

ORIGINAL ARTICLE

A long-term follow-up of allergic diseases in Iceland

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Abstract

Introduction: Allergic disorders are an increasing health problem in many countries, in particular among children. We have evaluated the prevalence and manifestations of allergy in a cohort of young Icelanders for more than two decades. Variations in the epidemiology and clinical expression of allergy in different communities may help to identify etiological factors contributing to these disorders.

Methods: A cohort of 179 children has been monitored for allergic manifestations for two decades, at the ages of two, four, eight, and 15 years, and most recently at the age of 21 years involving 120 of the participants.

Results: Cumulative prevalences of 40%, 45%, and 29% have been observed, respectively, for rhinoconjunctivitis, eczema, and asthma during the study period. None had developed rhinoconjunctivitis at the age of about 2 years, but the point prevalence gradually increased to 33% at the age of 21 years. Conversely, the prevalence of eczema was 31% at the age of 2 years, but gradually declined to 8% at the age of 21 years. The prevalence of asthma peaked at 28% at the age of 4 years, but declined thereafter and has remained stable at about 13% from the age of eight to 21 years.

Discussion: The prevalence of allergic diseases is high in Iceland among children and young individuals. Asthma and atopic eczema are very common in childhood, but decreases with age while the prevalence of rhinoconjunctivitis increases markedly. The very high and increasing prevalence of rhinoconjunctivitis among 15- to 21-year-old individuals is noteworthy.

The prevalence of allergic rhinoconjunctivitis, atopic dermatitis, and asthma bronchialis may be increasing as several studies and review papers have indicated (1–5), although other studies suggest a steady state during the last several years (5–10). The increasing prevalence of atopic diseases has been especially evident in children (2, 5).

A prevalence of allergic rhinoconjunctivitis up to 40% has been reported in Western countries (2, 6), while atopic dermatitis has been reported to affect 7–30% of children (2–4, 6, 11, 12) and 2–10% of adults. Thus, it has become evident that the prevalence of atopic diseases may have doubled or tripled in Western societies during the last thirty years as recently reviewed (3). The prevalence of asthma is also increasing throughout the world, particularly among children (2, 5, 13), and a recent Icelandic study revealed 9% prevalence of childhood asthma (4). However, the prevalence of atopic disorders varies in different parts of the world (2, 5, 6,

11, 14), but seems to be increasing (2, 13, 14), although, this increase may be slowing down or reaching a plateau in younger age groups (5, 10, 14).

The clinical symptoms of allergic diseases vary with age, seasons, countries, and race, as well as study periods (2, 12, 15, 16). While atopic dermatitis is common during infancy and improves in late childhood (2, 3, 12, 15), allergic rhinoconjunctivitis, which is rare in infancy, has an increasing prevalence during childhood, but has been reported to diminish again in teenagers in some studies (2, 15). Symptoms of asthma are also common in the first years of life, but diminish in late childhood, although, some may continue to wheeze into adulthood (2, 16–18).

Several prophylactic measures against allergy have been proposed, including avoidance of certain allergenic nutrients or environmental factors to influence the immune response (19–21), but the results have often been disappointing and

controversial (22, 23). Several attempts have been made to identify at birth individuals prone to develop atopic diseases later in life (19–21). A few studies have found a correlation between high cord blood IgE levels and atopy during early childhood (24) and even in teenagers and adults (25), but others have not identified any such connections (12, 26). In our study cohort, such association has not been observed (15, 27, 28).

The prevalence and clinical presentation of allergic diseases are apparently changing. This development warrants close attention. Our study group has evaluated the prevalence and manifestations of allergy in a cohort from birth to the age of 21 years for the prevalence of eczema, asthma, and rhinoconjunctivitis. Our study provides an opportunity to follow closely the development of allergic diseases in this cohort over a long period of time.

Patients and methods

In the initial study, the cohort was recruited from infants who were consecutively vaginally born at Landspítali University Hospital, Iceland, in June to October 1987 (25). The cohort consisted of individuals with relatively high versus low levels of cord blood IgE, as well as a randomly selected group (27).

Of the children originally enrolled, 179 were enrolled for evaluation of allergic disorders at the age of 18–23 months, and at the age of four, 161 of the 179 children were available for follow-up, 134 at the age of eight and 122 at 15–16 years of age (15, 27, 28). As no association or trend was observed between cord blood levels of IgE and prevalence or manifestations of allergy at the ages of about 2, 4, and 8 years (25, 26), the cohort has been considered to represent Icelanders born in 1987. The present report involves 120 members of the original cohort when they were approaching the age of 21 years.

The diagnostic criteria for allergic diseases were the same as in earlier studies (15, 27). Allergic rhinoconjunctivitis was defined as nasal congestion with clear nasal discharge, sneezing, and itching in the nose, with or without conjunctivitis, occurring during the summer months or in the presence of pets, but without any symptoms of upper airway infections. Asthma was defined by recurrent symptoms from lungs with wheezing, dyspnea, nocturnal coughing, and exercise-induced coughing, as well as a physician-confirmed diagnosis of asthma. Atopic dermatitis was defined as recurrent or continuous erythema, scaling, and itching in typical places for atopic dermatitis, the symptoms starting in early childhood (29). The individuals were recorded to have an active allergic disease if allergic symptoms had occurred during the previous year.

A skin prick test was performed (Soluprick®, ALK, Denmark) in a standardized manner and response to common allergens tested; grass pollen, dust mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), mold (*Cladosporium*), dogs, cats, rabbits, horses, birch, dandelion, and sorrel.

Statistical analysis was performed using the software Matlab. A statistical significance was set at $p < 0.05$. Changes in prevalence between the time points were tested

using a test for single population proportion. The observed prevalence of one time point was used as a reference point, and then it was tested whether the prevalence of another time point had the same value or not. Every participant was given a siblings index such that each sibling adds one unit to the index and each half sibling adds half a unit. The coefficient corresponding to the sibling's index is denoted by β . The statistical significance of association between allergic diseases at age 21 and the number of siblings was tested by setting up a logistic regression model and applying a likelihood ratio test for the parameter β and evaluating whether it is equal to zero or not. When testing the association between allergy at age 21 and sex, and the association between allergy at age 21 and birth month, a standard chi-square test for independence was applied. The Ethical Committee at the University Hospital, The Data Protection Committee, and the hospital authorities approved the study.

Results

Of the 179 individuals in the original group, 120 (67%) participated at the age of 21 years, 61 women and 59 men. Four declined participation; others were living abroad or had moved outside the capital area in Iceland and could not be reached or were not included because of other health issues or pregnancy.

A positive history of allergic rhinoconjunctivitis was given by 48 (40%) of the 120 participants, 22 women and 26 men, and the diagnosis was confirmed with a positive skin prick test in 40 (83%) or 33% of the current cohort. Of those, 36 had at some time been treated for this disorder. At the age of 18–23 months, none of these participants was diagnosed with allergic rhinoconjunctivitis, and the prevalence was 7% at the age of four, 10% at 8 years of age, 25% at 15–16 years, and 33% in the current study at 21 years of age (Fig. 1). The prevalence of rhinoconjunctivitis increased significantly from the age of 18–23 months until 21 years of age ($p \leq 0.0001$).

Twenty-eight (23%) of the participants had history of atopic dermatitis, whereas 54 (45%) reported any symptoms from the skin. Nine (8%) individuals had symptoms at the

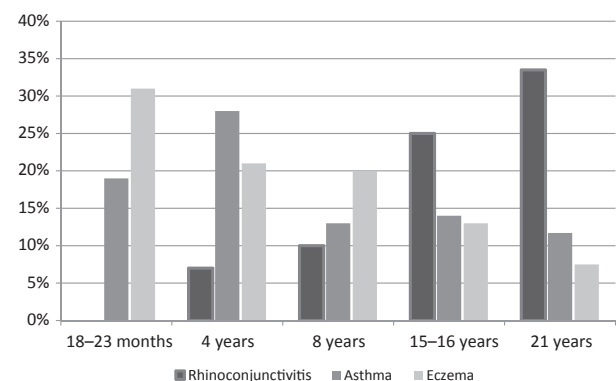


Fig. 1. Prevalence of allergic diseases in a cohort of 120 Icelandic individuals, followed up for two decades.

time of examination and five of those had one or more positive skin prick tests. Twenty-six individuals (23%) had used medical treatment for their skin disorders. The prevalence of atopic dermatitis declined over the whole period from 31% at the age of 18–23 months to 21%, 20%, and 13% at the ages of four, eight, and 15–16 years, respectively (Fig. 1), and was 8% at the age of 21 years. The decrease in prevalence was statistically significant over the whole study period ($p \leq 0.0001$).

Thirty-five of the 120 participants (29%) had at some stage been diagnosed with asthma, but 66 (55%) reported any lung symptoms. Sixteen (13%) of the participants had current symptoms or reported wheezing during the last 12 months, eight women and eight men. Thirteen had been treated for asthma during the last year, but none had been hospitalized. Of the 16 asthmatic individuals, seven reported less than ten episodes of asthma in the past year, whereas six reported over ten episodes, three were uncertain. Six had exercise-induced asthma, asthma attacks were triggered by respiratory tract infections in two and allergy in one, but seven of the 16 individuals had more than one possible trigger for the wheezing. The asthma prevalence over the 20-year period was 19% at 18–23 months of age, 28% at the age of four, 13% at 8 years of age, and 14% at 15–16 years (Fig. 1). The prevalence of asthma was highest at the age of 4 years (28%) and decreased significantly ($p = 0.0002$) between the age of four and 8 years of age, but remained relatively stable thereafter. No sex difference was noted for rhinoconjunctivitis, atopic dermatitis, or asthma ($p = 0.371, 0.690$, and 0.943).

Nine individuals reported drug reactions, including two with confirmed allergy to penicillin. Urticaria at some stage was reported by 27 (23%) with various or unknown triggers.

A positive first-degree family history of allergic diseases was found in 57 (48%), 27 (23%) in mothers, 17 in the fathers (14%), and 13 individuals had siblings with allergic disorders. Of the 57 individuals with positive family history, 46 had allergic diseases themselves and 46 had positive skin prick tests. No correlation between number of siblings and allergic diseases was observed for rhinoconjunctivitis, atopic dermatitis, or asthma ($p = 0.324, 0.804$, and 0.147).

Of the 120 participants 29 (24%) smoked, 14 women and 15 men, in addition to seven who claimed to have recently stopped smoking. Smoking was reported in 37 (31%) of the households, and smoking was recently stopped in additional seven. Of the 16 individuals with active asthma, three were current smokers and smoking was in one or two of the households.

Pets were in 50 (42%) of the households, most often a dog ($n = 25$) or a cat ($n = 18$). Pet ownership was common, even among individuals with allergic reactions, as 12 participants held pets, despite positive allergic tests. Pet ownership was not different between individuals with or without allergic disorders.

Skin prick test was positive in 44 (37%) of the participants, most often for grass ($n = 37$), cat allergens ($n = 28$), and dog allergens ($n = 12$). Twenty-six individuals reacted to more than one allergen. Of the 44 with a positive skin prick test, 40 had allergic rhinoconjunctivitis or 33% of the total cohort. No sex difference was found in skin prick tests.

In the original study in 1987, individuals were enrolled in the study during a 5-month period, June to October. The number of individuals enrolled in each month varied considerably; in June, 41 were enrolled, 26 in July, 31 in August, 10 in September, and 12 in October (Table I). No correlation between the month of birth and allergic diseases was found for rhinoconjunctivitis, atopic dermatitis, or asthma ($p = 0.267, 0.066$, and 0.281) nor for positive skin prick test ($p = 0.437$).

Discussion

The study cohort has been followed from birth for 21 years to evaluate the prevalence and manifestations of allergy at different ages (15, 27, 28). It consists of a randomly selected group of children in addition to individuals with relatively high versus low levels of cord blood IgE (27). As no association or trend was observed between cord blood levels of IgE and prevalence or manifestations of allergy at the ages of about 2 and 4 years (27, 28), the cohort has been considered to represent Icelanders born in 1987. It should be emphasized that the clinical evaluations have all been supervised by the same pediatric allergologist (BÁ), and they have been based on physical examinations and prick tests in addition to detailed questionnaires.

As expected, the prevalence of allergic rhinoconjunctivitis has increased constantly from the age of 4 years, and notably, it increased from 25% to 41% between the age of 15–16 and 21 years. In another recent study in Iceland, 17% prevalence of allergic rhinoconjunctivitis was reported among 10-year-old children (4).

In contrast to rhinoconjunctivitis, the highest prevalence of asthma (27%) was observed in our cohort at the age of 4 years, but declined to about 13% at age of 8 years and has not changed significantly after that (15). This is slightly higher than in a recent study on 10-year-old children in Iceland (4) and in Sweden (10). It is well known that the prevalence of asthma changes with age throughout childhood (16), but the prevalence remains rather high compared with our earlier results. Several other studies are, however, in keeping with our results, although differences between studies are seen (2, 5, 6, 13, 18). In our cohort, none was severely affected or had been hospitalized for asthma during the last 12 months.

Atopic dermatitis was now diagnosed in 8% of the cohort and has decreased steadily with age as expected (2, 3, 12). Reported atopic dermatitis during 12 months has recently been described to be as high as 27% in 10-year-old Icelandic children (4). Our results are in concordance with other studies in children and adults (3, 6, 12).

The prevalence of positive prick test has increased from 29% at the age of 15–16 to 37% in the current study. This prevalence is within the range that has been reported for individuals with known allergy (30), and therefore relatively high, especially as we consider our cohort to be population based. (22, 31). Furthermore, positive prick tests to dust mites are very rare in Iceland (32), a finding that was confirmed in the present study. A positive prick test was observed in 20% of adult Icelanders about 10 years ago (33). As is known from

other studies, a positive skin prick test is more related to allergic rhinoconjunctivitis than to asthma or atopic dermatitis (8), and our present study confirms that. Thus, the high prevalence of positive skin tests in our study may reflect the increasing prevalence of allergic rhinoconjunctivitis that we observed.

In the initial study, the individuals were enrolled during the months June to October, thus are born in this period (27). Several researchers have studied the effect of the season of birth on the development of allergy with very conflicting results (24, 26, 34–37). Our results are in good harmony with a recent epidemiological study on 10-year-old Icelandic children revealing a high and probably increasing prevalence of allergic disorders in Icelandic children (4).

Our results are in concordance with several studies revealing a strong family history in allergic diseases supported by interesting genetic studies as recently reviewed (3, 23).

Almost one-fourth of the individuals smoked in addition to those who claimed to have recently stopped. These numbers are high, but comparable to a survey on smoking in teenagers in Iceland (http://www2.lydheilsustod.is/media/tobaksvarnir/rannsoknir/reykingskysla_2005.pdf). It is bizarre that few patients with asthma were active smokers. Pet ownership was in 42% of households, even sometimes despite confirmed pet allergy. Although this is strange, one might keep in mind that symptoms of asthma and allergy were mild in our group. Drug reactions were uncommon.

Our results confirm that allergic diseases are common in Iceland and in many aspects comparable to other Western countries (1, 2, 6, 10, 11). The high early age prevalence of asthma and atopic dermatitis shifting to lower prevalence with increasing age agrees with several other studies (1, 2). However, the high and steadily increasing prevalence of allergic rhinoconjunctivitis warrants attention.

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