ACTA MEDICA LITUANICA. 2017. Vol. 24. No. 3. P. 145–152

Investigation of markers of allergic sensitization and viral infections in children with allergy and asthma

Rūta Dubakienė[1],

Vilija Rubinaitė[2],

Malvina Petronytė[1],

Indrė Dalgėdienė[2],

Odilija Rudzevičienė[1],

Dalia Dubakaitė[1],

Palmira Rudalevičienė[3],

Aurelija Žvirblienė[1, 2]

[1] *Faculty of Medicine, Vilnius University, Vilnius, Lithuania*

[2] *Institute of Biotechnology, Vilnius University Life Sciences Centre, Vilnius, Lithuania*

[3] *Mykolas Romeris University, Vilnius, Lithuania*

Background. Allergic diseases are the most prevalent chronic diseases in the developed countries. It is believed that early allergic sensitization and respiratory viral infections play an important role in the development of allergic diseases and asthma.

Methods. The current study investigated the correlation between asthma, allergy, and various markers – allergen-specific IgE, IgG4 and IgA, ECP, IgM, and IgG antibodies against respiratory viruses hRSV and hPIV1-4 – in blood serum samples from 80 children (mean age 5.2 years) recruited from the Lithuanian birth cohort. Children were divided into three groups according to their diagnosis: asthma (n = 25), allergy without asthma (n = 14), and control group (n = 41).

Results. Based on retrospective data, airway infections and bronchitis by the age of two years were associated with asthma in later childhood. The presence of IgM and IgG antibodies against hRSV and hPIV1–4 at the age of five years were not associated with asthma and allergy: a high rate of persistent or past respiratory viral infections was revealed in all three groups. Among allergic children, increased levels of allergen-specific IgE and d1-specific IgG4 were determined.

Conclusion. The current study provides new insights into the relationships between allergic sensitization and respiratory virus infections in children.

Keywords: allergy markers, human respiratory viruses, asthma, allergy, birth cohort

INTRODUCTION

Allergic diseases, including allergic asthma, are among the most prevalent chronic diseases in the developed countries. It is estimated that there are approximately 300 million of asthma-affected individuals worldwide independently of their age or ethnic group (1). According to the Lithuanian Department of Statistics, the prevalence of asthma in Lithuanian population was 2.7% (2) in 2014. It is believed that these numbers might significantly increase in the next few decades. Therefore, it is of great importance to identify factors that cause allergy and asthma in order to predict disease progress and prevent the development of new cases of asthma.

Correspondence to: Aurelija Žvirblienė, Institute of Biotechnology, Vilnius University Life Sciences Centre, Saulėtekio 7, Vilnius, LT-10257, Lithuania. Email: azvirb@ibt.lt

Acute asthma exacerbations are frequently caused by respiratory viral infections (3) and allergic sensitization (4). In infancy, illnesses such as bronchiolitis share many clinical features with acute asthma, including wheezing, rapid breathing, prolonged expiratory phase inflammation, and respiratory compromise (4). Accumulating evidence indicates that the aetiology of virus-induced asthma is linked to viral respiratory infections. Respiratory viruses are detected in the majority of asthma exacerbations in both children (80–85%) and adults (75–80%) (1, 3, 5–7). Previous studies have shown that human respiratory syncytial virus (hRSV), human metapneumovirus (hMPV), human parainfluenza virus (hPIV), and human rhinovirus infections may be associated with virus-induced asthma (1, 5, 6). Polymerase chain reaction (PCR) analysis revealed that hRSV and hMPV are the most frequently detected pathogens in children with acute wheezing: the prevalence of hRSV and hMPV is similar (36% and 42%, respectively) in children younger than 2 years of age, but differs (27% and 66%, respectively) in older children (1). Moreover, it was suggested that hRSV is the dominant species detected in patients with no history of wheezing and/or asthma, while hMPV is dominant in patients with such a history (3). Thus, the main causative viral agent of asthma depends on previous illness and age. Around one-third of infants who have acute wheezing develop recurring wheezing, indicating that viral respiratory illnesses in early life may promote asthma (6). Recently, the "two-hit" hypothesis has been proposed, whereby viral infections promote asthma mainly in predisposed children (1). Infants who develop virus-induced wheezing episodes are at an increased risk for subsequent asthma, although most acute wheezing illnesses in infancy resolve with no long-term sequelae (3). Indicators of an increased risk for developing asthma include wheezing episodes caused by respiratory viral infections and the development of atopic features such as atopic dermatitis, allergen-specific IgE for food or inhalant allergens (e.g., house dust, mites, cat or dog dander), and blood eosinophilia (4–6). In infancy, atopy is an important risk factor for acute episodes of virus-induced wheezing. Once asthma has been established, respiratory viral infections are the most common cause of acute exacerbations, especially in children (4). Thus, it is believed that the main etiological causes of asthma are allergic sensitization and acute respiratory illness. However, the relationships between viral infections, host immune response, early allergy sensitization and host factors in the pathophysiology of asthma remain unclear. To gain a better understanding of the development of virus-induced asthma, it is important to assess both the characteristics of the respiratory viral infections and allergy-related markers.

Long-term cohort studies provide opportunities to investigate risk factors of allergic diseases in various countries. The aim of the current study was to investigate the links between allergy markers (the levels of allergen-specific IgE, IgG4, IgA antibodies and eosinophil cationic protein (ECP) in serum) and the infectivity with viruses that cause most of the airway infections in a group of children with allergy and asthma from the Lithuanian birth cohort. In order to evaluate the impact of respiratory viral infections to the development of allergy and asthma in paediatric patients, we investigated the levels of virus-specific IgG and IgM antibodies in patients' serum and compared these results with the data obtained from the evaluation of allergic condition and the ECP level.

MATERIALS AND METHODS

Study subjects

The study population included 80 children who were selected from the Lithuanian birth cohort ALRIGEN (n = 1556), which was established as a part of the multicentre "EuroPrevall" birth cohort including over 12,000 newborns in nine European countries. The "EuroPrevall" cohort was established in 2005–2009 using a standardised approach.

Children included in this study were born in 2006 and 2007 inclusively. On the day of blood collection, they were 4–7 years of age (mean age 5.21 years). These children were divided into three groups according to the asthma diagnosis and their allergic condition: the asthma group (children diagnosed with asthma, n = 25), the allergy group (children sensitized to f1, d1 and/or d202 allergens and/or having a positive skin prick test (SPT), and not diagnosed with asthma, n = 14) and the control group (apparently healthy children that were neither diagnosed with asthma nor sensitized to any of the allergens, n = 41).

Each participant of the study was skin-prick tested for 23 commercially available allergens and their mixes, and the serum of each participant was tested

for: (1) allergen-specific IgE, IgG4, (2) ECP levels, and (3) hPIV1-4 and hRSV specific IgM and IgG.

SPTs were performed with 23 commercial allergens and their mixes (*D. pteronyssinus*, *D. farinae*, cat, dog, grass mix, tree pollen mix, timothy grass, birch, mugworth, carrot, thistle, hazelnut, buckwheat, kiwifruit, egg, peanut, milk, shrimp, celery, apple, horse, codfish, soy) (ALK, Denmark) according to standard protocols.

Collection of blood serum samples

Blood specimens were collected at the Children Pulmonology and Allergology Centre of Vilnius University Children Hospital. The study was approved by the Lithuanian Bioethics Committee (approval No. 6B-12-306).

From each participant 4–5 ml of blood were collected by venepuncture. Blood samples were collected into 6 ml non-heparinised tubes (Vacuette Z Serum Clot Activator, Greiner Bio-one, Austria). After coagulation, blood serum was collected into 3.5 ml tubes (Röhner Tubes, Sarstedt, Germany). Immediately after collection, the aliquots of serum were used to perform allergy testing and the remaining samples were frozen and stored at –70°C for further analysis.

Detection of allergen-specific IgE, IgA and IgG4 antibodies and ECP

Blood serum from each sample was analyzed for allergen-specific IgE antibodies to the dust mite (d1 – *Dermatophagoides pteronyssinus* and d202 – *D. pteronyssinus* Der p 1 protein) and hen egg white (f1), IgA and IgG4 to d1 and f1 antigens as well as for ECP levels by using the Phadia ImmunoCAP assay (Phadia, Uppsala, Sweden).

Blood serum specimens with 0.35 kU/l or higher levels of IgE antibodies to any of the allergens tested were considered positive and indicative of allergen sensitization. In the case of IgA and IgG4, blood serum samples were considered positive when the levels of allergen-specific antibodies were higher than 0 kU/l. ECP levels of 13.0 μg/dl or higher were considered positive and indicative of increased eosinophilia.

Detection of virus-specific IgG and IgM antibodies by ELISA

IgM and IgG antibodies against hRSV and hPIV1-4 in blood serum specimens were detected using commercial ELISA kits (Euroimmun, Germany) according to the manufacturer's protocols.

Statistical analysis

Statistical analysis was performed using Origin 8.0 statistical software. Where applicable, the data were given as either means or geometric means ± appropriate standard deviation. The acquired data were compared by either *t*-test (continuous parameters) or by Fisher's exact test (categorical parameters). *P* values of 0.05 or less were considered to be of statistical significance. Due to the small sample size, more complex statistical methods were not used.

RESULTS

Study population

A total of 1556 newborns were recruited into the Lithuanian birth cohort in 2006–2007. At 24 months, a telephone survey was conducted to evaluate the prevalence of allergic diseases. In total, parents of 1126 children (72.4% of the whole cohort) completed the survey; 430 (27.6%) refused to participate. According to the acquired data, 27 children (2.4% of those that completed the survey) had already been diagnosed with asthma at the age of 24 months, while further 177 children (15.7%) had had asthma-like symptoms (episodes of wheezing, shortness of breath, or obstructive bronchitis). Allergy was diagnosed in 118 children (10.5% of those that completed the survey). Based on these data, 80 participants of the Lithuanian birth cohort were recruited into the current study. The participants were 4–7 years old (mean age 5.21 years), 42 of 80 children (53%) were boys and 38 (47%) girls. All participants were divided into three age- and gender-matched groups: healthy controls (n = 41; 51.3% of all participants), asthma group (n = 25; 31.2% of all participants) and allergy group (n = 14; 17.5% of all participants) as determined by skin prick tests and allergen-specific IgE sensitization to f1 (hen's egg white), d1 or d202 (house dust mite) allergens.

Based on the retrospective data, it was determined that by the age of two years, 16 children (20% of all participants) already had asthma-like symptoms, 35 children (43.75% of all participants) had bronchitis, and 21 children (26.25% of all participants) had various viral respiratory tract

infections (VRTI). Significant differences were detected between the asthma group and the control group according to these parameters (Table 1). Both asthma-like symptoms and bronchitis were more common among the currently asthmatic participants (both $p < 0.0001$), while previous viral infections were more common in the control group ($p = 0.01$). No differences were detected between the allergy group and the control group according to these parameters (Table 1).

Evaluation of atopy-related and virological markers

The levels of allergen-specific IgE, IgG4 and IgA and ECP in blood serum samples were measured in all three groups (asthma group, allergy group, and control group) in order to evaluate the sensitization differences between them. In parallel with the assessment of the allergic conditions, the presence of IgG and IgM antibodies against hRSV and hPIV1–4 in blood serum samples was also investigated.

It was determined that six out of 80 participants (7.5%) had an allergen-specific IgE sensitization to hen egg white (f1), 17 participants (21.3%) were sensitized to the house dust mite *D. pteronyssinus* (d1), and ten participants (12.5%) were sensitized to *D. pteronyssinus* main allergen Der p 1 (d202). Data on the allergy sensitization pattern in three different groups are summarized in Table 2. None of the participants of the control group had increased levels of allergen-specific IgE, while in the allergy group all children were sensitized to one or more investigated allergens. In the asthma group, only six participants (6/25, 24.0%) were sensitized to any of the investigated allergens – one participant was sensitized to all three allergens, one – to two allergens and four participants had increased IgE levels against a single allergen.

A total of 31 participant of the study (38.75%) had increased ECP levels. Due to great variation in ECP levels (47.14 ± 56.73 μg/dl in the control group, 53.88 ± 81.71 μg/dl in the asthma group, and 44.88 ± 29.22 μg/dl in the allergy group), the geometric mean of this parameter was analysed. It was demonstrated that the overall ECP levels were below the cut-off positive value for all three groups (11.31 ± 3.33 μg/dl in the control group, 7.18 ± 2.60 μg/dl in the asthma group, and 12.08 ± 3.35 μg/dl in the allergy group). However, the levels of increased ECP differed significantly between the groups as compared to apparently healthy children: the asthmatic children had lower ECP levels (28.11 ± 3.02 μg/dl versus 31.21 ± 2.27 μg/dl; $p = 0.017$), while the allergic children had higher ECP levels (39.08 ± 1.73 μg/dl versus 31.21 ± 2.27 μg/dl; $p < 0.0001$). These findings can be partly explained by a high number of apparently healthy controls with elevated ECP levels.

Analysis of allergen-specific IgG4 levels in blood serum revealed that while the control and the two atopic groups did not differ according to f1-specific IgG4 levels (5.26 ± 6.41 kU/l in the control group, 4.95 ± 4.67 kU/l in the asthma group, and 7.06 ± 8.30 kU/l in the allergy group; $p > 0.1$), there was a significant increase in d1-specific IgG4 levels among the allergic participants as compared to the healthy controls (0.49 ± 0.37 kU/l versus 0.19 ± 0.11 kU/l; $p < 0.0001$) (Table 2).

None of the participants of the current study were positive for f1-specific IgA antibodies. However, a nearly significant decrease in the levels of d1-specific IgA among the asthmatic children was determined (1.25 ± 0.19 kU/l as compared to 1.48 ± 0.43 kU/l in the control group; $p = 0.07$). Similar decrease in d1-specific IgA levels was

Table 1. Characterization of the participants of the current study ($N = 80$)

	Control group ($n = 41$)	**Asthma group ($n = 25$)**	***P***	**Allergy group ($n = 14$)**	***P***
Boys	21 (51.2%)	14 (56.0%)	0.80	7 (50.0%)	0.99
Girls	20 (48.8%)	11 (44.0%)		7 (50.0%)	
Age (yrs; mean ± SD)	5.32 ± 0.69	5.08 ± 0.70	0.18	5.57 ± 0.76	0.25
Asthma-like symptoms by 2 yrs.	1 (2.4%)	15 (60.0%)	**<0.0001**	0	0.99
Bronchitis by 2 yrs	11 (26.8%)	21 (84.0%)	**<0.0001**	3 (21.4%)	0.99
VRTI by the age of 2 yrs	15 (36.6%)	2 (8.0%)	**0.01**	4 (28.6%)	0.75

Table 2. The levels of allergen-specific IgE, IgG4, and IgA antibodies and ECP among the participants of three different study groups ($N = 80$)

	Control group ($n = 41$)		Asthma group ($n = 25$)		p	Allergy group ($n = 14$)		p
	Positive	Mean ± SD	Positive	Mean ± SD		Positive	Mean ± SD	
IgE f1, kU/l	0	–	2 (8.0%)	1.12 ± 0.04	n/a	4 (28.6%)	0.43 ± 0.07	n/a
IgE d202, kU/l	0	–	2 (8.0%)	5.05 ± 1.53	n/a	8 (57.1%)	26.56 ± 41.02	n/a
IgE d1, kU/l	0	–	5 (20.0%)	2.37 ± 1.45	n/a	12 (85.7%)	29.38 ± 36.28	n/a
ECP, µg/dl*	20 (48.7%)	31.21 ± 2.27	5 (20.0%)	28.11 ± 3.02	**0.017**	6 (42.9%)	39.08 ± 1.73	**<0.0001**
IgG4 d1, kU/l	38 (92.7%)	0.19 ± 0.11	25 (100%)	0.25 ± 0.17	0.12	14 (100%)	0.49 ± 0.37	**<0.0001**
IgG4 f1, kU/l	36 (87.8%)	5.26 ± 6.41	22 (88.0%)	4.95 ± 4.67	0.84	14 (100%)	7.06 ± 8.30	0.42
IgA d1, kU/l	19 (46.3%)	1.48 ± 0.43	11 (44.0%)	1.25 ± 0.19	0.07	6 (42.9%)	1.24 ± 0.20	0.15
IgA f1, kU/l	0	–	0	–	n/a	0	–	n/a

n/a – not applicable; * geometric mean and standard deviation

observed in the allergy group (1.24 ± 0.20 kU/l), but the difference was found to be insignificant due to small number of IgA-positive children ($n = 6$; $p = 0.15$).

Serologic tests revealed that all three study groups were similar in terms of previous viral infections as determined by virus-specific IgG and IgM levels in blood serum samples (Table 3) and no significant differences were detected. It was found that 65 children (94.2% of all participants) were positive for IgG against hRSV and 57 children (89.1%) were positive for IgG against hPIV1-4. Furthermore, serologic tests revealed that five children (8.2%) had IgM antibodies against hRSV and 22 children (36.1%) had IgM antibodies against hPIV1–4, which indicates acute viral infections (Table 3).

DISCUSSION

The burden of allergic diseases is increasing and asthma alone affects ~300 million people worldwide (1).

Table 3. The prevalence of hRSV or hPIV1–4 specific IgM and IgG antibodies in serum samples of the participants of three different study groups ($N = 80$)

	Control group ($n = 41$)		Asthma group ($n = 25$)		p	Allergy group ($n = 14$)		p
	Positive	Negative	Positive	Negative		Positive	Negative	
hRSV IgG*	34 (94.4%)	2	22 (91.7%)	2	0.99	9 (100%)	0	0.99
hPIV1–4 IgG*	27 (81.8%)	6	23 (95.8%)	1	0.22	7 (100%)	0	0.57
hRSV IgM*	2 (6.7%)	30	2 (10.0%)	18	0.63	1 (11.1%)	8	0.53
hPIV1–4 IgM*	10 (32.3%)	21	9 (39.1%)	14	0.77	3 (42.8%)	4	0.67

* Serum samples with non-informative results (the antibody titer is borderline as compared to the calibration sample and no conclusive results can be made) were excluded from each test.

It is believed that viral respiratory tract infections and IgE-specific allergies in cooperation may increase the risk of asthma onset by magnifying the sensitivity of the asthmatic respiratory tract to environmental allergens (6, 8). In the current study, we have analysed potential allergy and asthma risk factors in the group of children (mean age 5.21 years) recruited from the Lithuanian birth cohort.

Previous studies have demonstrated that hRSV-induced respiratory tract infections may be the risk factor for the development of asthma in later life (1, 9–14), but it is not known whether hRSV acts as a disease-causing agent in the development of asthma or it just reinforces the occurrence of first asthma symptoms (9, 15). Based on retrospective data, we have demonstrated that healthy children and those currently diagnosed with asthma differed according to previous respiratory infections (VRTI) and bronchitis at the age of two years. Previous bronchitis was more common among the currently asthmatic patients than among the apparently healthy children (84.0% and 26.8%, respectively). Curiously, previous VRTI at the age of two years showed a lower rate among the currently asthmatic as compared to healthy children (8.0% and 36.6%, respectively) according to the telephone survey data. Since bronchitis may be caused by viruses (16), it is possible that the observed tendency shows not the raw occurrence of viral infections, but the pattern of viral infections transitioning into bronchitis among the asthmatic children.

In contrast to the survey data, no association between asthma and respiratory virus infections at the age of five years was detected ($p > 0.05$), possibly due to high infectivity rate in all three studied groups of children (asthma group, allergy group and control group) as confirmed by the presence of virus-specific IgG in blood serum samples. This lack of difference between the groups might be explained by preschool attendance, where viral transmission occurs easily due to a high number of interacting children (17). Based on data from the Lithuanian Department of Statistics (2), during the time of the telephone survey at two years, preschool attendance among the 1–3-year-old children was 35%, while during the data acquisition step of this study (2011–2013) the preschool attendance among the 3–6-year-old children increased to 85%. This might explain the significant difference in VRTI and bronchitis frequency at the age of two years and the lack of significance in the prevalence of virological serum markers at age of five years.

Previous studies have detected associations between increased serum ECP levels and airway inflammation (18, 19), therefore this marker may be used to assess the severity of asthma (20). However, we found increased ECP levels across all three study groups – asthmatic, allergic, and apparently healthy children. We assume that other health conditions – e.g., bacterial or rhinovirus infections (20) – might cause the increase of this inflammation-related marker among children with high preschool attendance.

Allergic inflammation is mainly associated with increased IgE levels; however, studies have shown that serum IgG4 and IgA levels may also provide valuable information about the severity of the disease (21, 22). We found that among allergic non-asthmatic children, increased allergen-specific IgE levels correlate with increased IgG4 levels in the case of the house dust mite (d1 antigen). However, in the case of egg white (f1 antigen) no such correlation was detected. Increased IgG4 levels to harmless inhalant allergens may be indicatory of an additional non-IgE-dependent allergic sensitization mechanism that may increase the risk of allergy progression to asthma (23). No association between the presence of allergen-specific IgE and asthma was detected among the asthmatic children because we found that only six of 25 asthmatic children had an IgE-dependent sensitization to any of the investigated allergens, possibly hinting at non-classic, i.e., non-allergic phenotype of their asthma. Only a few participants of our study were positive for either f1- or d1-specific IgA, therefore no conclusive associations between allergen-specific serum IgA levels and either asthma or allergy may be made.

CONCLUSIONS

The current study provides insights into the associations between allergy sensitization, respiratory virus infections, and the progression of allergy and asthma in the Lithuanian birth cohort. Analysis of allergy-related markers in three study groups revealed significantly higher levels of allergen-specific

IgE among allergic non-asthmatic children as compared to healthy controls. In addition, the allergy group was characterized by significantly higher levels of d1-specific IgG4 antibodies that might be indicative for an increased risk of developing asthma. Based on the retrospective data, viral respiratory tract infections and bronchitis by the age of two years were determined to be associated with asthma in later childhood (at the age of five years). However, the infection with hRSV and hPIV1–4 as determined by the presence of virus-specific IgG and IgM antibodies in blood serum was found to be not associated with asthma and allergy at the age of five years, possibly due to a high infectivity rate in all three study groups.

ACKNOWLEDGEMENTS

This research was supported by the Research Council of Lithuania, grant No. LIG-02/2012 (ALRIGEN).

Conflicts of Interest

The authors declare no conflict of interest.

Received 12 June 2017
Accepted 25 September 2017

References

1. Tauro S, Su YC, Thomas S, Schwarze J, Matthaei KI, Townsend D, Simson L, Tripp RA, Mahalingam S. Molecular and cellular mechanisms in the viral exacerbation of asthma. Microbes and Infection. 2008; 10: 1014–23.
2. Statistics Lithuania. https://osp.stat.gov.lt/statistiniu-rodikliu-analize#/. Accessed 20 May 2017.
3. Wark PAB, Johnston SL, Moric I, Simpson JL, Hensley MJ, Gibson PG. Neutrophil degranulation and cell lysis is associated with clinical severity in virus-induced asthma. Eur Respir J. 2002; 19: 68–75.
4. Murray CS, Simpson A, Custovic A. Allergens, Viruses, and Asthma Exacerbations. Proc Am Thorac Soc. 2004; 1: 99–104.
5. Vallet C, Pons-Catalano C, Mandelcwajg A, Wang A, Raymond J, Lebon P, Gendrel D. Human Bocavirus: A Cause of Severe Asthma Exacerbation in Children. J Pediatr. 2009; 155(2): 286–288.
6. Message SD, Johnston SL. Viruses in asthma. British Medical Bulletin. 2012; 61(1): 29–43.
7. Peebles RS. Viral infections, atopy, and asthma: Is there a causal relationship? J Allergy Clin Immunol. 2004; 113(1): S15–8.
8. Baraldo S, Contoli M, Bazzan E, Turato G, Padovani A, Marku B, Fiorella Calabrese F, Caramori G, Ballarin A, Snijders D, Barbato A, Saetta M, Papi A. Deficient antiviral immune responses in childhood: distinct roles of atopy and asthma. J Allergy Clin Immunol. 2012; 130: 1307–14.
9. Adamko DJ, Friesen M. Why does respiratory syncytial virus appear to cause asthma? J Allergy Clin Immunol. 2012; 130: 101–2.
10. Barends M, van Oosten M, de Rond CGH, Dormans JAMA, Osterhaus ADME, Neijens HJ, Kimman TG. Timing of Infection and Prior Immunization with Respiratory Syncytial Virus (RSV) in RSV-Enhanced Allergic Inflammation. The Journal of Infectious Diseases. 2004; 189(10): 1866–72.
11. Choi J, Callaway Z, Kim HB, Fujisawa T, Kim CK. The role of TNF-alpha in eosinophilic inflammation associated with RSV bronchiolitis. Pediatr Allergy Immunol. 2010; 21: 474.
12. Kusel MMH, de Klerk NH, Kebadze T, Vohma V, Holt PG, Johnston SL, Sly PD. Early – life respiratory viral infections, atopic sensitization, and risk of subsequent development of persistent asthma. J Allergy Clin Immunol. 2007; 119: 1105–10.
13. Piedimonte G, Simoes EAF. Respiratory syncytial virus and subsequent asthma: one step closer to unravelling the Gordian knot? Eur Respir J. 2002; 20: 515–7.
14. Zeng R, Li C, Li N, Wei L, Cui Y. The role of cytokines and chemokines in severe respiratory syncytial virus infection and subsequent asthma. Cytokine. 2011; 53: 1–7.
15. Hansbro NG, Horvat JC, Wark PA, Hansbro PM. Understanding the mechanisms of viral induced asthma: new therapeutic directions. Pharmacology & Therapeutics. 2008; 117(3): 313–53.
16. Wenzel RP, Fowler AA. Acute bronchitis. N Engl J Med. 2006; 355: 2125–30.
17. Monto AS. Occurrence of respiratory virus: time, place and person. Pediatr Infect Dis J. 2004; 23: S58–64.
18. Joseph-Bowen J, de Klerk N, Holt PG, Sly PD. Relationship of asthma, atopy, and bronchial responsiveness to serum eosinophil cationic proteins in

early childhood. J Allergy Clin Immunol. 2004; 114(5): 1040–5.
19. Kato M, Yamada Y, Maruyama K, Hayashi Y. Serum eosinophil cationic protein and 27 cytokines/chemokines in acute exacerbation of childhood asthma. Int Arch Allergy Immunol. 2010; 152(suppl 1): 62–6.
20. Koh GCH, Shek LPC, Goh DYT, Van Bever H, Koh DSQ. Eosinophil cationic protein: is it useful in asthma? A systematic review. Respiratory Medicine. 2007; 101: 696–705.
21. Savilahti EM, Saarinen KM, Savilahti E. Duration of clinical reactivity in cow's milk allergy is associated with levels of specific immunoglobulin G4 and immunoglobulin A antibodies to β-lactoglobulin. Clinical & Experimental Allergy. 2010; 40(2): 251–6.
22. Lúðvíksson BR, Arason GJ, Thorarensen O, Ardal B, Valdimarsson H. Allergic diseases and asthma in relation to serum immunoglobulins and salivary immunoglobulin A in pre-school children: a follow-up community-based study. Clinical & Experimental Allergy. 2005; 35(1): 64–9.
23. Jarvis D, Zock JP, Heinrich J, et al. Cat and dust mite allergen levels, specific IgG and IgG4, and respiratory symptoms in adults. J Allergy Clin Immunol. 2007; 119(3): 697–704.

Rūta Dubakienė, Vilija Rubinaitė, Malvina Petronytė, Indrė Dalgėdienė, Odilija Rudzevičienė, Dalia Dubakaitė, Palmira Rudalevičienė, Aurelija Žvirblienė

ALERGINIO ĮSIJAUTRINIMO IR VIRUSINIŲ INFEKCIJŲ ŽYMENŲ TYRIMAI ALERGIJA IR ASTMA SERGANČIŲ VAIKŲ GRUPĖJE

Santrauka

Įvadas. Alerginės ligos – vienos iš labiausiai paplitusių lėtinių ligų išsivysčiusiose šalyse. Manoma, kad alerginis įsijautrinimas ir virusinės infekcijos ankstyvame amžiuje yra svarbūs alerginių ligų ir astmos vystymosi veiksniai.

Metodika. Tirtos sąsajos tarp astmos, alergijos ir įvairių veiksnių – alergenams savitų IgE, IgG4 ir IgA, ECP, IgM ir IgG antikūnų prieš kvėpavimo takų virusus hRSV ir hPIV1-4 – 80 vaikų (amžiaus vidurkis 5,2 metų), atrinktų iš Lietuvos naujagimių kohortos, kraujo serumo mėginiuose. Vaikai buvo suskirstyti į tris grupes pagal diagnozę: astma (n = 25), alergija be astmos simptomų (n = 14) ir kontrolinė grupė (n = 41).

Rezultatai. Retrospektyviniai duomenys parodė, kad kvėpavimo takų infekcijos ir bronchitas dvejų metų vaikams buvo susiję su astmos rizika vėlesniame amžiuje. IgM ir IgG klasės antikūnų prieš hRSV ir hPIV1-4 buvimas penkerių metų vaikų kraujo serume nebuvo susijęs su alergija ir astma: visose trijose grupėse buvo nustatytas aukštas lėtinių ar buvusių kvėpavimo takų virusinių infekcijų dažnis. Alergiškų vaikų grupėje nustatytas padidėjęs alergenams savitų IgE antikūnų ir dl savitų IgG4 antikūnų lygis.

Išvada. Šis tyrimas suteikia naujų duomenų apie sąsajas tarp vaikų alerginio įsijautrinimo ir kvėpavimo takų virusinių infekcijų.

Raktažodžiai: alergijos žymenys, žmogaus kvėpavimo takų virusai, astma, alergija, naujagimių kohorta