the guidelines of the Expert Panel Report (EPR-3) on Asthma Diagnosis and Treatment Guidelines [13]. Allergic rhinitis and rhino conjunctivitis were diagnosed by the presence of an inflammatory condition of the nose and conjunctiva characterized by sneezing, nasal blockage/ obstruction/congestion or nasal discharge [14].

Skin prick testing was carried out according the guidelines set by the European Academy of Allergy and Clinical Immunology [12]. The skin prick tests were carried out for common indoor aeroallergens (Allergropharma, UK) which included *Dermatophagoides pteronyssinus, Periplaneta americana* and an indoor mould panel which included *Aspergillus fumigatus, Mucormucedo, Penicillium notatum, Pullulariapullulans, Rhizopusnigricans, Serpulalacrymans*, dog dander, cat danderand positive (0.1% histamine) and negative controls. Briefly, single drops were put on volar surface of the forearm, spaced 3.5 cm from each other.The size of the wheal was recorded between 15-20 minutes. The test was considered positive if the wheal size was >3 mm of the negative control.

Statistical analysis was performed using Graph pad PRISM version 6. Degree of association between allergen sensitization and asthma and allergic rhinitis was expressed as the odds ratio (OR), which was obtained from standard contingency table analysis by Haldane's modification of Woolf's method. The Fisher's exact test was used to determine the *p* value.

## Results

The mean age of the patients was 6.8 years (SD ±3.2). Ninety five (60.8%) were females. Seventy five (48.1%) patients had asthma and AR, 80 (51.3%) had asthma only. Seventy seven (49.3%) children were sensitized to at least one allergen; 45 (28.8%) were sensitized to only one allergen, 28 (19.9%) to two allergens, and 10 (6.4%) sensitized to 3 or more allergens. Sensitivity tests were positive for house dust mite (HDM) in 59 (37.8%), cockroach in 37 (23.7%), the indoor mould panel in 9 (5.8%), cats in 19 (12.2%) and dogs in 14 (8.9%). A first degree relative with asthma or AR was present in 28

(17.9%). A family history of asthma or AR was a significant risk factor for allergen sensitization (OR 10.9, 95% CI 3.9 to 30.1; $p<0.001$). Twenty three out of 28 (82.1%) patients with a family history of AR or asthma were sensitized to at least one allergen, whereas only 54 out of 128 (42.2%) of those without a family history were sensitized to at least one allergen.

Allergen sensitization was commoner in children who had AR and asthma, compared to those who had asthma alone (Table 1). For instance, 26 (36.1%) children with both AR and asthma were sensitized to cockroach whereas only 10 (12.5%) with asthma alone were sensitized to cockroach. Sensitization to house dust mite and indoor moulds were also commoner in those who had both AR and asthma compared to those with asthma alone.

Children aged 4 years or older were significantly more likely to be sensitized to at least one aeroallergen compared to those who were aged less than 4 years (OR 8.3, 95% CI 2.9 to 23.24; $p<0.0001$). Only 5 (16.1%) children aged less than 4 years were sensitized to at least one aeroallergen, whereas 72 out of 117 (61.5%) children aged 4 years or older were sensitized. Of the 21 (26.9%) children reporting daily symptoms 21 (50%) were sensitized to at least one aeroallergen. However, no difference was seen between allergen sensitization and the frequency of symptoms ($p=0.46$) (Table 1). Sensitization to indoor moulds was not significantly associated with occurrence of daily symptoms (OR 2.1, 95% CI 0.55 to 8.4; ($p=0.22$)). Five out of 107 (4.7%) with less frequent symptoms were sensitized to indoor moulds whereas 4 out of 42 (9.5%) with daily symptoms were sensitized.

The type of fuel used for cooking was recorded in 151 patients (Table 2). Thirty five (38.4%) used gas as the sole source of fuel during cooking, 17 (11.2%) used kerosene and 30 (19.9%) used firewood alone. Frequency of symptoms was significantly higher in those who used firewood alone, compared to use of other fuels (OR 2.5, 95% CI 1.1 to 5.8; $p=0.02$). Although use of gas was associated with a lower frequency of symptoms this was not statistically significant (OR 0.61, 95% CI 0.29 to 1.3; $p=0.26$). Sensitization to allergens was commoner among the 35 (60.3%) who used only gas compared to those who used kerosene or firewood (23/47, 48.9%). However, this was not statistically significant (OR 1.59, 95% CI 0.73 to 3.4; $p=0.3$). Although allergen sensitization was higher in those who used mosquito coils this again was not statistically significant (OR 1.56, 95% CI 0.71 to 3.4; $p=0.33$) (Table 2).

**Table 1. Indoor aeroallergen sensitization patterns in patient with allergic rhinitis and asthma**

| | *All patients N = 156 (%)* | *Asthma and AR N = 72 (%)* | *Asthma only N = 80 (%)* | *Daily symptoms N = 43 (%)* |
|---|---|---|---|---|
| House dust mite | 59 (37.8) | 33 (45.83) | 25 (31.25) | 15 (34.88) |
| Cockroach | 37 (23.72) | 26 (36.11) | 10 (12.50) | 12 (27.91) |
| Indoor mould panel | 9 (5.77) | 6 (8.33) | 3 (3.75) | 4 (9.30) |
| Cat dander | 19 (12.18) | 10 (13.88) | 9 (11.25) | 5 (11.63) |
| Dog dander | 14 (8.97) | 8 (11.11) | 6 (7.50) | 3 (6.98) |
| House dust mite and cockroach | 24 (15.38) | 16 (22.22) | 7 (8.75) | 8 (18.60) |
| Cat and dog dander | 7 (4.49) | 3 (4.17) | 4 (5.00) | 3 (6.98) |
| House dust mite, cockroach and indoor mould panel | 4 (2.56) | 3 (4.17) | 1 (1.25) | 2 (4.65) |

**Table 2. Environmental risk factors and allergen sensitization and severity**

| | *Sensitization to at least one allergen N = 83 (%)* | *No allergen sensitization N = 73 (%)* | *Daily symptoms N = 43 (%)* | *Less frequent symptoms N = 109 (%)* |
|---|---|---|---|---|
| Gas only | 35 (42.17) | 24 (32.88) | 13 (30.23) | 45 (41.28) |
| Firewood only | 16 (19.28) | 14 (19.18) | 13 (30.23) | 16 (14.68) |
| Kerosene only | 7 (8.43) | 11 (15.07) | 5 (11.63) | 12 (11.01) |
| Use of mosquito coils | 21 (25.30) | 13 (17.81) | 9 (20.93) | 25 (22.94) |

## Discussion

In this study we have determined the indoor aeroallergen sensitization patterns in children with asthma and allergic rhinitis living in Colombo, Sri Lanka. Although many large scale studies have been carried out to determine patterns of allergen sensitization in US and European countries, such data were not available for Sri Lanka. As the environment is quite different in South Asian countries compared to temperate climates, patients with allergic diseases may have different allergen sensitization patterns. We found that 49.3% of children were sensitized to at least one allergen and that the patterns of aeroallergen sensitization was similar to temperate climates, with 37.8% of patients demonstrating sensitization to HDM and 23.7% showing sensitization to cockroach. Similar studies done in South Asia and the South East Asian region show that HDM and cockroach are the two commonest indoor aeroallergens [15, 16].

Sensitization rates for house dust mite was less frequent in our cohort than in other South Asian and South East Asian countries. Two large studies carried out in both adults and children in Kolkata and Mumbai, India showed that 75.6-77.13% of patients with asthma were sensitized to *Dermatophagoides pteronyssinus* [16, 17]. A similar study in both adults and children in Sri Lanka showed that 83.3% of individuals were sensitized to house dust mite [18]. The lower sensitization rates to HDM seen in our study is probably because only children were evaluated and because the SPT is less sensitive in identifying allergen sensitization in small children [19]. We found that children aged 4 year or older were significantly more likely to be sensitized to at least one aeroallergen than those who were aged less than 4 years. Although this suggests that the majority of children under 4 years of age are unlikely to have allergen induced asthma, it is also possible that children under 4 years of age were less likely to respond to the SPT. As we used only the SPT for determining sensitization to these allergens we may have underestimated the true allergen sensitization in many children in this age group.

Allergen sensitization was significantly higher in children with a first degree relative with asthma or AR consistent with the role of genes in predisposing individuals for atopic diseases [20]. Furthermore, sensitization to house dust mite, cockroach and indoor moulds were also significantly higher in children with other atopic diseases such as AR compared to those with asthma alone. However, the frequency of asthma symptoms was not higher in those with allergen sensitization except in children who were sensitized to moulds. Although only 4.7% of those with less frequent symptoms were sensitized to indoor moulds, 9.5% of those with daily symptoms were sensitized. These results are similar to other studies which have shown that fungal sensitization is associated with severe asthma [21, 22]. However, as lung function tests and monitoring of daily peak flow rates were not done in our patients, we could not determine if fungal sensitization was associated with more severe forms of asthma.

A control sample was not included in our study as skin prick testing is relevant only in those with type I mediated allergic diseases (asthma, allergic rhinitis, atopic eczema and food allergies) due to the difficulties in interpretation in the absence of disease. For instance, positive skin test result for an allergen in the absence of disease does not indicate that a person is allergic to that particular allergen [5, 13]. For this reason many previously published studies have not used a control sample [23-27].

Environmental pollutants are implicated in asthma and we found use of firewood as the sole source of cooking fuel was associated with more frequent asthma symptoms compared to other cooking fuels. The use of household gas for cooking appeared to be associated with less frequency of symptoms. Use of mosquito coils was not associated with increased frequency of symptoms nor with allergen sensitization.

In summary, we have determined the sensitization patterns to common indoor aeroallergens in patients with asthma and AR in Sri Lanka. Allergen avoidance has been shown to reduce asthma associated morbidity [8]. Therefore, determining allergen sensitization patterns in patients with asthma will help us educate patients regarding environmental modification. In addition, these finding may pave the way to initiate specific allergen immunotherapy in Sri Lanka.

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