

UDC: 616.248-036.001.33

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# Bronchial Asthma Phenotype with Obesity

**Key words:** *bronchial asthma, phenotype, obesity.*

Bronchial asthma (BA) comprises one of the most common diseases (5–25 % of general population) and has distinct tendency to increase [3, 13, 16]. According to calculations the frequency of the BA in Ukraine shall constitute 5–7 % [1, 2]. As of today approximately more than 300 million people suffer from the BA. However, as regards majority of the patients the BA is badly preventable or even unpreventable, that requires finding out new treatment approaches. Heterogeneity of the BA basing on the mechanisms, presentations and progress is considered one of reasons of bad preventability [8, 15]. Lastly, the attention was drawn to the tries to phenotype and genotype the BA, i.e. define main variants basing on the clinical characteristics and genetic markers for understanding of pathophysiological basis of the disease and optimization of remedial measures [8, 10, 12, 18]. Phenotyping of asthma is performed basing on the clinical characteristics (age, sex, duration, comorbid states), pathobiological inflammation appearances in sputum or bronchoscopic material [9, 15] and response to treatment. Phenotyping becomes particularly important to define the tactic of the treatment, namely while prescribing the systemic corticosteroids [10]. Obesity comprises one of the features under which the asthma is phenotyped and currently obesity turns to be the background of all diseases.

The **objective** of this paper is to analyse modern data regarding BA phenotyping considering obesity as well as findings obtained as a result of own observations.

According to the existing literature data up to now the attempts to combine all main criteria of phenotyping (clinical: age when the disease started, sex, presence or absence of the obesity; pathophysiological: eosinophilic, neutrophilic, pauci-immune inflammation; kind of response to treatment: good response or refractivity to treatment) were not successful. The described inflammatory characteristics and peculiarities of the respiratory function that asthma with obesity comprises separate phenotype of bad preventability [14]. Patients with obesity suffer from non-eosinophilic asthma in the light-medium or severe form (mostly women) [5, 11].

W. C. Moore, D. A. Meyers, S. E. Wenzel et al. (2010) provided more detailed characteristics. They performed cluster analysis of the results of diagnostics and treatment of 726 adult patients suffering from BA and formed 5 groups united on the basis of common clinical and functional features, character of treatment and response to it [6, 15]. According to their findings cluster consisting of 59 people (8 %) united mostly older women aged 34–68 years (average age 50 years) with obesity appeared to be unique. Their asthma was featured with non-atopic character, late appearance and moderate reduction of the peak volumetric rate and frequent use of the gluco-corticosteroids for exacerbations treatment. 17 % of such patients got systemic steroids. Notwithstanding the above, only 64 % of them after treatment managed to reach the norm of peak expiratory flow rate by means of three or more medicines including one inhalant gluco-corticosteroid

in high doses. It is important that the obesity degree of patients of this cluster is associated with the symptoms load. The history of such patients often revealed gastroesophageal reflux disease [4].

Asthma phenotyping is significantly important to define the tactic of treatment. While the patients with eosinophilic inflammation shall be prescribed with inhalant corticosteroids and prolonged  $\beta_2$ -agonists [5], the patients with non-eosinophilic neutrophilic inflammation would not respond to the therapy with inhalant and peroral corticosteroids and thus their first option shall be macrolide antibiotics [17]. Still most patients with the phenotyped of bad cases of asthma are resistant to standard therapy [7].

### Materials and methods

According to the Order of the Ministry of Health of Ukraine No 128 from 03.19. 2007, we performed complex clinical and laboratory examination of 90 patients with bronchial asthma, who were treated in the Department of Allergology in the Lviv 1<sup>st</sup> City Hospital. Lung function tests were made using computed spiograph «Pneumscreen» parameters were compared with predicted values for the same age, sex, and body mass. Body mass index (BMI) was calculated as body mass in kilograms divided into height in square meters. Statistical analysis was made using program Statistica for Windows, v. 6, with nonparametric methods, the results were given as median and [lower quartile; upper quartile].

### The results and discussion

The patients were divided into 3 groups basing on the criterion of body mass index (BMI): the first group consisted of 33 patients with normal body mass (BMI 18–24,9 kg/m<sup>2</sup>), the second one consisted of 29 patients with excessive body mass (BMI 25–29,9 kg/m<sup>2</sup>) and the third one consisted of 28 patients with obesity (BMI  $\geq$  30 kg/m<sup>2</sup>). The age of the groups did not sufficiently differ; age medians were 41,5 [25; 54], 42 [32; 53], 51 [45; 52] years respectfully. However, the difference in gender composition of groups was significant, since the number of women in the group with obesity was larger (64,3  $\pm$  9,0) % against (36,4  $\pm$  9,0) % and (41,4  $\pm$  9,1) % in group 1 and 2,  $p_{3-1} < 0,05$ ,  $p_{3-2} > 0,05$ .

While analysing the anamnesis data there was revealed that the disease of 93 % of women with obesity appeared in the mature age, while only 60 % ( $p = 0,05$ ) of men faced first symptoms in adulthood. Women with obesity more often suffer from pulmonary insufficiency of third degree (67 %,  $p = 0,05$ ) and pulmonary emphysema (56 %,  $p = 0,047$ ). Men with obesity suffered from the concomitant type 2 diabetes almost three times more often than women (60 % against 22 %,  $p = 0,048$ ).

Asthma with obesity is featured with inflammation of non-eosinophilic character that is confirmed by the fact that such patients significantly rarely suffered from allergic rhinitis (17,9  $\pm$  7,2%) than the patients with the excessive mass (46,4  $\pm$  9,3) %,  $p = 0,02$ ) and normal mass (36,4  $\pm$  8,4) %,  $p > 0,05$ ; and there was detected sufficiently lower level of eosinophils in peripheral blood (2 [2; 4] % against 4 [2; 5] %,  $p = 0,009$ , while it was in case of excessive and normal mass). At the same time the patients with obesity had significantly

higher ESR index (7,5 [6;12] mm/h, against 6 [4; 6] mm/h and 7 [6; 12] mm/h,  $p_{1-2} = 0,05$ ,  $p_{1-3} = 0,049$ ), that confirms that they had inflammation syndrome. Although the difference between the quantity of leukocytes and stab neutrophils was not significant, in case of obesity these indexes reached the maximum.

The BA of the patients with obesity significantly more often was complicated by lung tissue pneumosclerosis (21,3  $\pm$  7,7) % against (3,5  $\pm$  3,4) % in group 2,  $p = 0,04$ ); they were suffering from the comorbid states – hypertensive heart disease (42,9  $\pm$  9,4) % against (12,1  $\pm$  5,7) % in case of patients with normal mass,  $p < 0,05$  and (10,3  $\pm$  5,6) %,  $p < 0,05$  in case of patients with excessive mass) and type 2 diabetes (42,9  $\pm$  9,4) % against (17,1  $\pm$  7,1) %,  $p < 0,05$  in case of patients with excessive mass and (21,2  $\pm$  7,1) %  $p > 0,05$  in case of patients with normal mass). The subgroup consisting of the patients with obesity had sufficiently higher indexes of blood glucose (5,6 [4,7; 6,1] mmol/l against 4,6 [4,4; 5,2] mmol/l and 4,9 [4,5; 5,2] mmol/l,  $p_{1-3} = 0,01$ ,  $p_{2-3} = 0,02$ ).

Some indexes of the respiratory functions (RF) sufficiently differ: inspiratory vital capacity (IVC) was significantly lower in case of the patients with excessive mass (58,2 [42,3; 73,8] %,  $p = 0,009$ ) and in case of the patients with obesity (60,8 [38,4; 66,5] %,  $p = 0,02$ ) in comparison to patients with normal body mass (74,3 [61,5; 82,1] %), that confirmed more expressed restrictive disorders. The patients with obesity had the lowest wheezing indexes such as FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, FEF<sub>25-75</sub>, MEF<sub>25</sub>, MEF<sub>50</sub> and MEF<sub>75</sub>, however, these indexes did not reach the significance level.

Analysis of the RF indexes considering gender criterion demonstrated that in case of obesity women had significantly lower MEF<sub>75</sub>, index that confirms the obstructive changes in bronchial tubes (34,9 [24,4; 35,8] % against 45,9 [39,3; 53,7] % and 55,9 [24,5; 61,0] % in case of patients with normal and excessive body mass,  $p_{1-3} = 0,049$ ;  $p_{2-3} = 0,04$ ). At the same time men with excessive body mass and obesity were diagnosed significant changes of both volume and rate indexes. In case of obesity and excessive mass the indexes were sufficiently lower, as follows: forced VC (43,8 [37,9; 62,6] % and 47,7 [43,8; 68,7] % against 65,9 [59,4; 76,9] %,  $p_{1-2} = 0,04$ ,  $p_{1-3} = 0,009$ ), IVC (38,4 [34,1; 62,6] % and 43,0 [40,4; 58,0] % against 78,2 [66,5; 84,1] %,  $p_{1-2} = 0,0005$ ,  $p_{1-3} = 0,002$ ), Forced Expiratory Volume in 1 Second (FEV<sub>1</sub>) (28,8 [28,7; 51,4] % and 33,5 [31,0; 49,6] % against 55 [46,6; 59,4] %,  $p_{1-2} = 0,03$ ,  $p_{1-3} = 0,002$ ), peak volumetric rate (22,6 [17,6; 28,0] % and 25,5 [22,6; 27,6] % against 45,8 [32,9; 66,1] %,  $p_{1-2} = 0,008$ ,  $p_{1-3} = 0,007$ ).

Thus, basing on the existing data only part of the patients suffering from the BA may be phenotyped. The division of the BA to clusters makes possible to individualize the diagnostic and treatment approaches. It is reasonable to allocate within the clinical characteristics the cluster of bronchial asthma with obesity, that is featured with non-eosinophilic inflammation, is more often faced by women (64,3 %), and is accompanied with pneumosclerosis (21,3 %), arterial hypertension (42,9 %) and diabetes (42,9 %), worse RF indexes and its prevention requires three or more medicines including one inhalant corticosteroids.

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## ФЕНОТИП БРОНХІАЛЬНОЇ АСТМИ С ОЖИРЕННЯМ

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**Резюме.** Проблема фенотипування бронхіальної астми (БА) є важливою для практичної медицини та науки. Предложено виділяти окремий фенотип астми з ожиренням. З метою визначення особливостей БА з ожиренням проведено аналіз результатів

обстеження 90 хворих. Пацієнти були розділені на 3 групи: в першу вошли 33 пацієнта з нормальною масою тіла, во вторую — 29 хворих з избыточною масою і в третью — 28 хворих з ожиренням. У хворих з ожиренням БА достовірно частіше ускладнювалась пневмосклерозом і діагностувалися коморбідні стани — гіпертонічна хвороба і цукровий діабет 2-го типу. Достовірно рідше в групі з ожиренням виявляли алергічний риніт і еозинофілію. При аналізі показателів функції зовнішнього дихання встановлено, що у хворих з ожиренням і избыточною масою тіла спостерігалися більш виражені рестриктивні порушення функції зовнішнього дихання, ніж у пацієнтів з нормальною масою тіла. В групі з ожиренням більшість становили жінки, захворювання у них достовірно частіше, ніж у чоловіків, ускладнювалась легочною недостатністю III ступеня і емфіземой легких. Чоловіки з ожиренням достовірно частіше, ніж жінки, боліли цукровим діабетом 2-го типу.

**Ключові слова:** бронхіальна астма, фенотип, ожирення.

Научно-практический журнал «Астма и аллергия», 2014, № 2

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## PHENOTYPE OF BRONCHIAL ASTHMA WITH OBESITY

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**Abstract.** Problem of bronchial asthma (BA) phenotyping is important for clinical practice and science. It was proposed to separate asthma phenotype with obesity. For the determination of the specificity of asthma with obesity we analyzed the results of investigations of 90 patients with bronchial asthma (BA). Patients were divided into 3 groups: the first included 33 patients with normal body weight, the second — 29 patients being overweight and a third consisted of 28 patients with obesity. It was established, that patients with obesity had significantly more often lung tissue fibrosis, arterial hypertension and type 2 diabetes mellitus. But those patients had less often diagnosis of allergic rhinitis and peripheral blood eosinophilia. Lung function analysis showed that patients with obesity and overweight had more pronounced restrictive disorders than persons with normal body weight. We founded that group of patients with BA and obesity mostly included women in which disease was significantly more often complicated by respiratory insufficiency third degree and lung emphysema than in males. Men with BA and obesity suffered from type 2 diabetes significantly more often.

**Key words:** asthma, phenotype, obesity.

Theoretical and practical J. «Asthma and Allergy», 2014, 2

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