

## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

# Prevalence and comorbidity of asthma, allergic rhinitis, and eczema among schoolchildren in the Republic of Srpska – A cross-sectional study

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## SUMMARY

**Introduction/Objective** The incidence of comorbidity of asthma and allergic rhinitis was one of the reasons for changing guidelines for the treatment of asthma and allergic rhinitis. The World Health Organization and Allergic Rhinitis and its Impact on Asthma group proposed the new diagnostic and therapeutic concept – “one airway, one disease.” Further, the presence of allergic rhinitis in children with asthma contributes significantly to low control of asthma; also, the treatment of allergic rhinitis in children with asthma has positive effects in terms of reducing the severity of asthma symptoms.

The aim of this study was to determine the prevalence of allergic diseases among children in the Republic of Srpska, as well as to determine whether allergic rhinitis and eczema are more common in children with asthma.

**Methods** Our study was conducted as a cross-sectional study and included 3,000 children aged six to 15 years from 13 primary schools in the Republic of Srpska. The final data processing included 1,975 correctly completed questionnaires.

**Results** The prevalence of wheezing in the previous 12 months was 7.9%, of allergic rhinitis 12.7%, and of eczema 5%. Asthma was diagnosed by a doctor in 3.5% of the children, allergic rhinitis in 19.2%, and eczema was diagnosed in 14.5% of the children.

**Conclusion** Children with asthma had statistically significant higher prevalence of other allergic diseases compared to general population. Also, children with mild asthma had statistically significant risk to be undiagnosed. Undiagnosed asthma in comorbidity with other allergic diseases leads to poor asthma control in children.

**Keywords:** asthma; comorbidity; cross-sectional studies; eczema; prevalence; child

## INTRODUCTION

Allergic diseases have become a major worldwide public health problem and significantly burden the health care system [1]. The most significant allergic diseases in children are asthma and allergic rhinitis (AR). Because of similarities in anatomy, physiology, and pathophysiology between these two diseases, they are usually considered to be the cause of comorbidity in children [2]. AR has been identified as a risk factor for the development of asthma and the trigger for exacerbations in children with asthma [3]. For a long time, these two diseases have been considered to be two different entities. Recent studies suggest using the term terms “united respiratory diseases”, unifying rhinitis and asthma as a single respiratory disease in children [4, 5].

The incidence of comorbidity of asthma and AR was one of the reasons to change the guidelines for the treatment of asthma and AR [6, 7]. The World Health Organization (WHO) and Allergic Rhinitis and its Impact on Asthma (ARIA) group proposed a new diagnostic and therapeutic concept – “one airway, one disease” [8]. Furthermore, the presence of AR in chil-

dren with asthma contributes significantly to low control of asthma; also, the treatment of AR in children with asthma has positive effects in terms of reducing the severity of asthma symptoms [9]. Therefore, WHO recommends that adequate diagnostic tests for children with asthma should be made in order to detect AR, and combined therapeutic approach should eventually be used [7].

The aim of this study was to determine the prevalence of allergic diseases among children in the Republic of Srpska, as well as to determine whether AR and eczema are more common in children with asthma.

## METHODS

Our study was conducted as a cross-sectional study and included 3,000 children aged six to 15 years from 13 primary schools in the Republic of Srpska. Criteria for children's exclusion from the study were the age of the child under six years and above 15 years, the diagnosis of chronic respiratory disease (bronchopulmonary dysplasia, bronchiectasis, primary ciliary dyskinesia or

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cystic fibrosis). The study included children whose parents signed an informed consent for this study. The permissions for visiting the schools were obtained from the Ministry of Education and Culture of the Republic of Srpska and from principals of involved primary schools before the start of the study. The envelopes with written questionnaires were distributed to schools in June 2014 in Banja Luka, Trebinje, Gacko, and Bileća. In Bijeljina, Pale, and Han Pijesak, the questionnaire was distributed in October 2014. We again visited all the participating schools after four weeks, after they collected envelopes with filled out questionnaires.

In the study we used a questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC). These questionnaires are designed for multi-center studies concerning prevalence of asthma, AR, and eczema in children. In our study, all the questionnaires were completed by parents/guardians of the schoolchildren involved since the envelopes contained both the questionnaire and an informed consent form – parents/guardians also provided written consent to participate in the study for their child.

We organized lectures for teachers about the topic of the research and allergic diseases in children at the beginning of the study process. During the lectures, teachers were able to ask all the questions about any doubts and uncertainties related to the research or their participation in the study. Each teacher received ten envelopes with the questionnaire and the informed consent form, which they distributed to children who had been randomly enrolled into this study. Documents for parents/guardians contained all the necessary information about the research. At any time during the study, parents were able to ask the main researcher any additional questions either by phone or via email. The main researcher named one person in every included school as the contact person who would collect all the returned envelopes with the completed questionnaires.

The prevalence of asthma is defined by a positive answer to the question about occurrences of wheezing in the previous 12 months according to ISAAC methodology [10]. The prevalence of asthma undiagnosed by a doctor is defined as a difference between positive responses to the question about occurrences of wheezing in the previous 12 months and positive responses to the question, “Has your child ever had asthma?” Children who answered positively to questions concerning speech-limiting wheeze, sleep disturbance, and wheezing frequency in the previous 12 months were grouped as children with moderate to severe asthma, according to Global Initiative for Asthma (GINA) guidelines [11].

The prevalence of AR is defined as the percentage of positive responses to the question about the presence of the sneezing, runny or blocked nose, accompanied by itchy, watery eyes in the previous 12 months. The presence of eczema in children in the previous 12 months is defined by positive responses to the question about the presence of an itchy rash affecting any of the following places: the folds of the elbows, behind the knees, the front of the ankles, under the buttocks, or around the neck, ears, or eyes.

Children with a positive response to the question, “Have you ever had hay fever or eczema?” were grouped as children with the diagnosis of these diseases given by a doctor.

We calculated the frequencies and percentages for the descriptive data. We used Pearson's  $\chi^2$  test for testing the relationships between independent variables and the prevalence of asthma symptoms. The criterion for statistical significance was  $p < 0.05$ . All statistical analyses were performed using the statistical software package IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Ethical Review Board, Public Health Institute, Republic of Srpska, and the Commission for Ethics of Clinical Trials Involving Humans, Faculty of Medicine, University of Novi Sad. Written informed consent was obtained from all subjects.

## RESULTS

The final data processing included 1,975 correctly completed questionnaires.

Of all the children included in the study, 47.3% were boys, and 52.7% were girls. The average age of the children was 10.2 years (SD = 2.4). The prevalence of asthma in our study was 7.9%, of AR 12.7%, and of eczema 5%. Sixty-nine children (3.5%) had been diagnosed with asthma, 379 (19.2%) with AR, and 286 (14.5%) with eczema.

Children who had symptoms which are specific to one of the allergic diseases had not always been diagnosed with the diseases. Children with symptoms characteristic for AR (81.8%) and eczema (60.6%) had an appropriate diagnosis established more often than the children with asthma symptoms (29.9%). Children with mild asthma (one to three episodes of wheezing, with wheezing not affecting a child's sleep) (Table 1) had a significantly lower prevalence of asthma diagnosis.

The children included in the study usually had symptoms characteristic for one of the investigated allergic diseases. We found that AR was a comorbidity together with asthma in 3.6% of the children, and with eczema in 2% of the children. Twenty-six children had asthma and eczema (1.3%), and 17 children had persistent symptoms of all three allergic diseases (0.9%).

Children with asthma had significantly higher incidence of other allergic diseases compared to the general population, especially children with severe asthma (> 12 attacks of wheezing in the previous 12 months, speech-limiting wheeze, and > 1 sleep disturbance due to wheezing) (Table 2). The prevalence of the AR was significantly higher in children with exercised-induced asthma (51.3%) compared to the general population (12.7%) (Table 3).

## DISCUSSION

The intention of the authors was to include in our study as many children as possible, from different towns in the Republic of Srpska. Hence, our study covered the Repub-

**Table 1.** Prevalence of asthma diagnosed by a doctor in children with asthma symptoms

Symptoms		n	Number of patients (%)		p
			Diagnosed asthma		
			Yes	No	
Wheezing attacks within previous 12 months	Total	157	47 (29.9)	110 (70.1)	< 0.001
	1–3 attacks	132	34 (25.7)	98 (74.2)	< 0.001
	4–12 attacks	18	7 (38.9)	11 (61.1)	0.346
	> 12 attacks	7	6 (85.7)	1 (14.3)	0.059
Speech-limiting wheeze		30	15 (50)	15 (50)	1.000
Sleep disturbance due to wheezing	Never	88	15 (17)	73 (83)	< 0.001
	< 1 night/week	55	23 (41.8)	32 (58.2)	0.225
	> 1 night/week	14	9 (64.3)	5 (35.7)	0.285
Exercise-induced wheezing		67	35 (51.2)	32 (48.8)	0.714

**Table 2.** Prevalence of allergic rhinitis and eczema among children with asthma

Symptoms	Frequency of wheezing in previous 12 months					Frequency of sleep disturbance due to wheezing				Speech-limiting wheeze		
	Never n (%)	1–3 n (%)	4–12 n (%)	> 12 n (%)	p	Never n (%)	< 1 per week n (%)	> 1 per week n (%)	p	Yes n (%)	No n (%)	p
Eczema symptoms	73 (4.0)	21 (16.1)	2 (10.5)	3 (42.9)	0.000	81 (4.2)	13 (23.2)	5 (35.7)	0.000	6 (19.3)	93 (4.8)	0.000
Eczema diagnosis	240 (13.2)	36 (27.7)	7 (36.8)	3 (42.9)	0.000	265 (13.9)	15 (26.8)	6 (42.9)	0.000	9 (29.0)	277 (14.2)	0.020
Allergic rhinitis symptoms	179 (9.8)	61 (46.9)	5 (26.3)	6 (85.7)	0.000	213 (11.2)	31 (55.4)	7 (50.0)	0.000	14 (45.2)	237 (12.2)	0.000
Allergic rhinitis diagnosis	283 (15.6)	79 (60.8)	10 (52.6)	7 (100)	0.000	331 (17.4)	37 (66.1)	11 (78.6)	0.000	20 (64.5)	359 (18.5)	0.000

**Table 3.** Prevalence of allergic rhinitis and eczema among children with exercised-induced asthma

Symptoms	Number of patients (%)		p
	Exercised-induced asthma		
	Yes	No	
Eczema symptoms	19 (25)	80 (4.2)	0.000
Eczema diagnosis	27 (35.5)	259 (13.6)	0.000
Rhinitis symptoms	39 (51.3)	212 (11.2)	0.000
Rhinitis diagnosis	54 (71)	325 (17.1)	0.000

lic's entire territory, and to our knowledge it is the first study of its kind conducted in it. The prevalence of the allergic diseases (eczema, asthma, and AR) among children in our study was 5%, 7.9%, and 12.7%, respectively. These results are consistent with the results of studies in countries of the region [12, 13, 14]. In our study, children with asthma had significantly higher prevalence of AR and eczema, especially those with severe asthma symptoms, compared to the general population. Children with exercised-induced asthma have a significantly higher incidence of AR and eczema. Other epidemiological studies showed the same results [15, 16]. Ballardini et al. [1] found in their study that asthma was associated with AR and/or eczema in 67% of children. Children with asthma in Italy had a significantly higher incidence of AR (70.6%) compared to children without asthma symptoms (13%) [17]. A French study showed that a large percentage of children with asthma had symptoms of AR (58.7%) [18]. AR in these children was more common if asthma symptoms were more severe [18]. Studies suggest that AR in children with asthma statistically significantly affect asthma-related visits to hospital and the level of asthma control [19, 20].

Consequently, timely diagnosis of rhinitis in children with asthma is important in order to adequately treat them and to achieve better asthma control [15]. Available studies suggest that incidence of other allergic diseases was significantly higher in children with asthma compared to children with eczema or AR [1].

Prevalence of asthma diagnosis (3.49%) was significantly lower than prevalence of symptoms (7.9%), while prevalence of AR and eczema diagnosis (19.2% and 14.5%, respectively) was significantly higher than prevalence of symptoms (12.7% and 5.0%, respectively). In our study, children with asthma symptoms (29.9%) were at higher risk to be undiagnosed compared to children with AR (81.8%) or eczema symptoms (60.6%). Results of other epidemiological studies also suggest that children with asthmatic symptoms are more often undiagnosed [21, 22, 23]. Our study showed that higher percentage of children with diagnosed asthma had symptoms of severe asthma compared with other studies [21, 24]. A doctor diagnosed asthma in children with more than 12 attacks of wheezing in the previous 12 months, frequent attacks of speech-limiting wheeze, and sleep disturbance due to wheezing. However, children with less than 12 attacks of wheezing during the previous 12 months, without speech-limiting wheeze or sleep disturbance, had a significantly higher risk of being undiagnosed. A study by Brozek et al. [22] showed a higher percentage of children undiagnosed with asthma, classified by questionnaire, and then clinically, as mild asthma according to GINA guidelines [22]. One third of children with asthma were undiagnosed according to a study by Annesi-Maesano et al. [23]. Clinical examination

of these children showed that 4% of children have mild asthma and 5.8% have severe asthma. According to a Polish study, prevalence of asthma determined by a questionnaire was 5.4%, while corrected prevalence that included clinically confirmed diagnosis of asthma in children who had been undiagnosed by the questionnaire was 10.8% [22]. These results suggest that asthma is still not adequately diagnosed and controlled in children.

By including a large number of children from the entire territory of the Republic of Srpska and different centers we tried to reduce selection bias in a cross-section study. Random errors due to inaccurate definitions of allergic diseases in epidemiological studies cannot be completely avoided. Using international methodologies and the ISAAC questionnaire for the definition of allergic diseases in children, we tried to reduce this error to a minimum. Classification bias in the study could not be avoided as the questionnaires were filled by the parents of children included in the study, and their belief and understanding of the symptoms af-

fected the determination of the prevalence of symptoms of allergic diseases in children.

## CONCLUSION

Children with asthma had statistically significant higher prevalence of other allergic diseases compared to general population. Also, children with mild asthma had statistically significant risk to be undiagnosed. Undiagnosed asthma in comorbidity with other allergic diseases leads to poor asthma control in children.

## NOTE

The findings of this study will also form a part of a doctoral thesis which has been approved by the Senate of the University of Novi Sad.

## REFERENCES

- Ballardini N, Kull I, Lind T, Hallner E, Almqvist C, Ostblom E, et al. Development and comorbidity of eczema, asthma and rhinitis to age 12: data from the BAMSE birth cohort. *Allergy*. 2012; 67(4):537–44.
- de Groot EP, Duiverman EJ, Brand PLP. Comorbidities of asthma during childhood: possibly important, yet poorly studied. *Eur Respir J*. 2010; 36(3):671–8.
- Di Cara G, Carelli A, Latini A, Panfilì E, Bizzarri I, Ciprandi G, et al. Severity of allergic rhinitis and asthma development in children. *World Allergy Organ J*. 2015; 8(1):13.
- Papadopoulou A, Tsoukala D, Tsoumakas K. Rhinitis and asthma in children: comorbidity or united airway disease? *Curr Pediatr Rev*. 2014; 10(4):275–81.
- Bourdin A, Gras D, Vachier I, Chanez P. Upper airway x 1: allergic rhinitis and asthma: united disease through epithelial cells. *Thorax*. 2009; 64(11):999–1004.
- Bachert C, van Cauwenberge P. The WHO ARIA (allergic rhinitis and its impact on asthma) initiative. *Chem Immunol Allergy*. 2003; 82:119–26.
- Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008; 63 Suppl 86:8–160.
- Bousquet J, Schunemann HJ, Samolinski B, Demoly P, Baena-Cagnani CE, Bachert C, et al. Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. *J Allergy Clin Immunol*. 2012; 130(5):1049–62.
- Taha MS, Youssef T, Abd-Alsamee HF, Omran A, Ezzat WF. Allergic Rhinitis and its Impact on Asthma scores in asthmatic patients with and without allergic rhinitis. *Egypt J Otolaryngol*. 2014; 30(2):112.
- Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J*. 1998; 12(2):315–35.
- Global Initiative for Asthma. Pocket Guide for Asthma Management and Prevention (for adults and children older than 5 years). Global Initiative for Asthma; 2015. p. 32.
- Munivrana H, Vorko-Jovic A, Munivrana S, Kursar M, Medlobi-Gluhak M, Vlahek P. The prevalence of allergic diseases among Croatian school children according to the ISAAC Phase One questionnaire. *Med Sci Monit*. 2007; 13(11):CR505–9.
- Zivkovic Z, Vukasinovic Z, Cerovic S, Radulovic S, Zivanovic S, Panic E, et al. Prevalence of childhood asthma and allergies in Serbia and Montenegro. *World J Pediatr*. 2010; 6(4):331–6.
- Vlaski E, Stavric K, Isjanovska R, Seckova L, Kostovski A, Kimovska M. Prevalence and severity of asthma, allergic rhinitis and eczema in school children in Skopje (International Study of Asthma and Allergies in Childhood phase 3). *Maced J Med*. 2005; 51:24–34.
- de Groot EP, Nijkamp A, Duiverman EJ, Brand PLP. Allergic rhinitis is associated with poor asthma control in children with asthma. *Thorax*. 2012; 67(7):582–7.
- Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol*. 2000; 106(5 Suppl):S201–5.
- Bugiani M, Carosso A, Migliore E, Piccioni P, Corsico A, Olivieri M, et al. Allergic rhinitis and asthma comorbidity in a survey of young adults in Italy. *Allergy*. 2005; 60(2):165–70.
- Hamouda S, Karila C, Connault T, Scheinmann P, de Blic J. Allergic rhinitis in children with asthma: a questionnaire-based study. *Clin Exp Allergy*. 2008; 38(5):761–6.
- Thomas M. Allergic rhinitis: evidence for impact on asthma. *BMC Pulm Med*. 2006; 6(Suppl 1):S4.
- Sazonov Kocevar V, Thomas J 3rd, Jonsson L, Valovirta E, Kristensen F, Yin DD, et al. Association between allergic rhinitis and hospital resource use among asthmatic children in Norway. *Allergy*. 2005; 60(3):338–42.
- Luna MFG, Almeida PC, Silva MGC. Prevalence of asthma among adolescents in the city of Fortaleza, Brazil. *J Bras Pneumol*. 2009; 35(11):1060–7.
- Brozek GM, Farnik M, Lawson J, Zejda JE. Underdiagnosis of childhood asthma: A comparison of survey estimates to clinical evaluation. *Int J Occup Med Environ Health*. 2013; 26(6):900–9.
- Annesi-Maesano I, Sterlin C, Caillaud D, de Blay F, Lavaud F, Charpin D, et al. Factors related to under-diagnosis and under-treatment of childhood asthma in metropolitan France. *Multidiscip Respir Med*. 2012; 7(1):24.
- Karadag B, Karakoc F, Ersu R, Dagli E. Is childhood asthma still underdiagnosed and undertreated in Istanbul? *Pediatr Int*. 2007; 49(4):508–12.

## Преваленција и коморбидитет астме, алергијског ринитиса и екцема код школске деце у Републици Српској – студија пресека

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### САЖЕТАК

**Увод/Циљ** Учесталост коморбидитета астме и алергијског ринитиса била је повод за измену смерница у терапији астме и алергијског ринитиса. Светска здравствена организација и Група за алергијски ринитис и његов утицај на астму предлажу нови дијагностички и терапијски концепт – „један дисајни пут, једна болест“. Наиме, присуство алергијског ринитиса код деце са астмом значајно доприноси лошој контроли астме, док терапија алергијског ринитиса код деце са астмом има позитиван ефекат на побољшање степена тежине симптома.

Циљ ове студије био је одредити преваленцију алергијских обољења код деце у Републици Српској, као и да ли су алергијски ринитис и екцем чешћи код деце са астмом.

**Методe** Истраживање је спроведено у облику студије пресека путем ISAAC упитника и обухватало је 3.000 деце узраста од 6 до 15 година из 13 основних школа на територији

Републике Српске. У коначну обраду података укључено је 1.975 упитника који су правилно попуњени.

**Резултати** Преваленција визинга у последњих 12 месеци била је 7,9%, алергијског ринитиса 12,7% и екцема 5%. Дијагнозу астме постављену од стране лекара имало је 3,5% деце, дијагнозу алергијског ринитиса 19,2% и дијагнозу екцема 14,5% деце.

**Закључак** Деца са астмом имала су статистички значајно већу учесталост других алергијских обољења у односу на општу популацију. Такође, деца са умерено благом астмом имала су статистички значајно већи ризик да буду без постављене дијагнозе астме од стране лекара. Недијагностикована астма у коморбидитету са другим алергијским обољењима доводи до лоше контроле астме код деце.

**Кључне речи:** астма; коморбидитет; студије пресека; екцем; преваленција; дете