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Variability in the clinical profile of children with asthma referred to allergy clinic: a 10-year observation

Abstract

Background: Asthma is the most common chronic respiratory disease in the paediatric population. Underdiagnosis is a frequent phenomenon and is associated with undertreatment, which results in increased morbidity and mortality. The delay in the diagnosis of asthma reflects problems with the correct implementation of diagnostic goals set by the Global Initiative for Asthma (GINA). The aim of our study was to describe the clinical profile of children referred to the Clinic of Allergic Diseases and subsequently diagnosed with asthma. We evaluated the reasons for referral, demographic data and social data.

Material and methods: We analysed a group of 907 children up to 18 years of age diagnosed with asthma at allergy clinic between 2000 and 2009. This was a cross-sectional study to assess the patients' demographic, social and clinical data.

Results: Our study revealed a shift in the clinical profile of children referred to allergy clinics over a period of ten years, subsequently diagnosed with asthma. The profile is characterised by a younger age, a higher incidence of recurrent infections and a lower incidence of wheezing and atopy as the reasons for referral to allergologists.

Conclusions: The new clinical profile of children referred to allergologists reveals the necessity of conducting the costly differential diagnosis of asthma at specialist facilities. These data should be taken into account while developing new healthcare strategies in Poland.

Key words: asthma, children, clinical profile

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Introduction

Asthma is currently a disease which poses a public health risk worldwide [1]. According to the World Health Organization (WHO) estimates, 300 million people worldwide are currently affected by asthma and by 2050 the number of patients will increase to 100 million [2]. In Poland, about 4–5 million citizens have asthma [3]. Although it may develop at any age, asthma mainly affects children and is in fact the most common chronic childhood illness. The percentage of children suffering from asthma in Poland is as high as 8.6% [4].

In 2007 the European Union developed the Brussels Declaration: a plan to improve healthcare provided to patients with asthma in Europe. The Declaration is addressed to individuals responsible for health policies of member states and points to the fact that asthma is a serious public health problem. It recommends that each member state should recognise the fight against the increasing prevalence of asthma as being one of its priorities. The Declaration also encourages state governments to support development of research aimed at gaining a better understanding of the pathomechanism of asthma.

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The epidemiological, social, economic and diagnostic problems related to asthma have been addressed by the National Programme for Early Detection and Management of Asthma POLAST-MA developed by the Polish Allergy Society [5]. The aims of the Programme include improved detectability of asthma, early initiation of appropriate treatment, prevention of asthma complications, reduced healthcare costs and increased social awareness of asthma. The Programme also assumes education provided not only to the patients but also to persons caring for them, particularly primary care physicians.

Undiagnosed or poorly controlled and incorrectly managed asthma may have a severe course and may lead to frequent hospitalisations and even to disability or death. The considerable underdiagnosis rates are of concern in asthma [6–8]. According to both the ECAP (Epidemiology of Allergic Diseases in Poland) study and the previous analyses, asthma is detected too late in nearly 70% of the cases [9, 10]. A question therefore arises whether there exist some objective reasons that interfere with early detection of asthma, such as a changing profile of clinical symptoms in children presenting to their primary care physicians that makes it impossible to establish an unequivocal diagnosis of asthma and requires differential diagnosis.

The aim of our study was to describe the clinical profile of children referred to the Clinic of Allergic Diseases and subsequently diagnosed with asthma. We evaluated the reasons for referral, demographic data and social data.

Material and methods

Out of the 6400 children diagnosed with persistent asthma at the Clinic of Allergic Diseases of Nicolaus Copernicus Hospital in Lodz, Poland, between 2000 and 2009, we randomly selected 1000 patients. In accordance with the international guidelines, the diagnosis of asthma in all the cases was confirmed by the results of pulmonary function testing and/or by the response to antiasthmatic treatment. Data from the patients' medical records was compiled with the data obtained in a telephone interview conducted with the children's parents. Skin prick testing was performed with the use of the following standardised allergen extracts from Allergopharma: mixture of 5 grass species, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Alternaria*, *Cladosporium*, mugwort, paper birch, negative control solution (0.9% NaCl — glycerol) and a positive control solution (0.1% histamine at 10 mg/ml). Total

and allergen-specific IgE concentrations in the serum were determined by enzyme immunoassay (Dynex, DSX System) according to the manufacturer's instructions. The pulmonary function testing — resting spirometry (flow-volume curves) — was performed using MasterScreen (Jaeger, Germany).

The analysis included demographic data, information on housing conditions and social circumstances and data describing the clinical characteristics of the patients (Table 1). We assumed the following criteria: recurrent episodes of expiratory wheezing were defined as occurring more than four times a year and lasting for more than one day; chronic cough was defined as one persisting for more than four weeks; recurrent upper or lower respiratory infections were defined as ones occurring more than six times a year; adequate antiasthmatic treatment attempt was defined as treatment of at least three months' duration accompanied by an assessment of effectiveness and an assessment of the effects of treatment discontinuation; and poor housing conditions were defined as the presence of damp and/or lack of running water.

The study was approved by the Medical University of Lodz Ethics Committee.

Statistical analysis

The statistical analysis was performed using the chi-square test for categorical variables. Con-

Table 1. Variables in analysis

Variables analyzed

| |
|---|
| Demographic and anthropometric data |
| Age |
| Gender |
| Clinical data* |
| Recurrent wheezing |
| Chronic cough |
| Recurrent respiratory tract infections |
| Asthma symptoms at first visit |
| Atopy** |
| Initial anti-asthma therapy |
| Optimal anti-asthma therapy*** |
| House conditions |
| Exposure to environment tobacco smoke**** |
| Central heating |
| Living with single parent |
| Poor living conditions |

*Main complains during the first visit

**Positive skin prick test and/or the presence of one or more specific IgE

***Initial anti-asthma therapy \geq 3 months and evaluation of clinical improvement and/or lack of clinical improvement without anti-asthma therapy

****At least one smoker at home

tinuous variables were analysed by ANOVA for repeated measurements supplemented by an assessment of the linear trend.

Results

We analysed a group of 907 children between 5 and 18 years of age; 93 subjects were excluded from the analysis due to the lack of data that would enable us to describe their clinical characteristics. All the children have been treated in the Clinic of Allergic Diseases at Nicolaus Copernicus Hospital in Lodz, Poland. A total of 562 children (62%) had a family history of atopy, 707 children (78%) also had allergic rhinitis and 446 (49%) also had atopic dermatitis. In order to aggregate the findings we grouped the data from neighbouring years and assessed them over time. We found a significant difference in patient age between the subsequent years of follow-up. The ANOVA revealed a significant linear trend in patient age between the subsequent categories of the dependent variable, which confirms a significant gradual decrease in the age of patients presenting

to the clinic in subsequent years of follow-up (Table 2, Figure 1).

The relationships between the investigated nominal variables and the duration of follow-up are illustrated in Figure 1 and Table 2. We showed a significant and gradual increase in the percentage of children referred to the allergy clinic with recurrent upper and lower respiratory tract infections and a parallel decrease in the percentage of children referred with recurrent episodes of expiratory wheezing. We showed a nearly two-fold decrease in the prevalence of atopy in children referred to the allergy clinic in the subsequent years of follow-up and a significant increase in the percentage of children in whom antiasthmatic treatment was attempted prior to referral. The attempt was, however, adequate (i.e. treatment lasted at least three months and was accompanied by an assessment of effectiveness and an assessment of the effects of treatment discontinuation) only in a small percentage of children.

We observed a gradual improvement in parent-reported housing conditions of the patients and a significant increase in the percentage of ob-

Table 2. Demographic, medical, social and family data of patients with asthma diagnosed in outpatient allergy clinic in 2000–2009

| | Patients with newly-diagnosed asthma in allergy clinic (consecutive years of observation) | | | | | | | | | |
|---|--|------|----------------------|------|---------------------|------|----------------------|------|----------------------|------|
| | 2000–2001 n = 201 | | 2002–2003 n = 251 | | 2004–2005 n = 93 | | 2006–2007 n = 199 | | 2008–2009 n = 163 | |
| | n | % | n | % | n | % | n | % | n | % |
| Age mean ± SD | 13.5 ± 3.8 | | 12.1 ± 3.9 | | 11.6 ± 3.9 | | 9.3 ± 4.0 | | 7.3 ± 4.0 | |
| Male gender | 145 | 72.1 | 155 | 61.8 | 60 | 64.5 | 146 | 73.4 | 100 | 61.3 |
| Clinical data* | | | | | | | | | | |
| Recurrent wheezing | 191 | 95.0 | 221 | 88.0 | 78 | 83.9 | 165 | 82.9 | 125 | 76.7 |
| Chronic cough | 185 | 92.0 | 234 | 93.2 | 90 | 96.8 | 188 | 94.5 | 148 | 90.8 |
| Recurrent respiratory tract infections | 151 | 75.1 | 196 | 78.1 | 75 | 80.6 | 188 | 94.5 | 155 | 95.1 |
| Asthma symptoms at first visit | 71 | 35.3 | 91 | 36.3 | 33 | 35.5 | 77 | 38.7 | 57 | 35.0 |
| Atopy** | 197 | 98.0 | 240 | 95.6 | 77 | 82.8 | 156 | 78.4 | 116 | 71.2 |
| Initial anti-asthma therapy | 120 | 59.7 | 143 | 57.0 | 58 | 62.4 | 140 | 70.4 | 131 | 80.4 |
| Optimal anti-asthma therapy*** | 2 | 1.0 | 3 | 1.2 | 2 | 2.2 | 6 | 3.0 | 3 | 1.8 |
| House conditions | | | | | | | | | | |
| Exposure to environment tobacco smoke**** | 67 | 33.3 | 89 | 35.5 | 32 | 34.4 | 72 | 36.2 | 56 | 34.4 |
| Central heating | 165 | 82.1 | 196 | 78.1 | 77 | 82.8 | 171 | 85.9 | 155 | 95.1 |
| Living with single parent | 11 | 5.5 | 17 | 6.8 | 7 | 7.5 | 23 | 11.6 | 7 | 4.3 |
| Poor living conditions | 54 | 26.9 | 59 | 23.5 | 19 | 20.4 | 34 | 17.1 | 23 | 14.1 |

*Main complains during first visit

**Positive skin prick test and/or the presence of one or more specific IgE

***Initial anti-asthma therapy ≥ 3 months and evaluation of clinical improvement and/or lack of clinical improvement without anti-asthma therapy

****At least one smoker at home

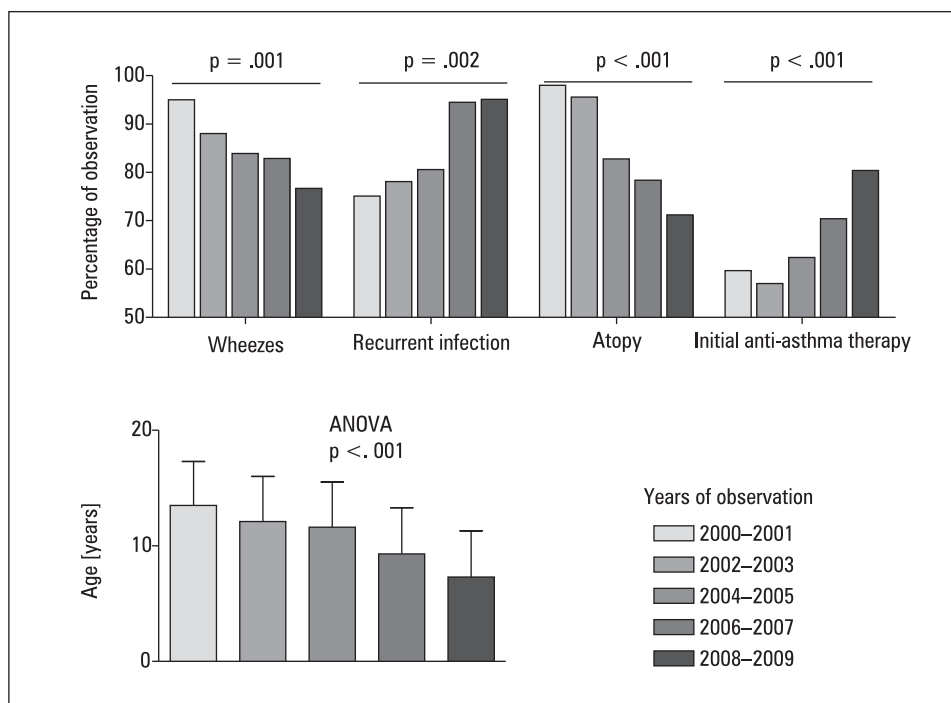


Figure 1. Medical characteristic of children consulted in outpatient allergy clinic between 2000–2009 with asthma diagnosis

servations within the variable “accommodation with central heating”. We did not, however, find any significant differences in the percentage of patients exposed to cigarette smoke in the subsequent years of follow-up.

Discussion

Our study showed a change in the clinical profile of children referred to the allergy clinic subsequently diagnosed with asthma over the period of ten years. We observed changes in patient age, in the clinical manifestations prompting the referral and in the atopy status. We found a gradual decrease in the age of patients being referred in the subsequent years of follow-up. Establishing the diagnosis of asthma in children below 5 years of age is a significant problem, as there are no uniform diagnostic criteria for this age group [11, 12]. Asthma in children is very often misdiagnosed as bronchitis, which leads to prescription of antibiotics and antitussives rather than antiasthmatics. Establishing the diagnosis of asthma in small children is particularly difficult and has serious clinical implications, as it means diagnosing a chronic inflammatory airway disease that requires specific management [1]. However, the decreasing age of patients referred for specialist treatment may suggest that primary care physicians are increasingly aware of early childhood asthma and of its manifestations and risk factors. Montnemery et al.

assessed the accuracy of a diagnosis of asthma by primary care physicians. They found that the accuracy of ruling out asthma was close to 100% but the percentage of accurate diagnoses of asthma was only 60% [13]. Most epidemiological studies have shown that underdiagnosis of asthma is an actual problem at the population level not only in Europe but worldwide [8, 14, 15]. In the Lodz district, 70% of children with manifestations of allergic diseases go undiagnosed and untreated [9].

We also observed an increase in the percentage of children referred with recurrent upper and lower respiratory infections and a decrease in the percentage of children referred with recurrent episodes of expiratory wheezing. In the first few years of follow-up patients with the classical manifestations of asthma prevailed, while in the subsequent period patients with recurrent respiratory infections predominated. This fact requires the specialists to carry out a thorough differential evaluation. The signs and symptoms of respiratory infections are often difficult to differentiate from the signs and symptoms of allergy (rhinitis or asthma) [16]. Respiratory infections, when recurrent and persistent, accompany allergic illnesses in about 60% of children. Allergists must consider the diagnosis of asthma in the children they see for consultation because, on the one hand, asthma may be induced by recurrent respiratory infections and, on the other, lower respiratory tract infections accompanied by airway obstruction in early chil-

hood have been linked to an increased risk of asthma at 6 years of age [17]. Children younger than 3 years of age are particularly prone to develop expiratory wheezing, which leads to overdiagnosis of asthma in this age group. A spontaneous resolution of this propensity by 5 years of age is observed in the majority of children. It should be borne in mind that only 30% of recurrent wheezing episodes are in fact asthma. The Multicentre Allergy Study (MAS) showed that 90% of non-atopic children with expiratory wheezing do not have any manifestations of asthma at school age and show normal pulmonary function during adolescence [18]. Therefore, the younger the child is, the more it is likely that wheezing is not caused by asthma. Our study suggests that the diagnostic evaluation of expiratory wheezing in children is carried out already at the level of the primary care physician.

Another finding in our study was the almost two-fold decrease in the prevalence of atopy in children referred for specialist treatment in the subsequent years of follow-up. This trend might be explained by the effects of early childhood viral infections and passive smoking on changes in the airways and lungs of small children leading to non-atopic asthma. The absence of atopy is the most frequent cause of delayed diagnosis of childhood asthma. More than 80% of the children suffer from IgE-mediated asthma with allergy to allergens commonly found in the environment (atopic asthma). The remaining children with asthma have negative skin prick tests using allergens commonly found in the environment and allergen-specific IgE antibodies cannot be detected in their serum (non-atopic asthma). Non-atopic asthma is more common in older children and is characterised by a more severe clinical course and a greater non-specific bronchial hyperreactivity. While population studies suggest a relationship between atopy and asthma, it is not a constant feature [19]. Results of many studies confirm that the absence of atopy is an important reason for underdiagnosis of asthma, and the results of our study indicate that primary care physicians are aware of that and refer non-atopic children to allergy clinics.

Our study also showed a significant increase in the percentage of children in whom antiasthmatic treatment had been attempted prior to referral. The attempt was, however, adequate (i.e. treatment lasted at least three months and was accompanied by an assessment of effectiveness and an assessment of the effects of treatment discontinuation) only in a small percentage of children. Physicians refer children who were only episodically treated with inhaled glucocorticosteroids, which will make

it impossible to assess the effectiveness of antiasthmatic treatment and therefore will not aid in the diagnosis. These results may indicate an ongoing phenomenon of “steroidophobia” among parents and physicians.

We observed a gradual improvement in parent-reported housing conditions, although we did not show any significant change in the percentage of children exposed to cigarette smoke in the subsequent years of follow-up, which is not a desired social phenomenon.

The constant increase in the incidence of asthma and the changes in patient profiles over the past decade with the resulting problems should come to the attention of persons responsible for the organisation and funding of healthcare. It seems that the above changes should be taken into account while planning the expenditure for healthcare and the fight against the ongoing problem of increasing prevalence of asthma among Polish children. Furthermore, given the need to improve the quality and accessibility of medical care, changes in the organisation of healthcare and the allocation of funds for the prevention and diagnosis of allergic diseases at specialised facilities are required. The results of the Programme for the Prevention of Allergic Diseases completed in the Lodz region between 2000 and 2003 [20–22] provided sufficient arguments to support the continuation and modification of future programmes for the prevention of allergy in Poland. The designed and implemented prevention programme launched on 1 January 2000 was the first project in Poland that comprehensively addressed the issue of prevention and care for patients with allergic diseases. The aims of the programme implemented in the Lodz region included: early detection of allergic diseases, improvement of treatment efficacy, prevention of acute exacerbations of asthma, increased accessibility to specialised facilities and health education of patients with allergic diseases and their families. Over the four years of the programme a total of 16,445 new diagnoses of allergic diseases in children were made, i.e. more than 26 new diagnoses per 1000 inhabitants of the province below 19 years of age. A total of 5002 new cases of asthma in children were diagnosed, which translates into more than 8 new cases of asthma per 1000 inhabitants of the province below 19 years of age. The systematic increase in the percentage of new cases in the subsequent years of the programme, particularly in children, proves the lack of satisfaction of the population needs in this respect and the need to continue similar preventive activities. The programme has also contributed to the reduced num-

ber and duration of hospitalisations for acute asthma exacerbations. Preventive activities and early pharmacological intervention currently seem to be the most effective form of combat against the asthma epidemic [23].

Conclusions

The results of our study point to some new issues in the diagnosis of asthma in children in the setting of allergy clinic. The increasing percentage of children with less asthma-specific manifestations, such as recurrent respiratory infections or chronic cough, requires — in line with the current guidelines — diagnostic evaluation for other chronic diseases [24, 25]. The change in the clinical profile of patients referred for specialist treatment revealed by our study suggests, on the one hand, need for high awareness and knowledge of the disease on the part of primary care physicians and, on the other, forces a thorough differential diagnosis of asthma-like symptoms at specialised facilities, which generates high cost, prolongs the diagnostic process and reduces the accessibility to specialist clinics [15].

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