Allergic sensitisation to common antigens among Ethiopian asthmatic patients

K Gidey, A Adem, M Guizaw, K-H Franz , and A Potthoff

Abstract

This review was conducted with the aim of identifying the allergic sensitisation patterns to common antigens among asthmatic patients and to assess for possible sociodemographic correlates. Records were reviewed retrospectively for patients who had undergone skin prick testing as part of a routine care for asthma between June 2012 and June 2013 at the Pulmonology clinic of Ayder Referral Hospital, Mekelle, Ethiopia. The records of 47 patients were eligible for the study and were hence reviewed. The mean age of these patients was 41.3 years. Skin prick testing was positive for one or more antigens in 53.2% of patients. The three most common positive antigen tests were for Dermatophagoides farinae (27.7% patients), Dermatophagoides pteronyssinus (25.5%), and dog hair (12.8%). The conclusions from the study are that allergic sensitisation among Ethiopian asthmatic patients was common and that house dust mites were the most commonest sensitisers. Further studies are recommended to investigate sensitisation for additional allergens and to better assess correlations with risk factors.

Introduction

Asthma is one of the most common chronic diseases globally and currently affects approximately 10–12% of adults and 15% of children worldwide. The prevalence in developing countries has increased in recent decades due to increased urbanisation.^{1,2}

Although there is lack of population-based prevalence reports in Ethiopia, a report in 1997 from Jimma (southwest Ethiopia) showed that 3.6% of the urban population in the area had asthma. Additionally, the overall prevalence of wheezes in rural areas was lower than in urban groups.³ Another report in 2003 among school children from Gondar Town, Ethiopia showed a prevalence of 16.2%.⁴ A more recent cohort of 1006 newborns who were followed for 5 years in the Butajira cohort study showed a prevalence of wheeze among 1 year olds (as reported by their mothers) of 11.5%.⁵

Kibreab Gidey and Amir Adem, Department of Internal Medicine; Mairie Guizaw, Department of Dermatology and Venereology, all at Ayder Referral Hospital, Mekelle University, Ethiopia; Karl-Heinz Franz, Lungenpraxis Witten/Filialpraxis Witten – Herbede, Germany; Anja Potthoff, Chefärztin des Fachklinikums Borkum, Fachärztin für Dermatologie, Germany. Correspondene to: Amir Adem, Department of Internal Medicine, Ayder Referral Hospital, Mekelle University, Ethiopia. Email: amiradem@gmail.com With changes in lifestyle, the prevalence of asthma also changes, as seen from a 1999 report among Ethiopian immigrants in Israel. According to the report, 2.5% of the immigrants had asthma at the time of immigration and this figure increased to 17% after 8–17 years spent living in Israel.⁶

Asthmaisa heterogeneous disease with interplay between genetic and environmental factors. Several risk factors and triggers are involved in the pathogenesis of asthma. Endogenous factors such as genetic predisposition, atopy, and airway hyper-responsiveness, and environmental factors such as indoor allergens, outdoor allergens, and occupational sensitisers etc. are all known to contribute. Many triggers have been identified – for example, allergens, upper respiratory tract infection, cold air, stress, irritants (household spray, paint fumes), etc.^{1,7} In the Butajira birth cohort study, the incidence of wheeze and eczema was increased with early-in-life use of paracetamol,⁸ but in a similar group of patients the incidence was lower among children with *Helicobacter pylori* infection.⁹

Most patients with asthma are atopic, with sensitisation to various allergens. Many allergens have been tested and identified worldwide, for example *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* (house dust mites), cat hair, dog fur, *Alternaria alternata* (*A. tenuis*), cockroach (*Blatella germanica*), olive (*Olea europaea*), and many others. The pattern of allergic sensitisation to different allergens is believed to differ from country to country.¹⁰ To our knowledge there are no published data about patterns of sensitisation in northern Ethiopia.

Asthma is usually diagnosed clinically with history of cough, shortness of breath and with findings of diffuse wheezes on chest examination. Further investigations may include lung function tests to show any reversible obstructive features.¹¹Skin prick testing is an essential test procedure to confirm sensitisation in immunoglobulin E (IgE)-mediated allergic disease in subjects with rhinoconjunctivitis, asthma, urticaria, anaphylaxis, atopic eczema, and food and drug allergies.¹⁰

The aim of this study was to assess common sensitising allergens among asthmatic patients who presented to the emergency department of Ayder Referral Hospital, Mekelle, Ethiopia.

Methods

The study was conducted in the Ayder Referral Hospital of Mekelle University, which is located in Mekelle city 783 km north of the Ethiopian capital Addis Ababa. The hospital is the biggest referral hospital in the region with a catchment area of 8 million including inhabitants from neighbouring regions of Amhara and Afar.

A retrospective record review was carried out of the skin prick test recording book in the Pulmonology Unit; data were analysed over a 1-year period. The skin prick test was carried out for patients who came to the emergency clinic over the study period (June 2012 to June 2013) with a diagnosis of an acute asthmatic attack with subsequent improvement after therapy. The documents of all patients who appeared during the stated period were reviewed for the purposes of the current study. Information on the registry includes patients' identification, age, sex, place of residence, diagnosis and response to allergic prick tests.

Adult patients (aged ≥20 years) who visited the medical emergency clinic of the hospital in the study period and who were given a diagnosis of acute exacerbation of asthma were included in the current study. The diagnosis of asthma was made by the treating physician and was retrieved from patients' records. All patients having a chronic disease characterised by recurrent attacks of breathlessness and wheezing, fulfilled the World Health Organization clinical definition of asthma. The presence of wheezing was confirmed by physical examination, and was apparent in all patients as they appeared during an acute attack and subsequent improvement/resolution with therapy.

The skin prick test was carried out as a part of comprehensive asthma care. One trained medical resident performed and analysed all the tests. The test was performed once the patients were stabilised and had been treated for the acute exacerbation in the hospital. The necessary precautions for the management of complications were taken. No cases of anaphylaxis were encountered.

Skin prick testing was performed using 14 common allergens selected based on data from prior publications and on availability. There were positive (histamine, 1 mg/ml; Allergopharma, Germany) and negative (saline) controls. The allergens used were as follows: (1) Dermatophagoides pteronyssinus; (2) D. farina; (3) Tyrophagus putrescentiae; (4) cows' milk; (5) chicken egg; (6) chicken feathers; (7) dog hair; (8) cow hair; (9) grass pollen; (10) wheat pollen; (11) mould-1 (Alternaria tenuis, Botrytis cinerea, Cladosporium herbarum, Curvularia lunata, Helminthosporium, Fusarium moniliforme); (12) mould-2 (Aspergillus fumigatus, Mucor mucedo, Penicillium notatum, Pullularia pullulans, Rhizopus nigricans, Serpula lacrymans); (13) Candida albicans; (14) Alternaria alternata. Allergens 7 and 8 were obtained from ALK-Abello (Denmark) and the remaining allergens were from Allergopharma (Germany).

Drops of each allergen were placed over the volar aspect of the forearm, nearly two fingers away from the wrist joint and ante-cubital fossa. The allergens were spaced 2 cm from each other. A prick of about 1 mm was made through the allergens over the skin using sterile lancets. The results were read 15 minutes after the test and positivity was defined as maximal wheal diameter of 3 mm or more in the case of absent reaction to negative control or 3 mm or more reaction compared with the negative control in those with reaction to saline. Patients were excluded if they showed severe dermatographism, as assessed by a positive reaction of 3 mm or more for the negative control, or had less than 3 mm reaction to histamine as documented on the patients' card.10,12 There was only one patient with a 3 mm reaction to saline; despite this the patient was enrolled in the analysis because he had a 7 mm reaction to *D. pteronyssinus* and a <3 mm reaction to all other antigens. There were no patients with <3 mm reactions to histamine.

Patients were subsequently monitored for 30 minutes for complications. Emergency medications (adrenaline and hydrocortisone) were made available for management of complications.

The data collected were cleared and entered in to the statistical software SPSS (version 21). We prepared descriptive statistics of the sociodemographic parameters, proportions of skin test positivity to any of the antigens and possible sociodemographic correlates were assessed using the same statistical software. Ethical clearance was obtained from the institutional review board of the College of Health Sciences, Mekelle University.

Results

A total of 47 patients were included. All were known asthmatic patients who had been having follow-up appointments. The mean duration of asthma was recorded for 40 (85.1%) patients, and was 10.2 ± 11.8 years. There was no record of asthma duration for 7 patients. Twenty-four patients (51.1%) were female; the age of the participants ranged from 20 to 73 years with a mean age of 41.3±14.32 years; 39 patients (83.0%) were from urban areas of the region (Table 1).

The mean age of onset of asthma was recorded in 40 (85.1%) patients and was 31.1±14.5 years (8–62 years); association with all the tested allergens was sought, but

Variables		v t
Sex (n=47) Male, n (%)	23 (48.9%)	r (
Female, n (%)	24 (51.1%)	F (
Age in years (mean ± SD)		ŗ
Total (n=47)	41.3 ± 14.3	n
Male (n=23)	42.9 ± 14.3	а
Female (n=24)	40.7 ± 14.6	ע 1
Place of residence		F
Urban, n (%)	39 (83%)	F
Male, n (%)	19 (82.6%)	a
Female n (%)	20 (83.3%)	8 7
Rural, n (%)	8 (17%)	n
Male, n (%)	4 (17.4%)	t
Female, n (%)	4 (16.7%)	e

Table 1: Sociodemographic characteristics of patients

was found to be statistically non-significant p 0.08–0.9).

Among the patients, 25 (53.2%) were positivetooneor more allergens and 22 (46.8%) were negative. There was skinprick-testing positivity to all tested allergens except for *Alternaria alternata* (Figure 1).

Among patients who tested positive for the allergens, 10 patients (40%)

Original Article

reacted to a single allergen. There were 10, 4 (16%), and 1 (4%) patients who had positive tests for 2, 3, and 4 allergens respectively. Four (16%) of the patients reacted to food allergens, all of whom showed additional aeroallergen sensitivity. There were no clinically relevant symptoms after ingestion of food in the above patients. None of the positive tests for the allergens showed significant correlation with patients' places of residence.

Discussion

Asthma is classified as allergic and nonallergic; the former is mediated by immunologic mechanisms. The allergic type plays an important role in around 80% of childhood asthma and in 40–50% of adult

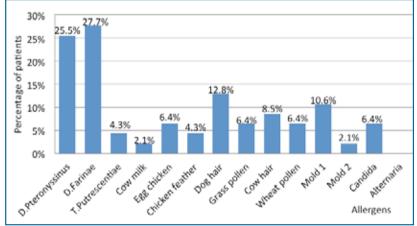
onset asthma cases; the allergic type is differentiated from the non-allergic type by the presence of a positive skin prick test to usual aeroallergens.¹³

Skin prick testing is an essential test procedure to confirm sensitisation in IgE-mediated allergic disease in subjects with rhinoconjunctivitis, asthma, urticaria, anaphylaxis, atopic eczema, and food and drug allergy.¹⁰ Our patients' ages ranged from 20 to 73 years with a mean age of 41.32±14.32 years. Most studies have shown that the prevalence of skin-prick-test positivity peaks in young adults and diminishes with age regardless of the type of allergen.¹⁴ Despite this, the skin-prick-test positivity in our patients was significant. Of our patients, 53.2% had reactivity for one or more allergens. All of these patients had aeroallergen sensitivity, while four patients (16%) were additionally sensitised to food allergens. An older report from Addis Ababa in the year 1989, reported 54 positive skin prick tests for house dust mite among 77 asthmatic patients; this figure is higher than in our report. Additionally, a publication from Saudi Arabia in 2006 reported skin-prick-test positivity to one or more allergens in 113 of 151 (74.8%) asthmatic patients. These difference could partly be attributed to variation in age among the patient groups, in the Saudi Arabian study, the mean age of the patients was 30±13 years and females constituted 65.5%.^{15,16}

House dust mites were the commonest sensitisers in our report with *D. farinae* accounting for 27.7% and *D. pteronyssinus* for 25.5%, which, despite being magnitude large proportion is less than the report from Saudi Arabia, which showed sensitisation to *D. pteronyssinus* in 87%, *D. farinae* in 84%, cat in 44%, and cockroach in 33%.¹⁶

Åretrospective study from Iraq recruited 130 asthmatic patients from September 2008 to May 2010 and 61% of the patients having skin-prick-test positivity were sensitive to pollens and 17% were sensitive to moulds. Of these patients 52% were male.¹⁷ This demonstrates the fact that allergic sensitisation varies significantly between geographical areas.

In a report of skin-prick-test reactivity to common allergens among women aged 14 years or older in Entebbe,



plays an important role in around 80% of Figure 1: Pattern of skin-prick-test positivity for common allergens

Uganda, skin- prick-test positivity was significantly associated with a history of asthma (70% to any allergen), among which 60% were positive for *Dermatophagoides* mixtures and 20% positive for dogs.¹⁸

In contrast to an older report from Switzerland stating that there are very few house dust mites in high mountainous areas, our findings suggest their frequent occurrence in the northern Ethiopian highlands. In comparison with Ethiopia, the weather in Switzerland was cold and had lower humidity.¹⁹ Another report from the highlands of Venezuela showed, if the humidity is high, that dust mites are common despite the high altitude.²⁰

The limitations of this study include the fact that it is a retrospective record review. The strength of the evidence is weak due to the lack of a control group and the low number of patients. There were incomplete recordings of treatment history (use of medications), although none of the patients were reported to be on antihistamines/ antidepressants during the time of testing. The use of systemic corticosteroids was also not consistently recorded. The type, severity, family history of asthma and presence of other atopic diseases were not consistently reported.

Conclusion

Aeroallergen sensitivity among asthmatics from the northern Ethiopian highlands is high. House dust mites were the commonest sensitisers identified. Large-scale prospective trials are recommended to investigate sensitisation to additional allergens and to better assess correlations with risk factors.

References

- Barnes PJ. Asthma. In *Harrison's Principles of Internal Medicine*, 18th edition. Eds Longo DL, Fauci AS, Kasper DL, et al. USA: McGraw-Hill Companies, 2012.
- Gemert FV, Molen TVD, Jones R, et al. The impact of asthma and COPD in sub-Saharan Africa. *Prim Care Respir J* 2011;20(3):240–48.
- 3. Haile Y, Zegaye B, Venn A, et al. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. *Lancet* 1997; 350: 85–90.
- Hailu S, Tessema T, Silverwan M. Prevalence of symptoms of asthma and allergies in school children in Gondar town and its vicinity, northwest Ethiopia. *Pediatr Pulmonol* 2003 Jun; 35(6): 427–32.

- Belyhun Y, Amberbir A, Medhin G, et al. Prevalence and risk factors of wheeze and eczema in 1-year-old children: the Butajira birth cohort, Ethiopia. *Clin Exp Allergy* 2010 Apr; 40(4): 619–26.
- Rosenberg R, Vinker S, Zakut H, et al. An unusually high prevalence of asthma in Ethiopian immigrants to Israel. *Fam Med* 1999 Apr; 31(4): 276–9.
- Lemanske RF Jr, Busse WW. Asthma: clinical expression and molecular mechanisms. J Allergy Clin Immunol 2010 Feb; 125 (2 Suppl 2): S95–102.
- Amberbir A, Medhin G, Hanlon C, et al. Effects of early life paracetamol use on the incidence of allergic disease and sensitization: 5-year follow-up of an Ethiopian birth cohort. *PLoS One* 2014; 9(4): e93869. doi:10.1371/journal.pone.0093869. Epub 2014 Apr 9. (Accessed 30 June 2014).
- Amberbir A, Medhin G, Ábegaz WÉ, et al. Exposure to Helicobacter pylori infection in early childhood and the risk of allergic disease and atopic sensitization: a longitudinal birth cohort study. *Clin Exp Allergy* 2014 April; 44(4): 563–71.
- Heinzerling L, Mari A, Bergmann KC, et al. The skin prick test – European standards. *Clin Transl Allergy* 2013; 3: 3. Available online: http://www.ctajournal.com/content/3/1/3, Accessed 05 Nov 2013.
- 11. Kaplan AG, Balter MS, Bell AD, et al. Diagnosis of asthma in adults, review. *CMAJ* 2009; DOI:10.1503/cmaj.080006. (accessed 10 January 2014).
- 12. Australasian Society of Clinical Immunology and Allergy. Skin prick testing for the diagnosis of allergic disease. A manual for practitio-

ners, Updated Nov. 2013. Available online: http://www.allergy. org.au/images/stories/pospapers/ASCIA_SPT_Manual_November_2013.pdf. (Accessed 30 November 2013).

- Johansson SG, Hourihane JO, Bousquet J, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. *Allergy* 2001 Sep; 56(9): 813–24.
- 14. Boulet LP, Turcotte H, Laprise C, et al. Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma. *Clin Exp Allergy* 1997 Jan; 27(1): 52–9.
- 15. Teklu B. Bronchial asthma at high altitude: a clinical and laboratory study in Addis Ababa. Thorax 1989; 44: 586–87.
- Koshak EA. Skin test reactivity to indoor allergens correlates with asthma severity in Jeddah, Saudi Arabia. *Allergy, Asthma & Clin Immunol* 2006; 2: 11-19.
- 17. Saleh BT. Evaluation of skin prick test for common aeroallergens in patients presented with bronchial asthma in Tikrit Teaching Hospital. *Tikrit Med J* 2012; 18(1): 57–63.
- Mpairwe H, Muhangi L, Ndibazza J, et al. Skin prick test reactivity to common allergens among women in Entebbe, Uganda. *Trans R Soc Trop Med Hyg* 2008 April; 102(4): 367–73.
- 19. Spieksma FTM, Zuidema P, Leupen MJ. High altitude and house-dust mites. Br Med J 1971 Jan; 1(5740): 82–84.
- 20. Rangel A, Salmen S, Muñoz J, et al. Dermatophagoides sp. and IgE anti-D. pteronyssinus and D. farinae detection in a Venezuelan community at more than 2000 m above the sea level. *Clin Exp Allergy* 1998 Sep; 28(9): 1100–3.