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DEVELOPMENT OF RESPIRATORY ALLERGIES, ASTHMA AND ALLERGIC RHINITS IN CHILDREN WITH ATOPIC DERMATITIS

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SUMMARY – Children with atopic dermatitis (AD) usually develop symptoms when they reach the age of 6-7 years, but the risk of developing respiratory allergies, asthma and allergic rhinitis (AR) remains high. In most children with AD, the development of asthma and AR is associated with sensitization to food allergens and/or aeroallergens, while only a small percentage missed atopic diathesis. In about 35% of children with AD, food allergy is the provoking cause, and 60% of infants who had AD in the first 3 months of life were sensitized against aeroallergens by the age of 5. The aim of the study was to follow development of asthma and AR and to assess the most significant risk factors for developing respiratory allergy. A total of 114 children with AD were followed up for five years. At annual visits, the severity of disease, total immunoglobulin E (IgE) antibody values, skin prick tests, specific IgE antibodies to food allergens and aeroallergens, and absolute eosinophil count were assessed. Information on the family history of atopy and AD, feeding patterns during infancy, data on sensitivity to food allergens and/or aeroallergens, and on the occurrence of bronchial obstruction and nose symptoms were obtained. Asthma developed in 36 children, median age 7.7 years; 33 children had symptoms of AR, and 13 children with AD had both diseases associated; 38 children had sensitivity to food, of which 24 developed asthma and 13 AR; asthma developed in 18/23 children with sensitivity to aeroallergens, and almost an equal number of children developed AR. The increased absolute eosinophil count and specific IgE to aeroallergens and food allergens were the best asthma predictors, while AR predictors were family history and early onset of AD. In conclusion, children with AD are at a significant risk of developing respiratory allergies, and those with the increased absolute eosinophil count, positive specific IgE to aeroallergens and food allergens, heredity of AD, and early onset of AD are at the highest risk. Identification of risk factors will enable us to improve the treatments of AD in order to reduce the severity of disease and prevent manifestation of respiratory allergy.

Key words: *Dermatitis, atopic; Child; Child, preschool; Asthma; Rhinitis, allergic*

Introduction

Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases in children, with the highest incidence during the first three months of life, and up to 85% of children suffer from AD before 5 years of age[1]. The prognosis of AD is usually good, but the risk of developing asthma and allergic rhinitis (AR) is very high[2]. Up to 80% of children with AD will develop some allergic respiratory disease; in about 50% of children it manifests as asthma[3]. Clinical experience shows the risk to be approximately 70% in children with severe form, about 30% of children

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with moderate form, and only children with mild AD will not develop either asthma or AR[4,5]. In most children with AD, the development of asthma and AR is associated with sensitization to food allergens and/or aeroallergens, increased serum immunoglobulin E (IgE) antibodies, while only a low percentage will miss atopic diathesis[6]. Commonly, AD and food allergy coexist in children with AD, while in about 35% of children with AD food allergy is the provoking cause[7]. About 69% of infants who had AD during the first 3 months of life were sensitized against aeroallergens by the age of 5 years[8].

The aim of the study was to monitor the development of asthma and AR in children with AD and observe the most significant risk factors for developing respiratory allergies.

Patients and Methods

A prospective cross-sectional study was conducted at the Clinical Department for Children's Diseases, Tuzla University Clinical Center (UCC), during the period from January 2010 to January 2015. The inclusion criteria were satisfying at least three major and three minor criteria according to the Hanifin and Rajka diagnostic criteria for AD[9], and duration of the pruritic skin changes of at least 3 months. The children were examined once a year for the next five years; the severity of disease was assessed, and total IgE antibody values, skin prick tests (SPTs) and specific IgE antibodies to food allergens and aeroallergens were determined. Bronchial asthma was defined as three or more episodes of bronchial obstruction diagnosed by a physician. Allergic rhinitis was defined as development of rhinitis at least twice after exposure to a particular allergen and unrelated to infection. Urticaria was defined as the history of typical symptoms. Atopic heredity was regarded as present if at least one of the family members had shown symptoms of AD, bronchial asthma, or AR. At the first visit, a questionnaire was filled out including information about the age and sex of children, age of the child when the first signs of AD appeared, severity of the disease, background factors such as heredity of atopy and AD, symptoms of bronchial obstruction, feeding patterns during infancy, other possible allergic symptoms, and data on sensitivity to food allergens and/or aeroallergens. At the follow-up visits, a written form based on an interview was filled out containing questions about exposures and events since the last visit: furry animals at home, exposure to tobacco smoke, occurrence of bronchial obstruction, and rhinitis. The exclusion criteria were failing to meet the diagnostic criteria, duration of pruritic skin changes of less than 3 months, acute and/or chronic disease with no atopic basis, an associated systemic disorder, and the parents' refusal to enroll their child in the study. All background factors are listed in Table 1.

Table 1. Background factors on study enrolment

Background factors Explanatory factors		n	%
Heredity	Family history of atopy	34	29.8
	Family history of AD	28	24.5
Feeding patterns during infancy	Breastfeeding ended before 6 months of age	40	35.0
	Introduction of cow's milk-based formula before 4 months of age	29	25.4
	Introduction of other food (apart from breastfeeding) before 6 months of age	27	23.6
AD	Onset of AD before 4 months of age	60	52.6
	AD score at first visit >40 points	21	18.4
Food reactions	Adverse food reaction before 36 months of age	43	37.7

AD = atopic dermatitis

The SCORing Atopic Dermatitis (SCORAD) index[10] was used to assess the severity of disease. We assessed the following (Table 2): (A) spread of skin changes, expressed in a range of 0-100; (B) intensity of skin changes graded on a 0-3 scale, where 0 indicated absence of changes, 1 minor changes, 2 moderate changes, and 3 intense changes; (C) subjective signs were presented on a 1-10 scale, where 0 signifies "never better" and 10 "never worse". The child (if it was an older child over 5 years of age) or the child's caretaker expressed an opinion on the intensity of subjective signs.

The values of the SCORAD index were calculated according to the formula A/5+7B/2+C. The maximum SCORAD index value was 103. According to the SCORAD index values, the severity of the disease was

Table 2. Parameters of SCORAD index

Parameters of SCORAD index			
Spread of changes (A)		Intensity of changes (B)	Subjective signs (C)
In a front and behind area:	Head	Erythema	Scratching
	Neck Upper extremities Trunk Genitals Lower extremities	Edema/papule Crust Excoriation Lichenification Excoriations	Interrupted sleep (due to scratching in the previous three days and nights)
		Dry skin	

SCORAD index = SCORing Atopic Dermatitis index

assessed as mild (<15 points), moderate (15-40 points), or severe (>40 points). Food allergen and aeroallergen testing by SPTs was performed at the Allergy Testing Department, Clinical Department for Children's Diseases, Tuzla UCC. Testing was carried out for groups of food allergens (cow's milk, eggs, flour, meat I and II, fruit I, II and III, vegetables I and II) and for groups of aeroallergens (grass pollen, weed pollen, tree pollen, house dust, *Dermatophagoides pteronyssinus*, animal hair-fur, feathers, vegetable fibers, fabrics, fungi, bacteria) using dialyzed extracts of allergens in a solution of a mixture of 50% glycerol solution in buffered saline solution (allergens preparations for SPT; Institute of Immunology, Zagreb, Croatia). Urticaria of >3 mm was taken as a positive test result.

The absolute eosinophil count in peripheral blood was determined. The smear was stained with May-Grünwald and the number of eosinophils *per* 100 white blood cells was counted. The obtained number was multiplied by the total number of leukocytes of the subjects. The eosinophil values ≥450x10^6/L were considered pathologic.

Blood for determination of total IgE antibody values and specific IgE antibodies to food allergens and/or aeroallergens was obtained by the standard procedure and analyzed at the Polyclinic for Laboratory Diagnosis, Immunology Department, Tuzla UCC. Blood samples were centrifuged at 2000 rpm for 10 minutes. To determine total IgE antibodies, the samples were analyzed within 24 hours by immunonephelometry (Nephelometer Dade Behring, Marburg, Germany). Total IgE antibody values of 0-100 IU/mL were considered normal. The separated serum was stored at -80 °C until used to determine specific IgE antibodies to food allergens and/or aeroallergens (the most common allergens: cow's milk, eggs, flour, soya, peanuts and fish; house dust, *Dermatophagoides pteronyssinus*, animal hair-fur, grass pollen and weed pollen), allergens for which the children had positive SPTs, and allergens suspected to be responsible for sensitivity based on medical history. Testing was performed using the ELISA method (Enzyme Linked ImmunoSorbent Assay; Hy Tec 288 Plus apparatus, Agilent Technologies Company, Biomedical, Garden Grove, Ca, United States). The values >0.35 IU/mL were considered positive.

This study was approved by the Ethics Committee of the Tuzla University Clinical Center in Tuzla. The informed consent form was signed by the participants' parents.

Statistical data analysis was performed using MedCalc for Windows, version 15.11.4 (MedCalc Software, Ostend, Belgium). Numerical data and variables with distorted distribution were expressed by median as a measure of central value and interquartile range, while χ^2-test contingency was used to analyze differentiation in the frequency of the parameters analyzed. Two-sided p value <0.05 was considered significant. To identify the factors that best predicted the outcome parameter, asthma and AR development, logistic regression was used. The selection method was the backward stepwise elimination with likelihood ratio.

Results

The study criteria included 114 children with AD (56 boys and 58 girls), median age on admission to the study 26.5 months, minimum 1.5 and maximum 96 months; by the end of the study, the children were

Table 3. Form of atopic dermatitis according to SCORAD index values on study entry and at the end of the study

Time of assessment	SCORAD index value (points)	Form of atopic dermatitis		
On study entry	28.5	Mild form (n=23)	Moderate form (n=70)	Severe form (n=21)
	Median	11.36	28.5	70.86
	Interquartile range	11.0-13.0	22-35.9	60.8-78
	Minimal value	4.7	16	39
	Maximum value	14.8	39	102
At the end of the study	21.6	Mild form (n=38)	Moderate form (n=65)	Severe form (n=11)
	Median	12.0	23.1	73.0
	Interquartile range	6.3-13.0	16.1-32.8	46.0-84.0
	Minimal value	4.7	16.0	42.0
	Maximum value	14.8	40.0	92.0

SCORAD index = SCORing Atopic Dermatitis index

Table 4. Results of examinations and history of visits I-VI

Time of examination	I	II	III	IV	V	VI
Age (months, median; interquartile range)	26.5 12.0-58.7	38 24-70.7	50 35.2-83.5	62 48.2-94.7	74 60-106.2	86 72-117
SCORAD (median, interquartile range)	28.5 17.4-38	24.0 15.5-34.0	22.0 12.7-34.2	14.0 10.7-27.2	23.0 11.7-34.2	21.6 13.1-32.8
Bronchial obstruction in last year, n (%)	51 (44.7)	18 (15.8)	28 (24.5)	26 (22.8)	36 (31.6)	47 (41.2)
AR in last year, n (%)	16 (14.0)	11 (9.6)	11 (9.6)	28 (25.8)	31 (27.2)	33 (28.94)
Adverse food reaction in last year, n (%)	43 (37.7)	11 (9.6)	28(24.5)	11 (9.6)	12 (10.5)	18 (15.8)
Furry animals at home, n (%)	16 (14.0)	18 (15.8)	11(9.6)	12 (10.5)	10 (8.8)	8 (7.0)
Exposure to environmental tobacco smoke, n (%)	25 (21.9)	22 (19.2)	13 (11.4)	11(9.6)	27 (23.7)	68 (59.6)
Value of total IgE antibodies (median, interquartile range)	288 (42-280)	345 (122-345)	328 (111-787)	238 (111-420)	122 (66-323)	234 (120-456)
Value of absolute eosinophil count (median, interquartile range)	620 (427-750)	620 (320-772)	663 (470-780)	680 (540-1820)	680 (540-200)	690 (320-240)
Severe form of disease (SCORAD >40), n (%)	21 (18.4)	14 (12.3)	16 (14.0)	14 (12.3)	16 (14.0)	11 (9.6)

SCORAD index = SCORing Atopic Dermatitis index; AR = allergic rhinitis

aged 5.1 to 13 years. Moderate form of AD was most common (Table 3); the median SCORAD index was 28.5 points at the first visit, but was lower (21.6 points) at the end of the study.

At the last visit, skin changes almost disappeared in 11 children (SCORAD 5 points) while in 9 children it was only 6. The results of examinations and the history of visits are shown in Table 4.

Table 5. Positive SPT findings and specific IgE to food allergens and aeroallergens in children with atopic dermatitis

SPT findings		Specific IgE antibody findings	
SPT to food allergens	Children with AD n	Specific IgE to food allergen	Children with AD n
Cow's milk	15	Cow's milk	17
Hen's egg	8	Hen's egg	8
Fruit (group I)	6	Fruit (group I)	8
Vegetables (group II)	3	Vegetables (group II)	4
Meat (group I)	6	Meat (veal, lamb)	7
Meat (group II)	1	Fish	4
Wheat flour	6	Wheat flour	6
Fruit (group I)	5	Soybean	4
Vegetables (group II)	4	Chocolate	3
SPT to aeroallergens	Children with AD n	Specific IgE to aeroallergens	Children with AD n
House dust	11	House dust	13
Dermatophagoides pteronyssinus	3	*Dermatophagoides pteronyssinus*	5
Grass pollen	4	Grass pollen	4
Weed pollen	4	Weed pollen	4
Tree pollen	3	Tree pollen	3
Animal hair-fur	2	Animal hair-fur	3
Feather	2	Feather	2

SPT = skin prick test; AD = atopic dermatitis; IgE = immunoglobulin E

At the first visit, 43 children had adverse food reactions, whereas at the end of the study sensitivity to one or more food allergens was found in 38 children. While manifestation and/or worsening of nasal symptoms and/or skin changes after exposure to aeroallergens was recorded in 26 children, sensitivity (positive SPTs and/or specific IgE) to one or more aeroallergens was found in 23 of these children. However, 8 children exhibited sensitivity to more than one allergen (food allergens and aeroallergens) by the end of the study. We found positive specific IgE to the following allergens: cow's milk, hen's egg, fruit (group I), vegetable (group II), meat, fish, soybean, chocolate, and house dust, *Dermatophagoides pteronyssinus*, pollen from grass, weed, tree, animal hair-fur, and feather. Positive SPT findings and specific IgE to food allergens and aeroallergens are shown in Table 5.

Table 6. Outcome parameters

Outcome parameter	n	%
Asthma	36	22.8
Urticaria at least once	42	36.8
Allergic rhinitis at least twice	33	28.9
Adverse food reaction after 36 months of age	22	19.3
Severe form of disease on last visit (SCORAD >40)	11	9.6
Positive SPT and specific IgE ELISA to one or more aeroallergens	23	20.1
Positive SPT and specific IgE ELISA to one or more food allergens	38	33.3

SCORAD index = SCORing Atopic Dermatitis index; SPT = skin prick tests; IgE = immunoglobulin E

At the first visit, 51 children, median age 16.7 months, had symptoms of bronchial obstruction (Table 4), although at the follow-up visits 31 of them were asymptomatic and 16 had obstructive symptoms by

Table 7. Children with or without diagnosis of asthma and with or without diagnosis of allergic rhinitis in relation to some explanatory factors

Explanatory factor	Children with atopic dermatitis					
	Diagnosis of asthma			Diagnosis of allergic rhinitis		
	Yes n=36	No n=78		Yes n=33	No n=81	
	n	n	p value Odds ratio (95% CI)	n	n	p value Odds ratio (95% CI)
Heredity of atopy	21	13	<0.0001 7.0 (2.8-17.0)	17	17	0.002 4.0 (1.6-9.5)
Heredity of AD	19	9	<0.0001 8.56 (3.3-22.2)	19	9	<0.0001 10.8 (4.0-28.8)
Breastfeeding ended before 6 months of age	17	23	0.10 2.1 (0.9-4.8)	11	49	0.01 0.3 (0.1-20.7)
Introduction of cow's milk based formula before 4 months of age	6	23	0.21 0.47 (0.17.1.3)	4	25	0.06 0.3 (0.09-0.9)
Introduction of other food (apart from breastfeeding) before 6 months of age	4	23	0.05 0.29 (0.09-098)	4	23	0.1 0.34 (0.1-1.1)
Onset of eczema before 4 months of age	29	31	0.0001 6.2 (2.4-16.1)	23	10	0.03 2.7 (1.1-6.5)
SCORAD >40 points at visit one	15	6	<0.001 8.5 (2.9-14.8)	16	5	<0.0001 14.3 (4.6-44.4)
Exposure to environmental tobacco smoke	17	51	0.10 0.4 (0.2-1.0)	12	56	0.002 0.25 (0.1-0.6)
Furry animals at home	8	10	0.31 1.9 (0.7-5.4)	7	11	0.46 1.7 (0.6-4.8)
Increased values of total IgE antibodies	31	33	<0.0001 8.4 (2-9-24.0)	26	38	0.003 4.2 (0.6-10.8)
Increased value of absolute eosinophil count	30	23	<0.0001 11.1 (4.3-32.5)	21	32	0.03 2.68 (1.1-6.2)
Positive SPT to one or more aeroallergens	17	6	<0.0001 10.7 (3.7-30.9)	16	7	0.0001 9.9 (3.5-22.9)
Positive SPT to one or more food allergens	21	17	0.003 5.0 (2.1-11.8)	18	20	0.004 3.6 (1.5-8.2)
Positive specific IgE to one or more aeroallergens	18	5	<0.0001 14.6 (4.7- 44.6)	17	6	<0.0001 13.2 (4.5-38.9)
Positive specific IgE to one or more food allergens	24	14	0.0001 9.1 (3.7-22.5)	13	25	0.5 1.45 (0.6-3.3)
Adverse reactions to food before 36 months of age	24	19	0.0002 5.1 (2.2-11.9)	13	30	0.9 1.1 (0.5-2.5)
Adverse food reaction after 36 months of age	11	11	0.06 2.4 (1.0-6.9)	7	15	0.94 1.2 (0.4-3.2)

AD = allergic rhinitis; IgE = immunoglobulin E; SPT = skin prick test; SCORAD index = SCORing Atopic Dermatitis index

Table 8. Significant findings in logistic regression analysis with explanatory and outcome parameters

Outcome parameter	Explanatory factor	OR (95% CI)	p
Asthma	Increased value of absolute eosinophil count	9.1 (2.9-28.0)	0.0001
	Positive specific IgE to one or more food allergens	5.4 (1.6-17.2)	0.0044
	Positive specific IgE to one or more aeroallergens	6.1 (1.3-28.6)	0.02
Allergic rhinitis	Heredity of atopic dermatitis	33.4 (8.4-132.1)	<0.0001
	Onset of eczema before 4 months of age	9.3 (2.6-33.2)	0.0006

the end of the study. During the study period, the number of children who experienced symptoms of AR increased twofold; at the first visit, 16 children had AR symptoms, and at follow-up visits 33 children with AD had allergic symptoms of the nose (17 boys and 16 girls). By the end of the study, 36 children developed asthma, including 20 boys and 16 girls, median age 7.7 years (interquartile range, 1.4- 9.2 years) (Table 6).

Fifteen of these children had the severe form of AD (at least twice at annual visits), an almost equal number of children (n=14) had the moderate form, and 7 children developed asthma although they had the mild form of AD. However, 13 children (9 and 4 children with the moderate and severe form of AD, respectively) developed associated asthma and AR. Comparative data between children who developed asthma and children who developed AR according to explanatory factors are shown in Table 7.

A significantly high risk of developing both diseases was found for heredity of atopy and AD, early onset, severe form of AD, increased values of total IgE antibodies, positive SPTs and specific IgE to food allergens and aeroallergens. However, multivariate analysis with relevant factors for asthma showed the increased absolute eosinophil count and positive specific IgE to aeroallergens and food allergens to be significant factors; for AR, family history of AD and AD onset before 4 months were significant factors too (Table 8).

Discussion

The nature of the relationship between AD, asthma and AR has been controversial. It has been commonly held that these disorders, while sharing genetic and environmental risk factors, are unrelated disorders that may develop sequentially along an atopic pathway. Conversely, the link between eczema and these later-onset respiratory disorders may be causal[11]. However, many studies suggest the significant risk of developing asthma and AR in children with AD in a wide range of 60%-80%[1,2,5,12]. Thus, Carmi *et al*.[13] found associated asthma and AR in 20.3% of children with AD, while Zhao *et al*.[14] found both diseases associated in 49.5% of children with AD. In their study, Samochocki *et al*.[15] report that children with AD developed asthma and AR in 17.4% and 32.1% of cases, respectively. Our results are in accordance with these, as out of 114 children enrolled in the study, 31.6% developed asthma, 28.9% experienced symptoms of AR, and 13 children had both diseases. Regarding the severity of AD, Gustafsson *et al*.[2], Ricci *et al*.[16] and Illi *et al*.[17] found that children with high severity scores were at an increased risk of developing asthma. Kobyletzki *et al*.[18] also found higher odds of developing asthma and AR for the moderate and severe forms of AD in comparison with the mild form of AD. Our results are slightly different from these, as we found a significantly high risk of developing both diseases for the severe and moderate forms of AD, whereas 7 children with the mild form of AD also developed asthma. The results of various studies suggest that the early onset of AD is one of the most important risk factors for developing asthma and AR in children with AD. Kobyletzki *et al*.[18] also point out that the early onset was a strong risk factor for the incidence of asthma (OR 3.44) and AR. Similar results were obtained by Illi *et al*.[17] and Kelbore *et al*.[19], who suggest that early onset, but also parental atopic history, increase the odds of developing asthma and AR. Our results are in accordance with the above; a significantly increased risk of developing asthma and AR was found in children with positive heredity of atopy and in children with early onset of AD. However, the multivariate analysis with relevant factors for asthma showed that the increased absolute eosinophil count was also a very important predictor of the devel-

opment of asthma. The increased values were observed in 31/36 children who developed asthma, and in 21/33 children with AR. This result was expected because the increased number of eosinophils is one of the major characteristics of AD, since eosinophils with their potent inflammatory function participate in the development and maintenance of skin change in AD. When the presence of IgE antibodies caused by hypersensitivity is suspected, SPT is a reliable method for recognizing the allergen to which the child is hypersensitive and against which the child will create specific IgE antibodies.

Studies show that within the first 2 to 4 years of life, children with AD and positive SPTs and specific IgE antibodies to food allergens and/or aeroallergens are at a higher risk of progressing into atopy[20-22]. Our results comply with this since it was found that positivity of IgE to aeroallergens and food allergens was the most significant predictor of developing asthma. The correlation between AD and food allergies was about 30%, particularly in those children with early onset, with the severe and persistent form of AD. Whether children with IgE-mediated food allergy are at an increased risk of developing subsequent asthma and AR is unclear[11]. Early manifestation of food allergy is accompanied by a very high risk of sensitization to aeroallergens and a high risk of developing asthma and AR in children with AD[20]. The results obtained by Lowe *et al.*[21] also suggested a greater risk of asthma and AR in children with AD and sensitivity to food allergens. Our study results comply with these, since out of 38 children with sensitivity to food, 24 children developed asthma and 13 developed AR. Malmberg *et al.*[23] and Saarinen *et al.*[24] point out that children with cow's milk allergy by the age of 7 months exhibited increased airway inflammation and bronchial responsiveness. In our study, at the first visit, 51 children with AD already had episodes of bronchial obstruction and 17 of them developed sensitivity to cow's milk in early infancy. On the other hand, data reported by Gustafsson *et al.*[2] show that 25% of children with symptoms of food allergy before 36 months of age failed to develop asthma or AR. Our results are different in comparison with these results, since 21% of children with AD and food allergy before 36 months of age developed asthma, and 11.41% of them developed AR. In their study on the significance of delayed solid food introduction to prevent the risk of developing asthma and AR in children with AD, Zutavern *et al.*[25] showed that the delayed introduction of solid food was not associated with decreased odds for developing asthma, AR or sensitization to food or inhalant allergens. Similarly, we did not find an increased risk of developing asthma or AR in children who were introduced solid food before 6 months of age. Opinions on the actual role of aeroallergens in the pathophysiology of AD are still divided, although research shows that at least one aeroallergen is present in 40%-50% of children with AD positivity and these children more often have associated asthma and AR[26,27].

In our study, 18 children developed asthma and almost an equal number developed AR out of 23 children with sensitivity to aeroallergens. It was observed that sensitivity to aeroallergens (positive SPTs, specific IgE) was a significant risk factor for development of asthma and AR. Also, in their studies, Jedrychowski *et al.*[28] and Arruda *et al.*[29] suggest that the presence of sensitivity to aeroallergens was a significant risk factor for developing asthma in children with AD. They also examined the effects of exposure to tobacco smoke in children with AD and emphasize that it was associated with the risk of developing asthma. However, in the study by Gustafsson *et al.*[2] on the effects of exposure to tobacco smoke or presence of furry animals at home, the increased risk of developing respiratory allergies was not observed. Our data are similar, and somewhat expected. It seems that families with atopic problems avoid keeping furry animals and smoking in comparison with the general population. The parents who deal with their children's atopy are likely to eliminate the risk factors which may worsen AD and may contribute to the development of respiratory allergy. Kotrulja *et al.*[30] emphasize that it is essential for parents to be informed and educated on AD, treatments and risk factors in order to improve their children's and the whole family's quality of life, but also to better monitor the disease.

Conclusion

Our study confirmed that the increased risk of developing respiratory allergy among children with AD, with the increased absolute eosinophil count, positive specific IgE to aeroallergens and food allergens, family history of AD, and early onset of AD are the best predictors. Identification of risk factors will enable us

to closely monitor and improve the treatment of children with AD in order to reduce the severity of disease and prevent the possible manifestation of respiratory allergy.

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Sažetak

RAZVOJ RESPIRACIJSKIH ALERGIJA, ASTME I ALERGIJSKOG RINITISA U DJECE S ATOPIJSKIM DERMATITISOM

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Djeca s atopijskim dermatitisom (AD), osobito ona s teškim oblikom i preosjetljivosti na alergene hrane ili aeroalergene, imaju visok rizik za razvoj astme i alergijskog rinitisa (AR). Cilj je bio pratiti razvoj astme i AR u djece s AD te uočiti najznačajnije rizične čimbenike za njihov nastanak. Ukupno je 114 djece s AD praćeno tijekom pet godina. Pri jednogodišnjim pregledima procjenjivala se težina bolesti, vrijednost apsolutnog broja eozinofila, ukupnih imunoglobulinskih E (IgE) protutijela, kožni ubodni test, specifična IgE protutijela na alergene hrane i aeroalergene te podaci o obiteljskoj povijesti atopije i AD, načinu prehrane u dojenačkoj dobi te o preosjetljivosti na hranu i aeroalergene, pojavi otežanog disanja i nosnih simptoma. Astma se razvila u 36 djece, uz gotovo jednak broj onih s umjerenim i teškim oblikom AD; simptome AR imalo je 33, a udružene obje bolesti 13 djece. Od 38 djece s preosjetljivošću na hranu 24 je razvilo astmu, a 13 AR; od 23 djece s preosjetljivošću na aeroalergene 18 je razvilo astmu, a 17 AR. Najbolji predskazatelji za razvoj astme bili su apsolutni broj eozinofila i specifična IgE protutijela, dok su predskazatelji za AR bili AD u srodnika i rani nastup AD. Zaključuje se da djeca s AD imaju značajan rizik za razvoj astme i AR. Prepoznavajući predskazatelje i ublažavajući težinu bolesti možda bi se mogao spriječiti razvoj respiracijske alergije.

Ključne riječi: *Dermatitis, atopijski; Dijete; Dijete, predškolsko; Astma; Rinitis, alergijski*