original article

Asthma and other allergic diseases among Saudi schoolchildren in Najran: the need for a comprehensive intervention program

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Ann Saudi Med 2016; 36(6): 379-385

DOI: 10.5144/0256-4947.2016.379

BACKGROUND: In the last three decades, an increasing incidence of allergic diseases has been associated with increasing morbidity and mortality in children and young adults.
OBJECTIVES: The study aimed to investigate the prevalence and risk factors associated with allergic diseases among Saudi schoolchildren in the southwestern Saudi region of Najran, and to determine the sensitization of patients to a set of allergens.
DESIGN: Cross-sectional observational study.
SETTING: Primary, intermediate and secondary schools, Najran, Saudi Arabia.
SUBJECTS AND METHODS: All participants completed the Arabic version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Skin prick tests (SPT) were performed, using a panel of standardized allergenic extracts.
MAIN OUTCOME MEASURE(S): Prevalence and risk factors associated with pediatric allergic diseases.
RESULTS: The study included 1700 Saudi schoolchildren. The overall prevalence of physician-diagnosed asthma, allergic rhinitis and atopic dermatitis was 27.5%, 6.3% and 12.5%, respectively. Multivariate analysis showed that male gender (adjusted odds ratio [aOR], 1.27), fast food consumption (aOR, 1.53), trucks passing near houses (aOR, 1.86), and having a dog or cat at home (aOR, 1.85) were significant risk factors. A total of 722 (42.5%) children had a positive SPT result to at least one allergen. The most prevalent allergens were grass pollens (60%), cat fur (41.6%), and house dust mites (25%).
CONCLUSIONS: The findings of this study highlight the urgent need for developing an effective intervention program including several components working in harmony to control and reduce the burden of allergic diseases.
LIMITATIONS: These results may not be generalizable to the rest of Saudi Arabia.

During the last three decades, an increasing incidence of allergic diseases, such as bronchial asthma, allergic rhinitis and atopic dermatitis has been associated with a dramatic increase in morbidity and mortality among children and young adults.[1,2] Pediatric allergic diseases are a major source of chronic conditions and the most common cause of school absence among children throughout the world.[3,4] Besides adverse outcomes at physical activities, allergic diseases also affect a child's emotions, behavior and quality of life, resulting in devastating socioeconomic consequences. Thus, allergic diseases are now a serious health problem and a significant burden, not only in terms of healthcare costs, but also in lost productivity and reduced participation in family life.[3,5]

The number of bronchial asthma and allergic rhinitis rhinitis patients worldwide are estimated at 334 and 400 million, respectively.[2] Asthma is associated with allergic rhinitis in 74% to 81% of cases and is one of highest ranking specific diseases in terms of years lost to disability adjusted life years (DALYs).[3] The causes of the increase are unknown, but appear linked to factors associated with westernization, improvement of socioeconomic standards and urbanization. In fact, countries undergoing rapid changes towards a western lifestyle concomitantly experience an increasing prevalence of

allergic diseases.[6,7] International multicenter population-based studies have documented significant variations in the prevalence of allergic diseases and sensitization against environmental allergens between and within countries.[8] Recent estimates have shown that the prevalence of allergic sensitization to the common allergen could be between 25% to 35% in the general population,[1] and the pattern of sensitization against allergens varies according to differences in environmental factors.

Atopy is defined as the genetic propensity to develop immunoglobulin E (IgE) antibodies in response to exposure to allergen and is assessed by positive skin-prick test (SPT) responses, which may contribute to the development of the clinical disorder.[9] Most studies make assessments based on the actual prevalence of allergic diseases using International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires.[10,11] These questionnaires enable the identification of the past and current state of diseases such as atopy, asthma, rhinitis, and dermatitis. They also help to identify the association between hereditary factors and environmental factors, and are used in studies that assess the relationship between allergic diseases and indoor/outdoor environmental pollution.[6,12,13]

Atopy is a consistent risk factor for asthma in many epidemiological studies. The proportion of asthma attributable to atopy in children has been estimated to be 38%,[14] but there is considerable variation between studies. Saudi Arabia is a vast country and includes regions with marked variability in meteorological and topographical conditions. The economy is growing rapidly and in parallel with the rapidly changing lifestyle and socioeconomic improvement, an increasing prevalence of allergic diseases has been reported in clinical studies. In Saudi Arabia, asthma ranks 19th in DALYs and 26th in deaths.[15] The prevalence of asthma has risen from 8% in 1986 to 25% in 2001.[16] In a more recent study, Al-Frayh et al[17] through questionnaire-based periodic assessments of prevalence rates determined the prevalence rates for childhood asthma, rhinitis, and eczema in different Saudi cities. The authors found higher prevalence rates for asthma, rhinitis, and eczema in Hofuf (33.7%, 48.2%, and 43.5%) compared with Riyadh (17.7%, 29%, and 32.6%) and Jeddah (14.1%, 24.3%, and 31.9%).

Characterization of risk factors of allergic diseases and patterns of sensitization obtained from prospective studies is a prerequisite for the continuous work on the prevention of allergic disorders. Primary and secondary prevention depend on the early identification of clinical markers preceding allergic disease.[18] This study aimed to investigate the prevalence and risk factors associated with asthma and other allergic diseases among a representative sample of Saudi schoolchildren, and to determine the sensitization of patients to a set of indoor and outdoor allergens by the skin prick test (SPT).

SUBJECTS AND METHODS

This cross-sectional study of a representative sample of Saudi school children in Najran Region, Southwestern Saudi Arabia was conducted between October 2014 and February 2016. Using the WHO Manual for Sample Size Determination in Health Studies,[19] the minimal sample size calculated for the study was 1537 subjects based on a conservative estimate of the anticipated population proportion of 15%,[20] and with an absolute precision of 2% and at a 95% confidence interval. To avoid loss of cases, a total sample of 1700 students (boys and girls) was included in the present study. A stratified proportional allocation random sample was selected. The stratification factors taken into consideration were the relative number and types of schools (primary, intermediate and secondary), the number of students, grades and male-female differences. The study was reviewed and approved by Ethics and Research committee of Najran University. Written consent was obtained from all participants.

Questionnaire interview

A well-constructed standardized questionnaire was distributed and completed by all participants. The questionnaire was a modification of the ISAAC Phase III questionnaire.[21,22] According to The ISAAC protocol recommendations for questionnaire translation, a focus group consisting of a pediatrician, an immunologist, an ear, nose and throat specialist, and an epidemiologist revised this translated questionnaire to fit with local colloquial Arabic terminology of Saudi Arabia used by physicians and health educators in the community. After translation and back translation, a panel of experts were asked to assess the preliminary questions and provide structured comments with respect to face and content validity, comprehensibility and comprehensiveness. The questionnaire was composed of four modules to address bronchial asthma, allergic rhinitis, atopic dermatitis and environmental risk factors. The asthma core questionnaire included several questions to identify physician-diagnosed asthma (have you ever had bronchial asthma at any time in the past?), current wheeze (have you had wheezing or whistling in the chest in the last 12 months?), wheeze ever (Have you ever had wheezing or whistling in the chest at any time in the past?), wheezing after exercise (in the last 12 months, has your chest

sounded wheezy during or after exercise?) and nocturnal cough (in the last 12 months, have you had a dry cough at night, apart from a cough associated with a cold or chest infection? The allergic rhinitis core questionnaire comprised questions to identify physician-diagnosed allergic rhinitis (have you ever had allergic rhinitis at any time in the past?), current rhinitis (in the past 12 months, have you had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu?), rhinitis ever (Have you ever had a problem with sneezing, or a runny, or blocked nose at any time in the past?), allergic rhinoconjunctivitis (in the past 12 months, has this nose problem been accompanied by itchy, watery eyes?). The atopic dermatitis score questionnaire included questions to identify physician-diagnosed AD, recurrent rash "ever" and recurrent rash in the last 12 months. The questionnaire included information about the following: (1) demographic data such as age, area of residence and crowding rate of the index child as well as the educational level of parents; (2) family history of asthma and other atopic conditions; (3) family pets (cat, bird, poultry, etc); (4) the presence of smokers in the family; and (5) monthly family income to categorize low and high income groups. In addition, it comprised questions about environmental tobacco smoke exposure, outdoor air pollution through the frequency of truck traffic on the street where children lived, the use of wood or coal as cooking fuel and consumption of different food types, as well as other questions regarding environmental risk factors.

Skin prick tests

The SPTs were performed, using a panel of standardized allergenic extracts and the Stallerpoint device (Stallergenes, Paris, France) according to the manufacturer's instructions. Histamine hypochloride (10 mg/mL) and normal saline (0.9% NaCl solution) were used as positive and negative controls, respectively. The allergens panel was determined by patient age, history, environment, and geographic location as well as meteorological and topographical conditions of Najran region. A positive SPT result was considered when the wheal diameter was >3 mm to at least one of the allergens or 3 mm larger than the negative control.

Statistical analysis

Data were coded, validated and analyzed using SPSS PC+ version 13 software package. Frequency, percentage, arithmetic mean, median and mode were used to present the data. Chi square and the *t* test were used as tests of significance at 5% level. Binary logistic regression analysis with adjusted odds ratio (aOR) and antecedent 95% confidence intervals (CI) were used to identify potential risk factors.

RESULTS

The study included 1700 students with an age range of 7-19 years with a median of 12 years. There were 851 (50.1%) male and 849 (49.9%) female. The majority of the study sample (990, 58.2%) were from primary schools, followed by intermediate (413, 24.3%) and secondary schools (297, 17.5%). **Table 1** shows the

Table 1. Prevalence of symptoms for diagnosed and current allergic diseases in schoolchildren.

Variable	Boys	Girls	Total	*P*
Age (mean, standard deviation)	12.2 (3.4)	12.3 (3.3)	12.2 (3.3)	.516
School type				
Primary	494 (58.0)	496 (58.4)	990 (58.2)	.910
Intermediate	205 (24.1)	208 (24.5)	413 (24.3)	
Secondary	152 (17.9)	145 (17.1)	297 (17.5)	
Asthma				
Wheeze "ever"	245 (28.8)	100 (11.8)	345 (20.3)	.001
Current wheeze	178 (21.0)	65 (7.7)	243 (14.3)	.001
Physician-diagnosed asthma	275 (32.3)	193 (22.7%)	468 (27.5)	.001
Exercise induced asthma	220 (25.9)	133 (15.7)	353 (20.8)	.001
Nocturnal cough	269 (31.6)	223 (26.3)	492 (28.9)	.009
Rhinitis				
Rhinitis "ever"	302 (35.5)	287 (33.8)	589 (34.6)	.249
Current rhinitis	248 (29.1)	232 (27.3)	480 (28.2)	.019
Rhinoconjunctivitis	114 (13.4)	137 (16.1)	251 (14.8)	.135
Physician-diagnosed AR	43 (5.1)	64 (7.5%)	107 (6.3)	.022
Dermatitis				
Recurrent rash "ever"	126 (14.8)	93 (11.0)	219 (12.9)	.011
Recurrent rash in last 12 months	102 (12.0)	77 (9.1)	179 (10.5)	.001
Recurrent rash typical eczema distribution	44 (5.2)	36 (4.2)	80 (4.7)	.001
Physician-diagnosed AD	110 (12.9)	103 (12.1)	213 (12.5)	.337

Values are numbers and percentor mean (standard deviation). Statistical comparisons by *t* test or chi-square test.

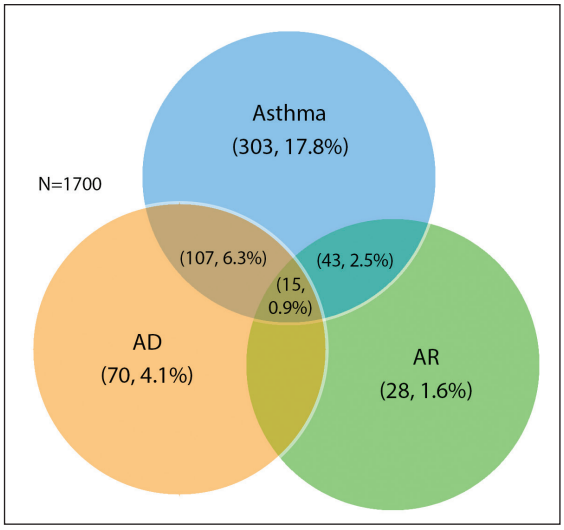

Figure 1. Venn diagram of patterns of co-morbid allergic disease among Saudi schoolchildren in Najran.

Table 2. Prevalence of allergen sensitizations among schoolchildren with different allergic diseases.

Allergen	Asthma (n=268)	Allergic rhinitis (n=107)	Atopic dermatitis (n=213)
Dermatophagoides pteronyssinus	20 (4.3)	8 (7.5)	4 (1.9)
Dermatophagoides farinae	16 (3.4)	8 (7.5)	0 (0)
Mugwort (*Artimisia*)	3 (0.6)	0 (0)	3 (1.4)
Chenopodium album	7 (1.5)	3 (2.8)	0 (0)
Pigweed (*Amaranthus retroflexus*)	15 (3.2)	0 (0)	0 (0)
Dog hair	12 (2.6)	0 (0)	0 (0)
Cat fur	109 (23.3)	9 (8.4)	28 (13.1)
Horse Hair	19 (4.1)	15 (14.0)	3 (1.4)
Cladosporium	41 (8.8)	13 (12.1)	31 (14.6)
Timothy grass (*Phleum pretense*)	24 (5.1)	0 (0)	8 (3.8)
Bermuda grass (*Cynodon dactylon*)	115 (24.6)	20 (18.7)	30 (14.1)
Ragweed (*Ambrosia*)	19 (4.1)	7 (6.5)	3 (1.4)
Candida albicans	0 (0)	0 (0)	0 (0)

Values are numbers and percent.

prevalence rates for each survey question pertaining to wheezing, asthma, allergic rhinitis, and atopic dermatitis. The overall prevalence of physician-diagnosed asthma, allergic rhinitis and atopic dermatitis was 27.5%, 6.3% and 12.5%, respectively. There was no significant difference in diagnosed atopic dermatitis between boys and girls (*P*=.337). However, boys were more likely to have diagnosed bronchial asthma (*P*=.001) and allergic rhinitis (*P*=.001), compared to girls. The boys reported more wheezing symptoms over the past 12 months (*P*=.001), wheeze at any time in the past (*P*=.001), exercise-induced wheeze (*P*=.001) and night cough (*P*=.009) compared to the girls.

Figure 1 shows the interrelated prevalence of allergic disease symptoms in the children in the study. While 587 (34.5%) of 1700 children show one or more symptoms of asthma, rhinitis and/or atopic dermatitis, 65.5% suffered none of the three disorders. The prevalence of bronchial asthma was 17.8% (303/1700), concomitant with atopic dermatitis 4.1%, allergic rhinitis 2.5% and both disorders occurred in 0.9% of the children.

A total of 722 (42.5%) students had a positive SPT to one or more allergens. Of those, 359 (49.7%) were sensitized to one allergen, 224 (31%) to two allergens and 139 (19.3%) to three or more allergens. The overall prevalence of positive SPT reactivity was 43.4% for Bermuda grass, 41.6% for cat fur, 16.6% for Timothy grass, 16.2% for *Cladosporium* ,14.8% for *Dermatophagoides pteronyssinus* and 10.2% for *Dermatophagoides farinae*. The distribution of SPT sensitization to various allergens in patients with asthma, rhinitis and dermatitis is listed in **Table 2**. The results clearly demonstrate that patients with asthma had increased positive SPT rates to Bermuda grass, cat fur and *Cladosporium* allergens. Sensitization to Bermuda grass, horse hair and *Cladosporium* was increased in patients with allergic rhinitis, while sensitization to *Cladosporium*, Bermuda grass and cat fur was more frequent among patients with atopic dermatitis.

The multiple logistic regression analysis with adjusted odds ratio (aOR) and antecedent 95% confidence intervals (CI) identified potential risk factors linked to allergic diseases (**Table 3**). The male schoolchildren had a significantly higher risk of developing allergic diseases to females (aOR=1.626, 95% CI: 1.296–2.040). Similarly, children consuming fast food had a significantly higher risk of developing allergic diseases (aOR=1.352, 95% CI: 1.074–1.703). Other significant risk factors were trucks regularly passing near houses (aOR=1.855, 95% CI: 1.316–2.557), having a dog or cat at home (aOR=1.853, 95% CI: 1.269–2.707), positive skin testing for Bermuda grass (aOR=3.221, 95% CI: 1.279–8.112)

and positive skin testing for cat fur (aOR=1.461, 95% CI: 1.081–1.973). On the other hand, other sociodemographic variables, consumed food items and environmental exposures were found to be of no significance in developing asthma.

DISCUSSION

This large cross-sectional study provides further evidence that the prevalence of physician-diagnosed asthma and other allergic diseases among schoolchildren is continuously rising in Saudi Arabia. Previous epidemiological studies investigating allergic disorders among Saudi schoolchildren have focused on children of certain age groups. For example, Nahhas et al[11] found that the prevalence of physician-diagnosed asthma, allergic rhinitis and atopic dermatitis among children aged 6-12 years was 15.5%, 4.2% and 14%, respectively, while Al Ghobian et al20 found that physician-diagnosed asthma was 19.6% among adolescents aged 16-18 years. This is, we believe, the largest cohort study on the prevalence of allergic disease in children and adolescents of all age groups (7-19 years) in Saudi Arabia.

The ISAAC-phase III study investigated the global prevalence and severity of asthma symptoms among >1 200 000 children from 98 countries and found that the mean global prevalence of current wheeze among children aged 6-7 years was 11.7%, with values ranging from 6.8% in the Indian subcontinent to 21.7% in Oceania, while it was 14.1% among 13-14 years aged children, compared to 5.1% in Northern and Eastern Europe, and 22% in Oceania children.[6] In this study, the overall prevalence of wheeze ever and current wheeze is high and alarming. Previous clinical studies showed that over 20% of children reporting severe symptoms of wheeze ever or current wheeze in developing countries had never received a diagnosis of asthma and that asthma care is likely poor in these countries.[22,23] These figures suggest that there might be less awareness of wheeze being a symptom of asthma, especially in those reporting ever wheezing. Children with frequent undiagnosed symptoms are also more likely to receive inadequate care for their asthma and may fall into a vicious circle of asthma control.

Previous epidemiological studies have shown an important overlap between bronchial asthma and other allergic diseases.[24] However, in practice, the number of patients following the classic 'atopic march' seems to be relatively low.[25] Similarly, only a minority of children in the present study suffered from all atopic disorders. However, coexistence of these diseases may be associated with greater functional impairment in terms of activity limitation and lower quality of life as compared with children who have one condition alone. Therefore, this group of children need to be considered by clinicians and researchers as a separate group with distinct characteristics for severity, causes, treatment or prognosis.

Table 3. Multivariate analysis of risk factors associated with allergic diseases.

Variable	aOR	95% CI		*P*
		Lower	Upper	
Gender: Males vs. Females	1.626	1.296	2.040	.001
Fast food consumption: Regular vs. Never	1.352	1.074	1.703	.001
Trucks passing near houses: Regular vs. Never	1.855	1.316	2.557	.001
Having a dog or cat at home: Yes vs. No	1.853	1.269	2.707	.002
Positive skin test for Bermuda grass: Yes vs. No	3.221	1.279	8.112	<.001
Positive skin test for Cat fur: Yes vs. No	1.461	1.081	1.973	.001

Cox/Snell R square=0.125, Nagelkerke R Square=0.178

Sensitization to atopic allergens has been recognized as the most important risk factor for allergic diseases.[26] Distribution of allergens may vary with different geographic areas, local climates, environments and lifestyles.[8,27] In this study, grass pollens, cat fur and house dust mites were the most frequent allergens in our region.

Worldwide, there is evidence to suggest that house dust mites are the most common indoor allergens associated with asthma and other allergic diseases in many countries.[26] In Saudi Arabia, house dust mites are the predominant indoor allergen in different regions with sensitization rates of 26% to 87%.[28,29] Contrary to these findings, 60% of atopic children in the present study were sensitized to grass pollens. This was not surprising as Najran is an agricultural area, and a high percentage of land is planted fields promoting a prolonged pollination period for grasses.[30] Moreover, Najran is geographically located in the southern region with a high altitude. Ozkaya et al[27] found that grass mixture pollen sensitization in patients who lived at high altitude was significantly greater than that of patients who lived at sea level. The independent effect of grass pollens is problematic, taking into account the high prevalence of poly-sensitization and/or cross-reactivity, especially between types of grass pollens (tropical and subtropical grasses) and the possible occurrence of epidemic-type asthma due to continuous exposure to high pollen concentrations as has been reported in previous clinical

studies.[30,31]

By analyzing patterns of allergen-specific sensitization profiles in the present study, it was clear that grass pollens and cat fur are significant allergens in all allergic diseases and could be one of the most important allergens in the atopic march[32] because the significant relationship was confirmed between sensitization to these two allergens and all atopic phenotypes.

Country and regional differences in allergic diseases estimates highlight the need to address the specific risk factors and consequently to design effective interventions and initiatives locally for proper management.[1] In this study, potential risk factors associated with allergic diseases were male gender, consuming fast food, trucks passing near houses, having a dog or cat at home, and a positive SPT for Bermuda grass or cat fur. Although part of these findings have already been described in previous studies investigating the epidemiology of asthma among children,[33,34] our results extend these findings to other allergic diseases.

This study had some limitations. Firstly, The questionnaire data may have been subject to recall bias and misclassification. However, the ISAAC core questionnaire and methodology used in this study has been extensively validated for the diagnosis and surveillance of allergic diseases in a population. Secondly, although our sample size was 1700 students and ISAAC recommended a sample size of 3000,[21] data from clinical and epidemiological studies including >1000 participants are generally accepted. Finally, specific IgE level, bronchial hyper-responsiveness test and spirometry were not performed for objective assessment and clinical classifications of asthma. Nevertheless, the SPT used in our study has proved to be a good procedure for detecting IgE-mediated allergic diseases, and it produces results comparable with other diagnostic techniques. Moreover, our study was limited to the southern Saudi region. Hence, the results presented here may not be generalized to the rest of Saudi Arabia.

In conclusion, the prevalence of asthma and other allergic diseases in our region is high and worrisome. The findings of this study draw attention to the necessity for development of an effective intervention program with multidisciplinary teams (pediatrician, immunologist, health educator, psychologist, social worker, rhinologist, and dermatologist) working in a harmony to control and reduce the burden of allergic diseases. This program should include establishment of school-based asthma clinics with facilities for accurate diagnosis of asthma in children to reduce morbidity and mortality due to under-, or over-diagnosis. Developing a comprehensive school-based asthma education program should be considered for allergic students, their parents and school staff to improve awareness about childhood allergic diseases. Meanwhile, determining allergen sensitization patterns in allergic patients will help pediatricians to educate patients regarding environmental modification, and will help health policy and decision makers to select proper treatment strategies including allergen-specific immunotherapy when applicable for the management of asthma and other allergies.

Conflict of interest

The author declares no potential conflicts of interest with respect to the authorship and/or publication of this article.

Funding

This work was supported by a grant (project No. AT-34-96) from King Abdulaziz City for Science and Technology (KACST). The author appreciates this support both in finance and in spirit.

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