

## IMMUNOGLOBULIN LEVELS IN CHILDREN WITH ALLERGIC AND NON - ALLERGIC CHILDHOOD ASTHMA

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*Immunoglobulin G and M levels were determined in children having non-allergic or allergic childhood asthma and in age-matched children without respiratory problems. Asthmatic children had higher IgG levels than the age-matched children without respiratory symptoms. Children having nonallergic asthma had lower IgG levels than the allergic group. Although higher concentrations were expected, the level of immunoglobulin M was normal and did not differ between groups having allergic or non-allergic childhood asthma. Low IgG levels (or/and IgA) may account for the susceptibility of asthmatic children to respiratory infections.*

Descriptors: CHILDHOOD ASTHMA, SERUM IMMUNOGLOBULINS

### INTRODUCTION

Childhood asthma is a special entity and differs from adult asthma. Epidemiological studies suggest an increasing prevalence of childhood asthma. That has been ascribed to an early and increasing exposure to allergens in pregnancy and postnatal period (1, 2). Imbalanced activation of the immunoglobulin heavy chain (IGHG) genes in more hygienic environments with a low pressure of infections has also been invoked (3, 4). A history of atopy in the mother is a risk factor for asthma in the infant, and events in fetal and infant life may lead to the adult illness (5, 6). Fetal and neonatal production of IL13, seem to be important (2, 7).

Development of the disease in childhood may be predicted and checked by an "early treatment of the atopic child" and that decreases the incidence of adult asthma (8). "Gut-associated lymphoid tissue" is an important source for generating in-

formation regarding the antigen specific database to the neonatal immune system and is exposed to the antigens due to breast-feeding (9). Allergic asthma in children shows an increase in the total IgE level in serum, which probably occurs due to the genes that regulate basal IgE production (7). In BALF of healthy children the IgG4 concentration was higher (10). Moreover, higher concentration of IgM (in cases of low IgA and IgG) could protect allergic children from infection (11). Etiopathogenetic role of other immunoglobulins is controversial, as well as protective roles of IgA, IgD and IgG (12, 13). The aim of this work was to collect basic information about the IgG and IgM levels in sera of children having non-allergic or allergic childhood asthma.

### PATIENTS AND METHODS

The study included children hospitalized in the Department of Pediatrics University Hospital Osijek. There were 79 patients having childhood asthma (moderate-persistent, by GINA guidelines) and 40 control subjects without such symptoms. Asthmatic patients were divided into two groups, allergic and non-allergic. All children assigned to the allergic childhood asthma group have had specific IgE antibodies against 5

inhalatory antigens common for eastern Croatia (Slavonia) and high total IgE levels (mean  $\pm$  standard deviation: 683.85  $\pm$  393.96 KIU/L). Control children were free of asthmatic symptoms and have had normal lung and immunological status.

Children having non-allergic asthma were younger than the allergic ones, the respective median ages were 1 yr 9 mo vs. 5 yr 1 mo ( $p < 0.001$ ). The control group was therefore divided into two comparable subgroups having median ages 2 yr 4 mo and 5 yr 3 mo. The differences between the matched groups were below statistical significance. Immunoglobulins G and M in plasma were measured by radial immunodiffusion assay on CombiRID plates (Immuno, Vienna, Austria). Concentrations of specific serum IgE antibodies (RAST) were determined by the Phadebas radio-allergo-sorbent test (Pharmacia Diagnostics AB, Sweden). Total IgE level in serum was measured by the commercial Delfia kit (Pharmacia Diagnostics AB, Uppsala, Sweden). The level of significance was set at  $p < 0.05$ .

### RESULTS

The general epidemiological trend of increasing asthma incidence is present in the eastern part of Croatia (Slavonia) and its capital Osijek (University Hospital) in

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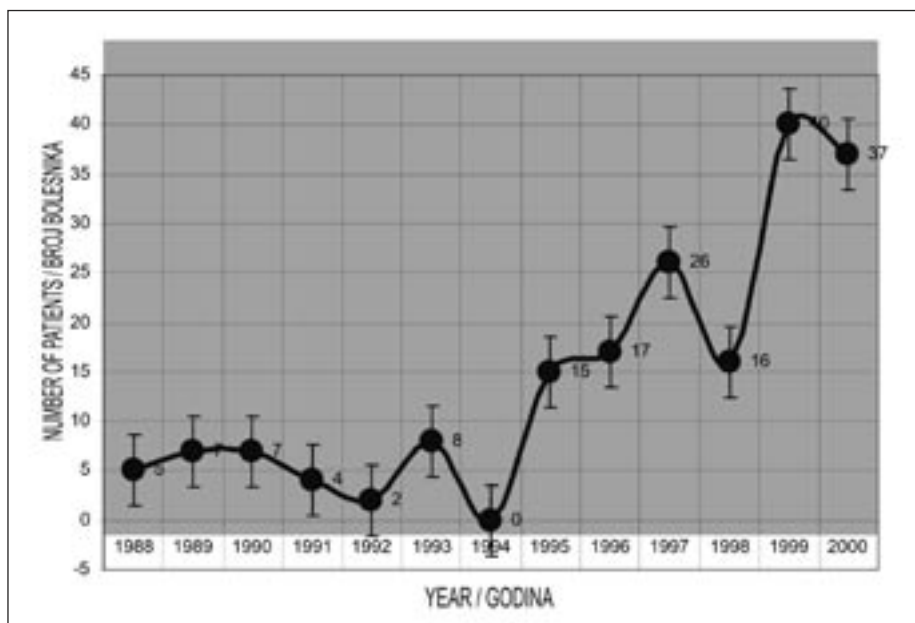


Figure 1  
New patients having childhood asthma (age 0-7) hospitalized at the University Hospital Osijek, from 1988 to 2000

Slika 1.  
Novootkriveni bolesnici s dječjom astmom (od 0-7 godina) koji su liječeni u Kliničkoj bolnici Osijek, od 1988. do 2000.

which this study was performed (Figure 1). As expected, asthma in the family was more frequently reported in the allergic asthma group (14 of 43 patients, 32.6%) than in the non-allergic asthma group (6 of 36 patients, 16.7%); ( $p \leq 0.001$ ). First attacks of asthma occurred significantly earlier in the non-allergic asthma group

than in the allergic group (median ages 10 vs. 18 mo;  $p \leq 0.005$ ).

Asthmatic patients (both the allergic and non-allergic ones) had higher IgG levels than the age-matched children without respiratory symptoms. Among the asthmatic patients, nonallergic group

had lower IgG levels than the allergic group. The serum concentration of IgM in asthmatic children having allergic and non-allergic childhood asthma were in normal ranges and the IgM levels of all four groups (asthmatic and control) were comparable. In non-allergic childhood asthma and allergic asthma group (mean  $\pm$  SD;  $1.93 \pm 0.63$  vs.  $1.53 \pm 0.59$ ) also in control group (younger/older) ( $1.39 \pm 6.2$  vs.  $1.35 \pm 0.49$ ) data on IgM concentration was not statistically significant ( $p \geq 0.05$ ) (Table 1).

#### DISCUSSION

High IgG level ( $10.48 \pm 2.77$  g/L), and normal IgM level ( $1.35 \pm 0.59$ ) were found in children having allergic asthma. In a similar study, authors compared immunoglobulin levels in children having moderate asthma to those in age-matched healthy children: IgD, IgE and IgM were elevated in asthmatic children whereas IgA and IgG were normal (13). Broncho-alveolar lavage fluids (BALF) of children having chronic chest disease (pneumonia, bronchitis) were reported to contain increased concentrations of IgG, IgA and IgM as compared to healthy controls (12). Allergen-specific IgA and specific IgG subclass were found in BALF and serum of asthmatic children and adults. High levels of IgG autoantibodies against bronchial epithelial cells were detected in adult patients having nonatopic asthma (14-17).

Other studies presented the role of infective agents in asthma and explored antibody responses to them. IgG antibodies against respiratory syncytial virus (RSV) were detected in nasal washes and sera from infants and wheezing. High titres of IgG to Chlamydia pneumoniae were associated with asthma morbidity. It has been presented that frequent infections may even protect from childhood asthma (3, 18, 19). In conclusion, our finding of increased IgG concentrations in asthmatic children is generally in accordance with selected literature data, normal concentration of IgM (we expected higher concentration) are not. It should be noted, however, that we have measured total IgG and IgM levels. Since an etiopathogenetic role has been postulated for the bacterial infections in

Table 1  
Serum IgG and IgM levels in children having allergic or non-allergic childhood asthma

Tablica 1.  
Serumske koncentracije IgG i IgM u djece s alergijskom i nealergijskom dječjom astmom

	Childhood asthma patients Bolesnici s dječjom astmom	Non-allergic nealergijska	Allergic alergijska	p
IgG	asthmatic children astmatična djeca	$8.38 \pm 1.93$	$10.48 \pm 2.77$	0.001
	age-matched children without respiratory symptoms djeca iste dobi bez respiratornih simptoma	$7.15 \pm 1.01$	$9.01 \pm 2.32$	0.007
	p	0.027	0.026	
IgM	asthmatic children astmatična djeca	$1.39 \pm 0.63$	$1.53 \pm 0.59$	0.273
	age-matched children without respiratory symptoms djeca iste dobi bez respiratornih simptoma	$1.39 \pm 0.62$	$1.35 \pm 0.49$	0.172
	p	0.997	0.065	

asthma, low serum IgG (or/and low IgA) could account for frequent infections in our patients with nonallergic childhood asthma (20).

#### LITERATURE

1. Van Duren-Schmidt K, Pichler J, Ener C. et al. Prenatal contact with inhalant allergens, *Pediatr Res* 1997; 41: 128-31.
2. Williams TJ, Jones AC, Miles EA, Warner JO, Warner JA. Fetal and neonatal IL-13 production during pregnancy and at birth and subsequent development of atopic symptoms. *J Allergy Clin Immunol* 2000; 105: 951-9.
3. Braback L. Do infections protect against atopic disease? *Acta Paediatrica* 1999; 88 (7): 705-8.
4. Oxelius VA. Imbalanced switch of the IGHG (immunoglobulin constant heavy G chain) Gm (bfn) genes in atopic childhood asthma. *Allergy* 2000; 55: 1063-8.
5. Corchia C, Bertollini R, Forastiere F, et al. Is maternal asthma a risk factor for low birth weight? Results of an epidemiologic survey. *Eur J Epidemiol* 1995; 11: 627-31.
6. Geary M, Hindmarsh PC. Childhood influences on adult disease. *Hospital Medicine* 1998; 59: 293-303.
7. Wills-Karp M, Luyimbazi J, Xu X. et al. Interleukin - 13: Central mediator of allergic asthma. *Science* 1998; 282: 2258-61.
8. Simons FE. Prospective, long-term safety evaluation of the H1-receptor antagonist cetirizine in very young children with atopic dermatitis. ETAC Study Group. *Early Treatment of the Atopic Child. J Allergy Clin Immunol* 1999; 104 (2 pt 1): 433-40.
9. Zeiger RS. Dietary aspects of food allergy prevention in infants and children. *J Pediatr Gastroenterol Nutrition* 2000; 30: 77-86.
10. Hanson LA, Soderstrom R, Avanzini A, Bengtsson U, Bjorkander J, Soderstrom T. Immunoglobulin subclass deficiency. *Pediatr Infect Dis J* 1988; 7: 17-21.
11. Williams H, McNicol KN. Prevalence, natural history, and relationship of wheezy bronchitis and asthma in children *Br Med J*. 1969; 4: 321-5.
12. Kitz R, Ahrens P, Zielen S. Immunoglobulin levels in bronchoalveolar lavage fluid of children with chronic chest disease. *Pediatric Pulmonology* 2000; 29: 443-51.
13. Najam FI, Giasuddin AS, Shembesh AH. Immunoglobulin isotypes in childhood asthma. *Indian Journal of Pediatrics* 1999; 66: 337-44.
14. Peebles RS Jr, Hamilton RG, Lichtenstein LM, Schlosberg M et al. Antigen specific IgE and IgA antibodies in bronchoalveolar lavage fluid are associated with stronger antigen-induced late phase reactions. *Clinical & Experimental Allergy* 2001; 31: 239-48.
15. Tang RB, Tsai LC, Chao PL, Hung MW. Significance of specific IgG subclass antibodies to house dust mites in asthmatic children. *Chinese Medical Journal* 2000; 63: 440-6.
16. Park HS, Kim HY, Kim YK, Son JW et al. Specific IgG1 and IgG4 antibodies to citrus red mite in citrus farmers: a study of their relationship in respiratory symptoms. *Journal of Korean Medical Science* 2000; 15: 407-12.
17. Nahm DH, Shin MJ, Yim H, Kang Y et al. Increased levels of circulating autoantibodies to cultured human bronchial epithelial cell in adult patients with nonatopic asthma. *Journal of Korean Medical Science* 2001; 16: 407-10.
18. Black PN, Scicchitano R, Jenkins CR, Blasi F et al. Serological evidence of infection with *Chlamydia pneumoniae* is related to the severity of asthma. *European Respiratory Journal* 2000; 15: 254-9.
19. De Alarcon A, Walsh EE, Carper HT, La Russa JB et al. Detection of IgA and IgG but not IgE antibody to respiratory syncytial virus in nasal washes and sera from infants with wheezing. *Journal of Pediatrics* 2001; 138: 311-7.
20. Kraft M. The role of bacterial infections in asthma. *Clinics in Chest Medicine* 2000; 21: 301-13.

#### Sažetak

#### KONCENTRACIJA IMUNOGLOBULINA U DJECE S ALERGIJSKOM I NEALERGIJSKOM DJEČJOM ASTMOM

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*Ispitali smo serumske koncentracije IgG i IgM u djece s alergijskom i nealergijskom dječjom astmom i u kontrolnoj skupini djece iste dobi, koja nisu imala respiratornih simptoma. Astmatična djece imala su više koncentracije IgG od kontrolne skupine djece bez respiratornih simptoma. Djeca s nealergijskom astmom imala su niže koncentracije IgG od djece s alergijskom dječjom astmom. Iako smo očekivali više vrijednosti IgM, koncentracije IgM bile su u granicama normale, i nisu bile vjerodostojno različite u djece s alergijskom i nealergijskom dječjom astmom. Niske koncentracije IgG (i/ili IgA) mogu biti razlog osjetljivosti djece s nealergijskom astmom na respiratorne infekcije.*

Deskriptori: DJEČJA ASTMA, SERUMSKI IMUNOGLOBULINI