



The frequency of sensitization to inhalatory allergens and concomitant rhinitis in asthmatic patients

Učestalost senzibilizacije na inhalatorne alergene i pridruženog rinitisa kod obolelih od astme

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Abstract

Background/Aim. Asthma is one of the most common chronic pulmonary diseases. The number of asthmatics has been continuously increasing all over the world. Depending on its causing agent, asthma is classified as allergic and nonallergic. Asthma is often associated with other allergic diseases, and it is most commonly preceded by the symptoms of rhinitis. The aim of this study was to establish the type and frequency of allergic sensitization to inhalatory allergens, frequency of concomitant rhinitis, gender and age-related distribution of asthma, and the presence of some risk factors in patients with diagnosed asthma. **Methods.** This retrospective and partially prospective analysis included 733 patients with asthma diagnosed in the Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica over the period January, 2004–December, 2008. The obtained data were statistically processed. **Results.** Females were significantly more often affected by asthma ($p < 0.05$), most frequently at 20–29 years of age. A hereditary predisposition to the diseases in terms of atopy was registered in 34.9% of the examined subjects. Most patients had allergic asthma (79.5%). Sensitization to internal and external inhalatory allergens was verified in 77.5% and 67.6% of the patients respectively, and combined hypersensitivity to both allergen types in 48.8% of the patients. Rhinitis was registered in 63.9% and 28% of the patients with allergic and nonallergic asthma, respectively. Rhinitis symptoms preceded the occurrence of asthma in 60% of the patients, with the precedence of rhinitis ranging from 1 to 27 years. A high correlation between rhinitis and asthma was established for the disease of both allergic ($r = 0.92$) and nonallergic ($r = 0.88$) etiology. **Conclusion.** The majority of the patients have allergic asthma, and they are females at 20–29 years of age. Sensitization to internal allergens is most common, and then to external ones. Rhinitis is the most common concomitant disease, usually preceding the occurrence of asthmatic symptoms.

Key words:
asthma; rhinitis; allergens; comorbidity.

Apstrakt

Uvod/Cilj. Astma je jedna od najčešćih hroničnih plućnih bolesti. Broj obolelih neprestano se povećava u celom svetu. U odnosu na uzročni faktor astma se klasifikuje na alergijsku i nealergijsku. Često postoji udruženost astme i drugih alergijskih bolesti, a najčešće njenoj pojavi prethode simptomi rinitisa. Cilj ovog rada bio je da se utvrde vrsta i učestalost alergijske senzibilizacije na inhalatorne alergene, postojanje drugih pridruženih alergijskih bolesti, distribucija astme u odnosu na pol i starost i postojanje nekih riziknih faktora kod osoba sa dijagnostikovanom astmom. **Metode.** Retrospektivno, delom prospektivno, analizirano je 733 bolesnika sa dijagnostikovanom astmom u Institutu za plućne bolesti Vojvodine u Sremskoj Kamenici, u periodu od januara 2004. do decembra 2008. godine. Dobijeni podaci statistički su obrađeni. **Rezultati.** Značajno češće od astme boluju žene ($p < 0,05$), a starost bolesnika najčešće je od 20 do 29 godina. Genetska predispozicija u smislu atopije postoji kod 34,9% ispitanika. U najvećem procentu dokazana je alergijska astma (79,5%). Senzibilizacija na unutrašnje inhalatorne alergene verifikovana je kod 77,5%, na spoljašnje kod 67,6%, a kombinovana na obe vrste alergena kod 48,8% ispitanika. Kod osoba sa alergijskom astmom rinitis postoji 63,9%, a kod onih sa nealergijskom astmom 28%. Simptomi rinitisa kod 60% obolelih javljaju se pre pojave astme u periodu od 1 do 27 godina. Visoka povezanost rinitisa i astme postoji i kod alergijske ($r = 0,92$) i kod nealergijske etiologije bolesti ($r = 0,88$). **Zaključak.** Najveći broj bolesnika ima alergijsku astmu, ženskog je pola i starosti od 20 do 29 godina. Najzastupljenija je senzibilizacija na unutrašnje alergene, a potom na spoljašnje. Najčešća pridružena alergijska bolest je rinitis, koji se većinom javlja znatno pre ispoljavanja simptoma astme.

Ključne reči:
astma; rinitis; alergeni; komorbiditet.

Introduction

Allergic diseases have been constantly increasing in number over the last two decades. Their higher frequency has been particularly evident in children, young adults and in economically undeveloped countries. These diseases are therefore regarded as the epidemic of the 21st century and the modern civilisation diseases. The allergic diseases include the respiratory tract ones, food allergies and atopic dermatitis. The most common of them are allergic diseases of the respiratory tract: allergic rhinitis and asthma¹.

In 2004, the World Health Organisation (WHO) reported about 300 million people in the world suffering from asthma. Parallel to the development of modern society and rapid industrialisation, further increase of the prevalence of asthma is predicted all over the world (it has been estimated that additional 100 million people will be affected until 2025). Due to these facts, WHO experts call asthma „the quiet tsunami“. It has been assessed that about 24% of the total world's population suffer from allergic rhinitis. It is not a severe, life-threatening disease, but can considerably disturb the quality of life of the affected subjects^{2,3}.

Asthma is a chronic inflammation of the airways in which the important role is played by a variety of cells, including mastocytes, eosinophils, T-lymphocytes and epithelial cells. In hypersensitive subjects, this inflammation induces recurrent episodes of wheezing, suffocation, chest tightness and cough, particularly during the night and/or early in the morning. These symptoms are associated with a disseminated and changing, spontaneously or by drugs, at least partially reversible obstruction of air flow through the airways. Inflammation also causes an elevated reactivity of the airways to diverse stimulants, which may be present even when neither the disease symptoms, nor bronchial obstruction are manifested. Depending on its inducing agents, asthma is classified as allergic (extrinsic) and nonallergic (intrinsic). Allergic rhinitis is an inflammation of the nasal mucosa, mediated by the immunoglobulin (Ig) E mechanism. It is clinically manifested by sneezing, nasal secretion, blocked and itching nose^{3,4}.

Risk factors for allergic respiratory tract diseases may be internal or external, acting usually in concomitance. Internal risk factors include genetic predisposition (atopy and hypersensitivity) and gender. Atopy is a predisposition of an organism to produce larger quantities of IgE antibodies in response to diverse substances from the external environment. External factors are allergens, infections, working environment, tobacco smoke, air pollution, live style and diet habits, food additives, drugs, and others^{3,4}.

Establishing the diagnosis of asthma is a continual process. The basic procedures include history taking, physical examination, lung function tests (spirometry, bronchial challenge, bronchodilation test), confirmation of hypersensitivity to inhalant allergens by cutaneous tests or measuring the levels of specific antibodies. The cutaneous prick test is painless, easy to perform and very sensitive and highly specific for establishing allergy^{1,4}.

The aim of this study was to define the frequency and type of sensitization to inhalant allergens in asthmatic subjects, as well the age-related distribution over the examined period, the presence of other allergic disorders, gender and age structure, as well as the presence of some predisposing and contribution factors for the disease genesis.

Methods

The study was retrospective and prospective in character. The data were collected from the files of 733 patients in the Allergy Unit of the Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, where the patients with asthma were diagnosed and controlled. The investigation was done for the period from January 1, 2004 to December 31, 2008. The inclusion criterion was that a patient had the diagnosis of asthma established by routine diagnostic procedures applied in this highly specialised health institution.

The following parameters were examined and analysed: annual distribution, sex structure, age structure, smoking habits, genetic predisposition, type of asthma depending on its etiological factor, concomitance of other allergic diseases (allergic rhinitis, food allergy and atopic dermatitis), time correlation of the genesis of allergic rhinitis and asthma, type and frequency of hypersensitivity to standard inhalatory allergens established by prick testing.

The obtained results were statistically processed by the Microsoft Excel 2003 software for statistical and tabular calculations. Common statistical methods were applied – Student's *t*-test i Pearson's correlation analysis.

Results

In the examined 5-year period, there were 733 patients with the established diagnosis of asthma registered in the Allergy Unit of the Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica. All the patients lived in Vojvodina, mostly in Novi Sad community.

The number of asthmatic patients registered per year, and the patients' gender structure in each year are given in Figure 1 and 2, respectively. A statistically significant difference ($p < 0.05$) was registered between the number of affected male and female patients. Females are more frequently affected with asthma than males.

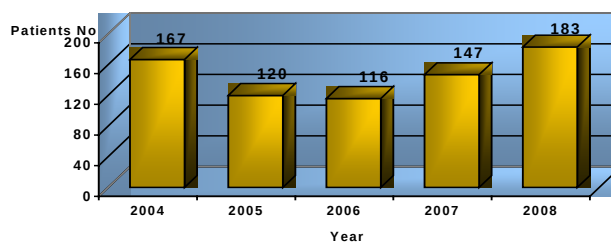


Fig. 1 – The number of the patients (n = 733) with the established diagnosis of asthma in a 5-year period

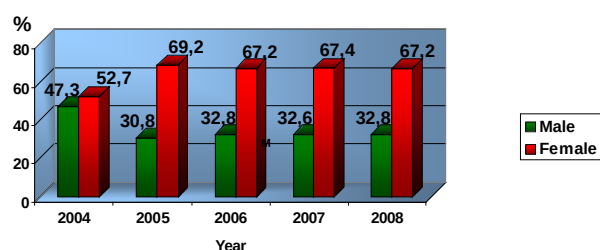


Fig. 2 – Distribution of the patients with the established diagnosis of asthma (n = 733) by gender in a 5-year period

The age structure of the affected patients is given in Figure 3. The age group from 20 to 29 is most frequently affected.

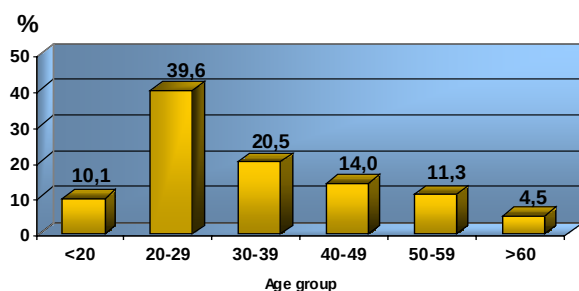


Fig. 3 – Age structure of the patients with the established diagnosis of asthma (n = 733)

The data on patients' smoking habits, genetic predisposition in terms of atopy, the distribution of nonallergic and allergic asthma established by cutaneous prick testing to standard inhalant allergens, concomitant allergic diseases, time correlation of allergic rhinitis and asthma occurrence, and frequency of rhinitis symptoms depending on asthma type are presented in table 1.

Table 1
Parameters examined in the patients with the established diagnosis of asthma (n = 733)

Parameters	% of patients
Smoking habits	
non-smokers	73.9
smokers	13.9
ex-smokers	12.2
Genetic predisposition	
positive atopy	34.9
negative atopy	65.1
Etiology-related type of asthma	
nonallergic asthma	20.5
allergic asthma	79.5
Concomitant allergic diseases (n = 583)	
allergic rhinitis	63.9
dermatitis	7.0
food allergy	3.1
Time correlation of allergic rhinitis and asthma occurrence	
earlier rhinitis	60.0
at the same time	40.0
Frequency of rhinitis symptoms depending on asthma type	
allergic asthma (n = 583)	64.0 (n = 373)
nonallergic asthma (n = 150)	28.0 (n = 42)

At least one concomitant allergic disease (allergic rhinitis, food allergy, atopic dermatitis) was registered in 74.1% of the patients with allergic asthma.

Three fifths of the patients (60%) developed the symptoms of allergic rhinitis prior to asthma over the period ranging from one to 27 years. A simultaneous onset of both diseases, within the same year, was registered in two fifths (40%) of the examined subjects.

The frequency of rhinitis symptoms in the patients with allergic and non-allergic asthma was found to be 64% and 28% of the patients, respectively.

By determining a correlation coefficient, a high correlation of rhinitis and asthma was demonstrated in allergic ($r = 0.92$) and non-allergic ($r = 0.88$) asthma.

Sensitization to at least one of the standard inhalant allergens, established by the cutaneous prick test, was found in 79.5% of the subjects. Distribution of sensitization to specific allergens is shown in Figure 4.

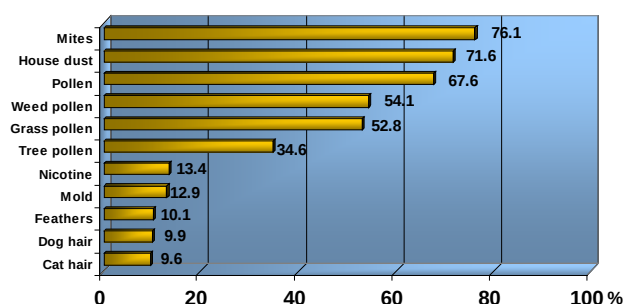


Fig. 4 – Type and frequency of hypersensitivity to standard inhalatory allergens (n = 583)

The incidence of sensitization to major inhalant allergens, classified into three classes depending on their origin (external, internal, and combined), is given in Figure 5.

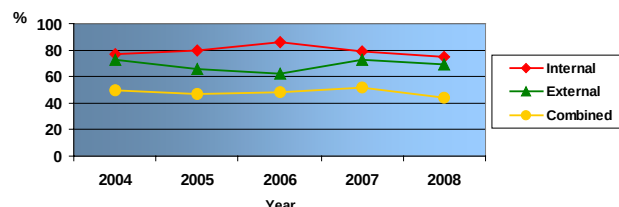


Fig. 5 – Incidence of sensitization to inhalatory allergens related to their origin

After examining exclusively the sensitization to pollens over the entire 5-year period, it was noticed that hypersensitivity to weed pollens is most common (54.1%), than to grass (52.8%) and tree (34.6%) pollens. The incidence of sensitization to pollens for each examined year is presented in Figure 6.

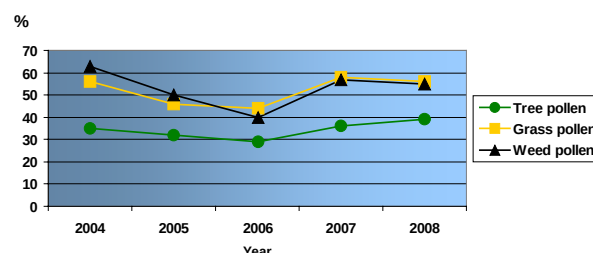


Fig. 6 – Incidence of sensitization related to the kind of pollen

Discussion

In the period from the beginning of 2004 to the end of 2008, there were 733 patients with the diagnosis of asthma registered in the Allergy Unit of the Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica. The smallest number of the patients were registered in 2006 (116), and the highest one in 2008 (183).

Asthma was significantly more often diagnosed in females (64.3%) than in males (35.7%), (female : male ratio = 1.8 : 1). This difference was statistically significant ($p < 0.05$), well correlating with the published articles, reporting the female : male ratio of asthmatic patients ranging from 1.04 to 1.9^{6,7}.

Most asthmatic patients belonged to the 20–29 year age group (39.6%), and then to the 30–39 year age group (20.5%). These results comply with the world trend. In this study, the fewest patients were older than 60 (4.5%), which is two times as few as reported in the literature^{1,8,9}.

It had long ago been clinically observed that asthma occurs more frequently in some families. In our examined group, genetic predisposition was registered in 34.9% of the subjects. Other authors report a higher percentage of atopy (44–53%) registered in the asthmatic families^{1,6}.

Smoking is considered a relevant risk factor for the occurrence and a bad course and prognosis of asthma. Asthmatics who are active or ex-smokers more frequently have acute asthmatic attacks, more often require hospitalisation, respond to therapy worse, and have a worse control of the disease. Of the subjects examined in this group, 73.9% were non-smokers, 12.2% ex-smokers, and 13.9% were active smokers. Some authors report a similar structure regarding smoking habits of their asthmatic patients^{1,4,7}.

Analysing the type of asthma depending on hypersensitivity to inhalatory allergens, confirmed by the cutaneous prick test, allergic asthma was found to be much more frequent (79.5%) than non-allergic asthma (20.5%). The literature data generally suggest that patients with allergic asthma make 70–90% of all asthmatic patients^{4,10}.

Allergy is a systemic disease of an organism, so allergic diseases are usually concomitant in one patient. At least one concomitant allergic disease was registered in 74.1% of the patients with allergic asthma. Food allergy was found in 3.1% of these patients, correlating to the literature data¹¹. Atopic dermatitis was registered in 7.0% of these subjects. Some authors report that even up to 38.3% of the patients with allergic asthma have atopic dermatitis in their case histories⁹. The most common concomitant allergic disease is allergic rhinitis, registered in 63.9% of our patients with allergic asthma. This finding correlates with the literature data^{2,3,7,10}. Symptoms of allergic rhinitis usually precede the onset of asthma (in 60% of the patients), ranging in precedence from 1 to 27 years. A simultaneous onset of both diseases (in the same year) was registered in 40% of the patients.

In this study, by estimating the correlation coefficient, a high correlation was established between rhinitis and asthma in allergic ($r = 0.92$) and non-allergic ($r = 0.88$) etiology of

the disease. The results obtained in our study correlate to the literature ones^{7,10}.

The concomitance of upper and lower airways diseases has been known more than two millenniums, and Galen emphasized that secretion removal from the nasal pathways alleviated respiratory symptoms. Numerous contemporary studies have shown a concomitant occurrence of allergic rhinitis and asthma in the same patient. It has been observed that allergic rhinitis usually precedes the occurrence of asthma, and is therefore included among the risk factors for the disease. In addition, the presence of allergic rhinitis, particularly when untreated, aggravates the symptoms of asthma and makes its control and treatment more difficult. The concomitance and mutual influence of the two diseases are due to the anatomical proximity and histological similarity of the upper and lower airways, as well as to the similar pathophysiology and risk factors for the occurrence of both allergic rhinitis and asthma. Inflammation plays a crucial role in the pathogenesis of both diseases. The mechanisms which further explain their correlation include: obstruction of the nose and breathing on the mouth, with the nose losing its important preparatory function; aspiration of the postnasal secretion with mediators and/or cells into the lungs; resorption of the inflammatory cells and/or mediators into the systemic circulation; nasobronchial reflex^{1,3,6,12}.

Exposure to inhalant allergens contributes to both exacerbation of the symptoms and the disease genesis itself, so the analysis of the frequency and the kind of sensitization to standard inhalatory allergens was particularly important. Hypersensitivity to at least one of standard inhalant allergens was registered in 79.5% of the patients. In most patients (77.5%), hypersensitivity to internal allergens was confirmed, while hypersensitivity to external allergens was established in 67.6% of the patients. Hypersensitivity to both allergen types was verified in 48.4% of the patients. Analysing hypersensitivity to single inhalant allergens, most patients were hypersensitive to mites (76.1%), correlating to the most internationally recognized results^{1,3,6,13}. In an international study, the European Community Respiratory Health Survey (ECRHS), it has been shown that rhinitis, with in fact an underlying hypersensitivity to only house dust mites, positively correlates to the occurrence of symptoms of asthma⁶. Hypersensitivity to weed pollens is most common (54.1%), then to grass pollen (52.8%), and tree pollen (34.6%). These results correlate to those obtained in the study which analyzed hypersensitivity to inhalant allergens in the population suffering from allergic respiratory diseases in the Novi Sad area, which may be due to the geographical features of Vojvodina⁵. In other countries, hypersensitivity to diverse pollens differs depending on the climatic and vegetation characteristics. Tree pollen allergy is most common in northern European countries, while hypersensitivity to grass pollens was most frequently verified in the majority of other European countries¹. Hypersensitivity to nicotine was much more rarely verified (13.4%), as well as to mold (12.9%), and feathers (10.1%). Hypersensitivity to animal hair was registered in 16.2% of the patients, with almost even frequency of hypersensitivity to dog (9.9%) and cat hair (9.6%). Some studies report cat hair as the most common allergen in adult

population, and in children with rhinitis and/or asthma, ranging from 15–50%^{3,14}. It may be due to the fact that cat is the most common pet in these environments.

The international ECRHS study has pointed out that geographical features of a particular environment determine the presence of different external factors which affect the prevalence of atopy and asthma. Taking into account the fact that allergy is the most common inducing agent of asthma, and that most asthmatics are hyperpersensitive to at least one allergen, as well as that a recurrent exposure to that allergen may “trigger” the symptoms of asthma, current guidelines for the treatment of asthma and allergic rhinitis recommend the avoidance of the allergen as a relevant preventive meas-

ure. Although most allergens are impossible to be entirely avoided, it is generally considered that their smaller concentration and exposure may have positive effects on the control and course of asthma^{3,4,15}.

Conclusion

The number of asthmatics has been constantly increasing in recent years, predominantly in female population at the third decade of life. A high proportion of asthmatics have a concomitant rhinitis, which precedes the onset of asthma with the precedence period ranging from 1 to 27 years and a verified allergy to inhalant allergens.

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