

Frequency of allergic diseases following measles

E. Kucukosmanoglu^a, F. Cetinkaya^b, F. Akcay^b and F. Pekun^b

^aDepartment of Pediatrics, Medical Faculty, Gaziantep University Istanbul, Turkey. ^bDepartment of Pediatrics Sisli Etfal Teaching Hospital, Istanbul, Turkey.

ABSTRACT

Objective: Viral and bacterial infections in childhood decrease the likelihood of allergic diseases in later life. The frequency of allergic diseases in patients with a history of measles has been reported to be low but some studies still suggest that measles can increase the frequency of allergic diseases. The aim of this study was to investigate the frequency of allergic diseases following measles in childhood.

Methods: Fifty-two children hospitalized in our clinic with measles were compared with 51 children without measles. Allergic diseases were investigated in both groups by using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. In all children, allergy skin tests were performed with the four most common allergens.

Results: Sensitivity to *Dermatophagoides pteronyssinus* was less frequent in children with measles than in those without ($p < 0.05$). A history of nebulized salbutamol use in the emergency room in the previous 12 months was also less frequent in the measles group ($p < 0.05$). Inhaled corticosteroid use was more common in the group without measles ($p < 0.05$).

Conclusion: The results of this study indicate that findings of allergic disease are less frequent in children with a history of measles. These children were less sensitive to *D. pteronyssinus*.

Key words: Allergic rhinitis. Asthma. Atopic dermatitis. Measles. Skin prick test. Wheezing.

INTRODUCTION

The prevalence of allergic diseases is steadily increasing in our country similar to the increase throughout the world¹⁻⁴. Allergic diseases are known to be more frequent in Western countries⁵⁻⁷. Similarly, the prevalence of atopy diagnosed by the skin prick test and specific IgE is also on the increase^{8,9}. These findings may be attributed to the hygiene hypothesis, which suggests an increase in the frequency of atopic diseases due to the decreasing number of children in families and a fall in the number of infections^{10,11}. According to this hypothesis, the cytokine profile with an innate predominance of allergenic Th2 profile, shifts to the non-allergenic Th1 profile with the influence of childhood infections^{12,13}. Although a number of studies demonstrate that measles and other viral infections prevent allergic conditions, other reports suggesting an increase in allergic diseases due to these infections are also present¹⁵⁻²⁰. Turkey is a country with a high prevalence of childhood diseases. The number of measles cases was 30,509 in 2001 and the morbidity rate was 44.97 per one hundred thousand²¹.

We aimed to investigate the correlation of allergic diseases with a history of measles.

Correspondence:

Ercan Kucukosmanoglu
Gaziantep Universitesi Tip Fakultesi
Pediatri Anabilim Dalı
Cocuk Allerjisi Uzmanı
Universite Bulvari 27310
Gaziantep, Turkey
E-mail: ercankosmanoglu@yahoo.com

METHODS

Fifty-two children with a diagnosis of measles who were hospitalized in the Pediatric Infectious Diseases Clinic in the Okmeydanı Teaching hospital during 1996 and 2002 were incorporated into the study. The control group consisted of fifty-one children who had been admitted to the outpatient clinic for other reasons and did not have a history of measles or a chronic disease. The diagnosis of measles was based on the presence of a maculopapular rash, high fever, rhinitis, conjunctivitis, cough, and Koplik spots on the buccal mucosa. Control cases without a history of measles were selected randomly among cases admitted to the pediatric outpatient clinic for other reasons. The number of measles vaccinations was recorded according to the children's vaccination cards.

The "International Study of Asthma and Allergies in Childhood" (ISAAC) questionnaire was applied to both groups. Sociodemographic questions were also asked. The parents of children enrolled in the study gave verbal consent. Prick skin tests with four allergens—*Dermatophagoides pteronyssinus*, *Mixture 5 Grasses*, *Alternaria* and cockroach antigens (Staller-genes, France) were performed. Sterile saline and histamine (10 mg/dl) were used as negative and positive controls respectively in the prick test simultaneously with the above-mentioned allergens. Tests results were evaluated 15 minutes after the procedure. The endurance diameter for each allergen was subtracted from that of the negative control and a resulting endurance of ≥ 3 mm was interpreted as positive. Moreover, when the endurance diameter of the allergen was subtracted from that of the negative control and the resulting number was divided by the endurance diameter of histamine, a value of at least 0.5 was also considered positive.

Statistical analyses were run with SPSS for windows. Fisher's exact test and independent t test were used for inter-group comparisons. A p value of < 0.05 was considered statistically significant.

RESULTS

The comparisons of age, height and weight in both groups did not yield a significant difference (table I). While the mean number of measles vaccinations was 0.94 in the measles group, it was 1.90 in the group without measles. The number of children living in the house was significantly higher in the measles group, compared to that of the control group.

The number of children using inhalation corticosteroids was significantly higher in the group without

Table I

Comparison of characteristics of the measles group and the control group

	Cases with measles (n = 52)	Cases without measles (n = 51)	p*
Age (years)	6,65 ± 1,85	6,57 ± 2,08	> 0,05
Weight (kg)	21,18 ± 5,68	20,11 ± 5,50	> 0,05
Height (cm)	117,04 ± 11,77	115,50 ± 13,58	> 0,05
Number of measles vaccinations	0,94 ± 0,96	1,90 ± 0,36	< 0,0001
Number of children living in the house	3,02 ± 1,48	2,35 ± 0,91	< 0,01

*Student's-t test.

measles than in the measles group ($p < 0.05$) (table II). There were significantly more children with a history of allergic dermatitis in the control group, compared to the group with measles ($p < 0.05$).

The primary attack of wheezing was significantly earlier in the measles group (table III).

History of experiencing a wheezing attack and use of nebulized salbutamol in the previous 12 months was significantly less frequent in the measles group (table III).

While the positivity of *D. pteronyssinus* allergy skin test was significantly higher in the group without measles, there was no significant difference between the two groups with regard to the results of other allergy skin tests (table IV).

DISCUSSION

Up to date, conflicting results on the correlation between allergic diseases and childhood infections have been obtained. While some reports suggest that childhood infections prevent the development of allergic diseases, others claim that they increase the frequency of these conditions¹⁴⁻²⁰. However, general opinion is that viral infections in childhood prevent the occurrence of asthma. A multi-center cohort study in Germany indicates that recurrent viral upper respiratory tract infections early in life decrease the likelihood of asthma, whereas a positive correlation is present between recurrent lower respiratory tract infections and wheezing attacks²². Authors attribute this to the predilection of the immature immune system towards Th1 phenotype with the stimulation of recurrent viral infections in early childhood, which consequently decreases the likelihood of asthma during the pre-school period²². Similarly, in vitro stud-

Table II
Comparison of various characteristics of the measles group and the control group

	Cases with measles (n = 52) (%)	Cases without measles (n = 51) (%)	p*
Allergic disease in the family	17 (32,6)	15 (29,4)	> 0,05
Allergic disease in the mother	9 (17,3)	5 (9,8)	> 0,05
Allergic disease in the father	3 (5,7)	3 (5,9)	> 0,05
Allergic disease in siblings	3 (5,7)	7 (13,7)	> 0,05
Case admitted to receive nebulized salbutamol in the emergency room	18 (34,6)	20 (39,2)	> 0,05
History of wheezing	29 (55,7)	29 (56,8)	> 0,05
Wheezing within the previous 12 months	11 (21,1)	14 (27,4)	> 0,05
History of inhaled steroid use	3 (5,8)	8 (15,6)	> 0,05
Current use of inhaled steroids	1 (2)	6 (13,3)	< 0,05
Allergic rhinitis findings within the previous 12 months	4 (7,7)	7 (13,7)	> 0,05
Allergic conjunctivitis findings within the previous 12 months	1 (2)	2 (3,9)	> 0,05
History of atopic dermatitis	–	4 (7,8)	< 0,05
Atopic dermatitis within the previous 12 months	–	3 (5,9)	> 0,05
Physician's diagnosis of asthma	1 (2)	3 (5,9)	> 0,05
Physician's diagnosis of allergic rhinitis	–	2 (3,9)	> 0,05
Physician's diagnosis of allergic dermatitis	–	1 (1,9)	> 0,05

*Fisher's exact test.

Table III

**Comparison of the two groups with regard to a history
of nebulized salbutamol use within the previous
12 months**

Use of nebulized salbutamol	Cases with measles (n = 52) (%)	Cases without measles (n = 51) (%)	p*
Never	8 (15,3)	3 (5,8)	< 0,05
1-3 times	3 (5,7)	7 (13,7)	
4 times or more	–	3 (5,8)	

*Fisher's exact test

Table IV

Comparison of allergy skin tests between the two groups

Skin test positivity	Measles (+) (n = 52)	Measles (-) (n = 51)	p*
Total	4 (7,7 %)	8 (15,7 %)	> 0,05
<i>D. pteronyssinus</i>	2 (3,8 %)	8 (15,7 %)	< 0,05
Mixture5grasses	0 (0 %)	3 (5,9 %)	> 0,05
<i>Alternaria</i>	1 (1,9 %)	2 (3,9 %)	> 0,05
Cockroach	1 (1,9 %)	2 (3,9 %)	> 0,05

*Fisher's exact test.

ies suggest that bacterial and viral infections prevent atopy by increasing the production of γ -interferon by Th1 type T lymphocytes^{23,24}. This cytokine prevents the development of atopy, ensuring the transformation of Th0 to Th1 instead of Th2.

In a study in Guinea Bissau, 395 children aged six years or younger were followed up for 14-16 years. Allergic diseases were 50 % less frequent in children who had contracted measles than in those who had not¹⁴. The hypothesis that measles prevented allergic diseases was investigated in Finland by evaluating

medical records between 1982 and 1986²⁰. Of the 547 910 children aged between 14 months and 19 years, 20 960 had experienced measles and the remaining had not. The results of the study showed that allergic diseases were more frequent in cases with measles. The results of this study were not consistent with the hypothesis that measles could prevent allergic diseases. The higher frequency of allergic diseases in cases with a history of measles was attributed to genetic predisposition. Another report from Denmark revealed that children vaccinated for

measles, rubella and varicella were not protected from atopy even when they were exposed to these infections during childhood²⁵.

The present study investigated the correlation between measles and atopy by comparing two groups of children with and without measles. Sensitivity to *D. pteronyssinus*—the most common cause of allergy—was more frequent in the control group without measles. While the *D. pteronyssinus* allergy skin test was positive in only two patients (3.8 %) in the measles group, 8 patients (15.7 %) were positive in the control group. The mean number of measles vaccinations was less than one in the measles group and almost two in the control group. A significant difference was present between the two groups in terms of age at which the wheezing episode first occurred. The age at which measles was contracted was three in the measles group. The age at which the first wheezing episode occurred in this group was less than two in 48 % of the cases; this percentage dropped to 4 % between the ages 2 and 4. No primary wheezing episode in this group was detected after the age of four. This decrease corresponds to the post-measles period. On the other hand, the decrease due to aging was slower in the control group. The history of experiencing a wheezing episode and receiving salbutamol in the emergency room during the previous 12 months was higher in the control group. Three children in the measles group and 10 children in the control group had received salbutamol in the emergency room; this difference was statistically significant ($p < 0.05$).

In conclusion, children with a history of measles in our study group had less frequent symptoms of allergic diseases. In children without a history of measles, sensitivity develops, particularly to the house dust mite.

REFERENCES

- Linneberg A, Nielsen NH, Madsen F, Frolund L, Dirksen A, Jorgensen T. Increasing prevalence of allergic rhinitis symptoms in adult Danish population. *Allergy*. 1999;54:1194-5.
- Ninan TK, Russel G. Respiratory symptoms and atopy in Aberdeen schoolchildren: evidence from two surveys 25 years apart. *BMJ*. 1999;304:760-4.
- Turktaş I, Selçuk ZT, Kalyoncu AF. Prevalence of asthma-associated symptoms in Turkish children. *Turk J Pediatr*. 2001;43(1):1-11.
- Akçakaya N, Kulak K, Hassanzadeh A, Camcıoğlu Y, Çokuğraş H. Prevalence of bronchial asthma and allergic rhinitis in Istanbul schoolchildren. *Eur J Epidemiol*. 2000;16(8):693-9.
- Van Niekerk CH, Weinberg EG, Shore SC, Heese HD, Van Shalkwyk DJ. Prevalence of asthma: a comparative study of urban and rural Xhosa children. *Clin Allergy*. 1979;9:319-24.
- Woolcock AJ, Green W, Alpers MP. Asthma in a rigid highland area of Papua New Guinea. *Am Rev Respir Dis*. 1981;123:565-7.
- Keeley DJ, Neill P, Galliva S. Comparison of the prevalence of reversible airways obstruction in rural and urban Zimbabwean children. *Thorax*. 1991;46:549-53.
- Ulrik CS, Backer V. Atopy in Danish children and adolescent: results from a longitudinal population study. *Ann Allergy Asthma Immunol*. 2000;85:293-7.
- Nakagawa T, Nakagomi T, Hisamatsu S, Itaya H, Nakagomi O, Mizushima Y. Increased prevalence of elevated serum IgE and IgG4 antibodies in students over decade. *J Allergy Clin Immunol*. 1996;97:1165-6.
- Strachan DP. Hay fever, hygiene and household size. *BMJ*. 1989;299:1259-60.
- Strachan DP. Family size, infection and atopy: the first decade of the "hygiene hypothesis". *Thorax*. 2000;55 Suppl 1: S2-10.
- Prescott SL, Macaubas C, Smallacombe T, Holt BJ, Sly PD, Holt PG. Development of allergen specific T-cell memory in atopic and normal children. *Lancet*. 1999;353:196-200.
- Martinez FD, Holt PG. Role of microbial burden in aetiology of allergy and asthma. *Lancet*. 1999;354 Suppl 2:S11 12-5.
- Shaheen SO, Aaby P, Hall AJ, Barker DJ, Heyes CD, Shell AW, et al. Measles and atopy in Guinea-Bissau. *Lancet*. 1996;347:1792-6.
- Bodner C, Godden D, Seaton A. Family size, childhood infections and atopic diseases. The Aberdeen WHEASE Group. *Thorax*. 1998;53:28-32.
- Wickens KL, Crane J, Kemp TJ, Lewis SJ, D'Souza WJ, Sawyer CM, et al. Family size, infections and asthma prevalence in New Zealand children. *Epidemiology*. 1999;10:699-705.
- Bodner C, Anderson WJ, Reid TS, Godden DJ. Childhood exposure to infection and risk of adult onset wheeze and atopy. *Thorax*. 2000;55:383-7.
- Farooqi IS, Hopkin JM. Early childhood infection and atopic disorder. *Thorax*. 1998;53:927-32.
- Matricardi PM, Rosmini F, Riondo S, Fantini M, Ferrigno L, Rapicetta M, et al. Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiologic study. *BMJ*. 2000;320:412-7.
- Paunio M, Heinonen OP, Virtanen M, et al. Measles history and atopic diseases: a population-based cross-sectional study. *JAMA*. 2000;283:343-6.
- www.saglik.gov.tr/extras/istatistikler/temel2001/105.htm
- Illı S, Mutius E, Lau S, Bergmann R, Niggemann B, Sommerfeld C, Wahn U. Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. *BMJ*. 2001;332:390-5.
- Romagnani S. Induction of Th1 and Th2 responses: a key role for the "natural" immune response? *Immunology Today*. 1992;13:379-81.
- Maggi E, Parronchi P, Manetti R, Simonelli C, Piccini MP, Ruggi FS, et al. Reciprocal regulatory effects of IFN- γ and IL-4 on the in vitro development of human Th1 and Th2 clones. *J Immunol*. 1992;148:2142-7.
- Bagger P, Westergaard T, Rostgaard K, Hjalgrim H, Melbye M. *Thorax*. 2002;57:379-82.