

## The analysis of several patogenetic and clinical paramethers among patients hospitalized due to asthma

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### ABSTRACT

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**Introduction:** Chronic diseases of the respiratory system are serious problem of modern medicine. Constant increase of occurrence of such diseases in the last few decades is particularly disturbing as it has a direct correlation to the rapid increase of costs intended for health care. Asthma is one of the most common chronic diseases of the respiratory system.

**Purpose:** The aim of this thesis was to evaluate chosen pathogenetic and clinical parameters among patients hospitalized because of asthma in the Department of Allergology and Internal Medicine between 2007 and 2009.

**Materials and methods:** The data included in the medical documentation of 544 patients hospitalized because of asthma, was undergone a statistical analysis.

**Results:** The analysis of the medical documentation shows that the presence of such symptoms as whizzing, dyspnea, intensifying of symptoms after exertion or contact with allergens and infections

can indicate asthma. Appearance of whizzing, exertion of symptoms after contact with allergens as well as the presence of allergies and asthma in the family are crucial in diagnosing asthma. Additionally, the presence of a cough, shortness of breath and the connection of the symptoms with exertion and infections were characteristic of high sensitivity and moderate chance of a positive prognosis. The measurements of the concentration of nitric oxide in the exhaled air was more specific and sensitive in recognizing asthma in comparison to spirometric tests, eosinophilia and the total concentration of IgE.

**Conclusion:** The results of the research conducted indicate a great demand for specialist care for asthmatic patients which include both diagnostic procedures and intensification of treatment during exacerbations.

**Key words:** asthma, epidemiology, diagnostic procedures

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## **INTRODUCTION**

Chronic diseases of the respiratory system are a serious problem of modern medicine. Constant increase of such diseases in the last few decades is particularly disturbing as it has a direct correlation to the rapid increase of costs intended for health care. Asthma is one of the most common chronic diseases of the respiratory system [1, 2].

An extremely worrying phenomenon is under-diagnosis of allergic diseases. According to an epidemiological study conducted in 1999-2000 and published in 2002, only 29% of children and 52% of adults with epidemiological diagnosis of asthma were diagnosed with the disease earlier [3].

The analysis of PMSEAD data (Polish Multicenter Study of Epidemiology of Allergic Diseases) from the area of Lodz region, showed a high rate of under - diagnosed cases of bronchial asthma reaching 50% in adults and up to 70% in children [4]

The analysis of data from the study conducted in the years 2006 - 2008 - ECAP, leads to similar conclusions. According to the ECAP research, every tenth polish citizen suffers from asthma, and nearly 70% of them have wrong diagnosis [5, 6]. The result is lack or inadequate treatment. In addition, asthma causes numerous hospitalizations, and they end with absence at work and school.

The increase in the incidence of asthma has changed its meaning in the social hierarchy of health care needs. Asthma is now perceived as a serious health, social and economic problem of the twenty-first century and the rapid increase in the incidence and prevalence, grow to epidemic proportions.

Environmental factors are considered the most important causes of the occurrence and the development of asthma among predisposed individuals. They may also contribute to strengthening or exacerbating the disease. The environmental factors that influence the development of asthma in predisposed individuals include: exposure to allergens and sensitizing occupational factors, viral and bacterial infections, diet, cigarette smoke, air pollution, socioeconomic status and family size [7].

Environmental factors affect not only the development of asthma among predisposed individuals, but also the severity of symptoms. Due to the variable course of the disease, it requires constant monitoring, education, adjusting of the medications and their dosages and routes of administration to the patient's individual needs [8].

The aim of this study was to evaluate selected pathogenic and clinical parameters in patients hospitalized for asthma in the Department of Allergology and Internal Diseases in 2007-2009.

## **MATERIALS AND METHODS**

The object of the analysis were data included in the questionnaires of 544 patients hospitalized in the Department of Allergology and Internal Medicine 2007-2009. The main components of the questionnaire included personal and demographic data, history, medical history, physical examination deviations, laboratory results, concomitant diseases, medications, current treatment of respiratory diseases, family history of allergic diseases, exercise tests performed during hospitalization and the classification of asthma on the basis of the documentation. The testing was approved by the Bioethics Committee of the Medical University of Bialystok (number of consent RI-002/98/2010).

### **Statistical analysis.**

Value distribution of particular quantitative variables in the study group of patients and in particular subgroups, is described by using mean, standard deviation, extreme values and median. Because of the lack of standard distribution of examined parameters, nonparametric methods were used in statistical inference. The assessment of the differences in distributions of variable values between the two groups of patients was performed using Mann-Whitney test, while in the case of larger number of subgroups we used Kruskal-Wallis test.

In order to determine the diagnostic usefulness of the quantitative parameters, such as IgE, FEV1, eosinophilia, FENO, a ROC curves were used, while for qualitative dichotomous variables (such as the clinical symptoms), the diagnostic value was described by sensitivity and specificity.

The relationship between qualitative variables were evaluated using Fisher's exact test or  $\chi^2$  test of independence (for the number of variants greater than 2).

All hypotheses were verified at the significance level  $\alpha = 0.05$ .

## **RESULTS**

The study involved the medical records of 544 patients, including 388 women and 156 men. Age of the patients ranged from 18 to 88 years. Mean age was  $45.63 \pm 16.66$  years. Among the 544 patients, 255 patients (47.3%), including 191 (49.6%) women and 64 (47.3%) men were hospitalized for diagnosis of reported symptoms of respiratory disease. Hospitalized with an exacerbation were 240 (44.5%) patients, including 164 (42.6%) women and 76 (49.4%) men. In order to verify the diagnosis, 36 patients (6.7%) of which 22 (5.7%) were women and 14 men (9.1%) were hospitalized.

Among diagnosed patients asthma diagnosis was confirmed in 151 (58%) patients, 114 (59.3%) women and 37 (54.8%) men. It is worth noticing that in 104 (41%) patients reporting symptoms of respiratory disease, after conducting

medical tests asthma was excluded. Among people diagnosed with asthma 177 (41.3%) were diagnosed with allergic disease and in 252 (58.7%) non-allergic. The results are shown in Table 1.

**Table 1.** Characteristics of patients surveyed divided into men and women.

parameters:	n - the number of patients % - The percentage of patients in the study group	Woman	Man	Total	p-value
<b>Purpose of hospitalization:</b>					
diagnostics	N %	191 49.3%	64 41.1%	255 46.9%	p= 0.173
exacerbation	N %	164 42.3%	76 48.7%	240 44.1%	
verification of diagnosis	N %	22 5.6%	14 9.0%	36 6.6%	
Other	N %	11 2.8%	2 1.2%	13 2.4%	
<b>Diagnostics</b>					
confirmed	N %	114 59.3%	37 54.8%	151 58.4%	p= 0.236
unconfirmed	N %	77 40.7%	27 45.2%	104 41.6%	
<b>Asthma</b>					
allergic	N %	121 39.2%	56 46.7%	177 41.3%	p= 0.096
Non - allergic	N %	188 60.8%	64 53.3%	252 58.7%	p= 0.158
<b>Primary diagnosis</b>					
Asthma	N %	241 62.1%	88 56.4%	329 60.5%	p= 0.016
COPD	N %	15 3.0%	17 10.9%	32 5.9%	
frequent infections	N %	59 15.2%	25 16.0%	84 15.4%	
Chronic bronchitis	N %	73 18.8%	26 16.7%	99 18.2%	
<b>Skin prick tests</b>					
Positive result	N %	123 45.9%	62 60.8%	185 50.0%	p=0.007
Negative result	N %	145 54.1%	40 39.2%	185 50.0%	

Table 2 shows the analysis of the selected parameters in patients with diagnosed or excluded asthma. There were no significant differences in the prevalence of asthma in the family among patients with confirmed and excluded asthma (p = 0.402). Family history of allergy was confirmed in 24.5% of patients with confirmed asthma and 11.8% with excluded asthma. The difference was statistically

significant (p=0.013). Shortness of breath and wheezing in the chest were more frequent in patients with confirmed asthma compared with patients among whom asthma was excluded as a result of a medical examination. The differences were statistically significant. Symptoms after exercise were significantly more frequent among patients with a confirmed diagnosis of asthma (p = 0.045).

**Table 2.** Characteristics of patients diagnosed because of symptoms suggesting the diagnosis of asthma, divided into diagnosed and excluded asthma.

parameters	n - the number of patients,% of patients in the group	Confirmed asthma	Excluded asthma	Total	p-value
<b>Family asthma</b>					
	N %	47 33.8%	29 28.4%	76 31.5%	p=0.402
<b>Family allergy</b>					
	N %	34 24.5%	12 11.8%	46 19,1%	p=0.013
<b>The symptoms of asthma</b>					
cough	N %	126 90.0%	100 98.0%	226 93.8%	p=0.028
dyspnea	N %	121 87.1%	70 68.6%	191 79.3%	p=0.001
wheezing	N %	54 35.8%	7 6.9%	61 23.9%	p=0.001
<b>The circumstances of the aggravating symptoms</b>					
During exercise	N %	105 75.5%	66 64.7%	171 71.0%	p=0.045
During contact with allergens	N %	82 59.0%	25 24.5%	107 44.4%	p=0.000
At work	N %	15 10.8%	14 13.7%	29 12.0%	p=0.550
After infection	N %	127 91.4%	82 80.4%	209 86.7%	p=0.020
<b>Smoking cigarettes</b>					
active	N %	40 28.8%	26 25.5%	66 27.4%	p=0.661
current	N %	21 15.1%	13 12.7%	34 14.1%	p=0.709
passive	N %	17 12.2%	16 15.7%	33 13.7	p=0.454
<b>Laryngological interview</b>					
• Chronic rhinitis	N %	90 64%	42 41.2%	132 54.8%	p=0.000
• Perennial rhinitis	N %	59 65.6%	26 61.9%	85 64.4%	p=0.700
• Seasonal rhinitis	N %	31 34.4%	16 38.1%	47 35.6%	p=0.700
• Chronic sinusitis	n %	22 15.8%	14 13.7%	36 14.9%	p=0.717
<b>GERD</b>					
	N %	22 15.8%	48 47.1%	70 29.0%	p=0.000

After contact with allergens it was (p = 0.000) and after infection (p = 0.020).

There were no significant differences concerning active, current or passive smoking in patients with confirmed and excluded asthma. Chronic rhinitis was present in 64% of patients with confirmed asthma and in 41.2% of patients with excluded asthma. This difference was statistically significant (p = 0.000). Among patients with

diagnosed asthma, 64% were cases of allergic asthma. Gastroesophageal reflux disease (GERD) occurred significantly more often (47.1%) among patients with excluded asthma compared with patients with confirmed asthma (15.8%) (p = 0.000). (Tab.2).

Analysis of medical records indicated that among patients with excluded diagnosis of asthma, the main causes of coughing and other symptoms of

respiratory disease were GERD (48 patients, 47.1%), and chronic rhinitis (42 patients, 41.2%). Coexistence of these two causes was observed in 21% of patients in the study group. A significantly higher eosinophilia in peripheral blood ( $p=0.015$ ),

IgE in total serum ( $p = 0.000$ ) and the concentration of the nitric oxide in exhaled air ( $p = 0.000$ ) were observed among patients with a confirmed diagnosis of asthma. The results are shown in Table 3.

**Table 3.** Characteristics of selected diagnostic parameters in patients with diagnosed and excluded asthma.

Parameters varied in quantity expressed as mean and standard deviation	Confirmed asthma	Excluded asthma	total	p-value
Eosinophils in the chamber 3 mm	163.78±159.32	144.12±217.9	155.05±187	p=0.015
IgE total KU/l	275.75±435.64	101.91±149.3	212.81±368	p=0.000
How many years are symptoms	2.31±3.18	2.20±2.89	2.26±3.053	p=0.963
FENO <sub>ppB</sub>	67.49±82.92	20.01±27.78	47.89±69.8	p=0.000

The next stage of the study analyzes the diagnostic value of the basic parameters collected during interviewing patients as well as from basic laboratory and functional parameters used in the diagnosis of patients with asthma and allergic diseases. The greatest specificity in the diagnosis of asthma was characterized by the occurrence of

wheezing, worsening of symptoms when exposed to allergens and after taking medication (especially NSAIDs). Cough, shortness of breath, and exacerbation of symptoms after exercise and infections was characterized by high sensitivity and low specificity. The results are shown in Table 4.

**Table 4.** Diagnostic indicators of particular symptoms possible to obtain from the interview in the diagnosis of asthma.

Diagnostic parameters	sensitivity	Specificity
wheezing	22.4%	92.7%
cough	91.4%	1.8%
dyspnea	85.5%	30.3%
Aggravation of symptoms during exercise	76.3%	33.9%
Family asthma	32.2%	73.4%
Family allergy	25.7%	89.0%
Aggravation of symptoms after taking medications	7.2%	92.7%
Aggravation of symptoms during contact with allergens	57.2%	75.2%
Aggravation of symptoms after infections	89.5%	20.2%

Table 5 shows the diagnostic value of selected studies used in the diagnosis of asthma. Measurements of nitric oxide in exhaled air were characterized by the highest specificity and

sensitivity in the diagnosis of asthma. The increase of the cut-off point was associated with the improvement of specificity with a significant reduction of sensitivity (Table 5).

Table 6 and Figure 1 show the results of evaluation of the diagnostic value of selected studies in the diagnosis of asthma by means of ROC curves. The highest AUC values had measurements of nitric oxide in exhaled air, which

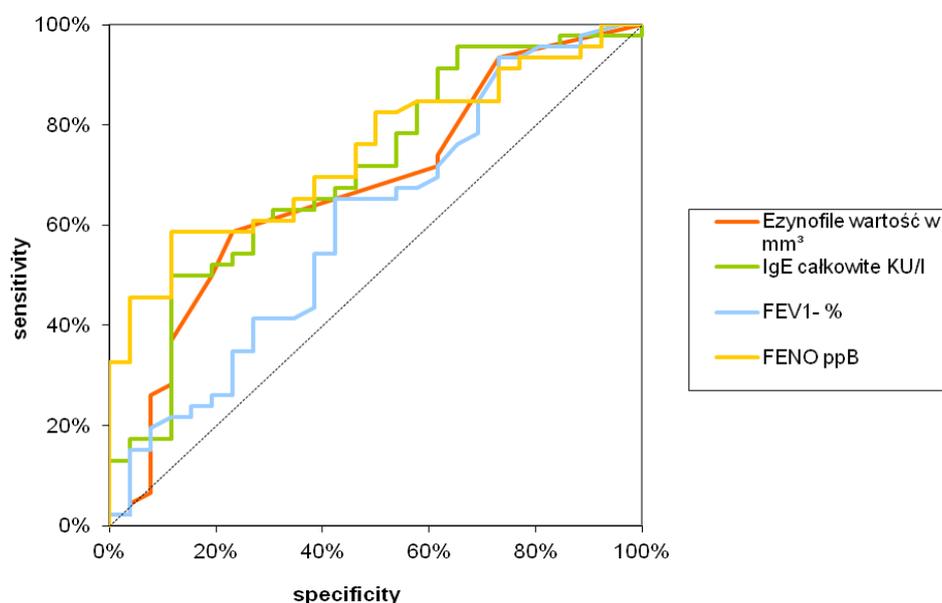
indicates that the test has a higher diagnostic utility compared to spirometry assessment (especially in patients with normal values of FEV<sub>1</sub>), examination of total IgE and evaluation eosinophilia in peripheral blood. (Table 6, Figure 1).

**Table 5.** The diagnostic value of the results of selected tests for the diagnosis of asthma.

Parameter	cut-off point	sensitivity	Specificity
<b>Eosinophils value in mm<sup>3</sup></b>	<b>&gt;100</b>	<b>64.71%</b>	<b>62.12%</b>
	>200	24.71%	83.33%
	>400	7.06%	92.42%
<b>IgE total KU/l</b>	<b>&gt;100</b>	<b>63.29%</b>	<b>68.18%</b>
	>200	39.23%	86.36%
	>400	18.99%	93.18%
<b>FEV<sub>1</sub>- % of predicted value</b>	<b>&lt;100</b>	<b>66.00%</b>	<b>49.54%</b>
	<80	18.00%	91.74%
	<60	4.00%	97.25%
<b>FE<sub>NO</sub> ppB</b>	<b>&gt;25</b>	<b>68.20%</b>	<b>86.76%</b>
	>35	47.90%	94.12%
	>50	38.78%	97.06%

**Table 6.** Evaluation of diagnostic value of particular parameters using ROC curves.

variable	AUC	p (AUC=0.5)
Eosinophils value in mm <sup>3</sup>	0.6756	<b>0.0080</b>
IgE total KU/l	0.7082	<b>0.0012</b>
FEV <sub>1</sub> - %	0.6045	<b>0.1440</b>
FE <sub>NO</sub> ppB	0.7437	<b>0.0000</b>



**Figure 1.** ROC curves for particular diagnostic parameters.

## DISCUSSION

Asthma is a common and chronic disease, chronic nature and severity of its symptoms affect family life, social and professional activities. Today, in many countries, it is perceived as a serious health, social and economic problem concerning a large part of the population and significantly impairing patients' quality of life [9, 10].

The basic symptoms of asthma include coughing, shortness of breath and wheezing in the chest. Symptoms usually occur at night and in the morning. Asthma can be characterized by various symptoms and bronchial hyperactivity, reflected by a readiness to bronchial muscle contraction, and as its consequence, obturation in exposure to specific factors (allergens) or by exposure to non-specific factors (cold humid air, exercise, intensive smells, fumes, strong emotions, laughter) [11, 12].

It should be noted that these symptoms may occur with other respiratory diseases. The analysis of the documentation of the studied population showed that most of the hospitalized patients reported cough and shortness of breath. Wheezing was observed in only half of the patients. A very characteristic symptom in more than 80% of patients is exacerbation of symptoms during or after exercise. In comparison, the presence of symptoms when exposed to allergens was observed in every third patient with asthma. At work it concerned every fifth man and every tenth woman (a statistically significant difference may be due to more frequent for men work-related physical activity). The intensification of symptoms after

NSAID stated 8% of women and 4.5% of men, it is consistent with the data in the literature [12].

240 patients were hospitalized because of asthma exacerbations. Despite finding the pathogenic base of the disease and the introduction of many modern drugs, there is still a group of patients with exacerbations for whom there is a need for intensification of the treatment and often hospitalization. Approximately 60% of the costs were generated by treatment of severe asthma, out of which 60% were indirect costs of the disease [13, 14]. The high economic burden concerns patients with poorly controlled asthma (more than one hospitalization during the 12 months of observation).

255 patients were hospitalized for diagnostic purposes. Basing on the conducted research, asthma was confirmed in 151 patients, and excluded in 104. This demonstrates the high demand for detailed diagnosis of patients with suspected asthma. It is worth noting that a detailed diagnosis prevents false diagnoses of asthma given only on the basis of data from the interview. It also prevents unnecessary treatment of patients and unnecessary expenditure associated with the purchase of drugs, both on behalf of the patients' and the state's budget.

Comparing selected parameters in a group of patients with confirmed and excluded asthma has brought interesting results. There was an increased incidence of asthma cases among the excluded patients in the older age groups. Asthma was confirmed statistically more often in patients born

and living in the city compared with those born and living in the village. Family history of allergy was observed more frequently among patients with a confirmed diagnosis of the disease.

The basic symptoms of asthma include coughing, shortness of breath and wheezing. Cough was reported by almost all patients with both confirmed and excluded asthma.

However, the presence of dyspnea and wheezing in the chest were reported by a larger group of patients with a confirmed asthma. Wheezing is the most common symptom of asthma and evidence of airway obstruction. In asthma they are paroxysmal and often occur with shortness of breath when exposed to provocative factors [15].

Cough that occurs among patients with asthma is a paroxysmal, dry, exhausting unrelated to colds frequently occurring at night and after exercise. The most common causes of chronic cough, besides asthma, include gastro-oesophageal reflux and cough syndrome associated with upper respiratory tract (chronic sinusitis and rhinitis) [8, 16].

Cough associated with other causes may be wrongly considered as a symptom of asthma, and patients unnecessarily treated with anti-asthmatic drugs. Therefore, it is important to get a specialized diagnosis of patients with chronic cough [12, 15].

Patients with the positive result of the diagnostic procedure more frequently reported a significant worsening of ailments of the respiratory system after exercise, contact with allergens and infections. These patients also more often reported symptoms of chronic rhinitis [8].

The analysis of the diagnostic value of the basic parameters available in the interview, revealed that the greatest specificity in the diagnosis of asthma was observed in the occurrence of wheezing, worsening of symptoms when exposed to allergens, and after taking drugs (mainly NSAIDs).

Occurrence of cough, shortness of breath, worsening of symptoms after exercise and infection, were characterized by high sensitivity along with low specificity. Among patients with excluded diagnosis of asthma the main causes of coughing and other symptoms of the respiratory system were gastro-oesophageal reflux and chronic rhinitis.

The basic additional examinations in the diagnosis of allergic diseases and asthma are: skin tests, evaluation of IgE, levels of nitric oxide in exhaled air and evaluation of eosinophilia. Each patient diagnosed because of symptoms which suggest asthma should have a skin test done to evaluate sensitization to inhalant allergens, and in

selected cases, an assessment of the level of immunoglobulin E should be performed.

The diagnosis of allergy to specific allergens simplifies treatment and the control of asthma. The other test used in the diagnosis of asthma is measuring the level of nitric oxide in exhaled air. F<sub>ENO</sub> measurements are a new non-invasive method of assessing the eosinophilic inflammation in the airways.

Direct measurement of inflammation in the bronchial tree complements the conventional tests used in the diagnosis and assessment of level of asthma control. The correlation between the value of F<sub>ENO</sub> and airway eosinophilia may be helpful in assessing the phenotype of asthma and in monitoring its treatment [17, 18].

In the group of patients with confirmed diagnosis of asthma, positive skin tests were observed much more frequently. These patients had significantly higher levels of nitric oxide in exhaled air, total IgE and increased level of eosinophilia in peripheral blood. Measurement of nitric oxide in the exhaled air was characterized by a higher specificity and sensitivity in the diagnosis of asthma compared with spirometric assessment (especially in patients without evidence of bronchial obstruction), eosinophilia in peripheral blood and concentration of total IgE.

## CONCLUSIONS

The analysis of the medical documentation indicates that the onset of symptoms of the patient's respiratory system, particularly shortness of breath and wheezing, worsening of symptoms after exercise, after contact with allergens and infections, may indicate a diagnosis of asthma. The likelihood increases in patients with atopy, positive skin tests, and chronic diseases of the upper respiratory tract. Occurrence of chronic rhinitis increases the likelihood of allergic asthma.

Results of this study indicate a great need for specialized care for patients with asthma. It concerns both diagnostic procedures as well as the intensification of treatment during exacerbations.

### Conflicts of interest

The authors declare that they have no competing interests in the publication of the manuscript.

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