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DISTINCTIVE FEATURES OF PHENOTYPIC CHARACTERISTICS OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE POPULATION OF AZERBAIJAN

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The study included 120 patients with the bronchitic phenotype, 20 patients with the emphysematous phenotype of chronic obstructive pulmonary disease, and 20 apparently healthy persons, aged 30–65 years. Body mass index was calculated using the formula: BMI = weight, kg / height, m² (kg/m²). Obesity was registered at a body mass index of ≥ 30 kg/m². Blood pressure was measured by the Korotkoff method. Systolic and diastolic blood pressure were determined. The study of the concentration of major lipids in blood plasma was performed on an empty stomach after a 14-hour fast, using the Cobas 6000 analyzer by an enzymatic colorimetric method. The body mass index data indicated a predominance of obesity in individuals with the bronchitic phenotype of chronic obstructive pulmonary disease. Contrary to the commonly accepted view that hyperlipidemia is characteristic of the bronchitic phenotype of chronic obstructive pulmonary disease, this form of lipid metabolism disorder was also detected in the emphysematous phenotype of the disease. Thus, the results of the study established a clear tendency toward the development of cardiovascular comorbid pathology in the presence of both the bronchitic and emphysematous phenotypes of chronic obstructive pulmonary disease.

Key words: chronic obstructive pulmonary disease, bronchitic phenotype, emphysematous phenotype, risk factors, plasma lipids, hyperlipidemia.

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ОСОБЛИВОСТІ ФЕНОТИПІЧНОЇ ХАРАКТЕРИСТИКИ ХВОРИХ НА ХРОНІЧНЕ ОБСТРУКТИВНЕ ЗАХВОРЮВАННЯ ЛЕГЕНІВ У ПОПУЛЯЦІЇ АЗЕРБАЙДЖАНУ

У дослідженні взяли участь 120 хворих із бронхітичним, 20 – з емфізематозним фенотипами хронічного обструктивного захворювання легень та 20 практично здорових осіб у віці від 30 до 65 років. Індекс маси тіла розраховували за формулою: ІМТ = вага, кг/зріст, м² (кг/м²). Ожиріння реєстрували при індексі маси тіла ≥ 30 кг/м². Артеріальний тиск вимірювали за методом Короткова. Визначали систолічний та діастолічний артеріальний тиск. Дослідження концентрації основних ліпідів у плазмі крові проводилося натщесерце після 14-годинного голодування на апараті Cobas 6000 за допомогою ензиматичного колориметричного методу. Дані індексу маси тіла вказували на переважання ожиріння у осіб із бронхітичним фенотипом хронічного обструктивного захворювання легень. На відміну від загальноприйнятої думки про те, що гіперліпідемія властива бронхітичному фенотипу хронічного обструктивного захворювання легень, ця форма порушення ліпідного обміну також виявлялася й при емфізематозному фенотипі захворювання. Таким чином, результати дослідження виявили явну тенденцію до формування серцево-судинної коморбідної патології за наявності як бронхітичного, так і емфізематозного фенотипів хронічного обструктивного захворювання легень.

Ключові слова: хронічне обструктивне захворювання легень, бронхітичний фенотип, емфізематозний фенотип, фактори ризику, плазмові ліпіди, гіперліпідемія.

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality [12, 17]. For an accurate assessment of the clinical forms of COPD, information on phenotypes is necessary. Phenotypes reflect clinical features and demonstrate the most important differences between patients [9]. The term “phenotype” was introduced to distinguish different subgroups of COPD patients. The latest GOLD classification is the closest to the phenotypic approach [14].

A phenotype is a physical type or a biochemical characteristic that reflects the interaction between phenotype and genotype, and it has a significant impact on prognosis [2, 13]. Based on the identification of the phenotype, the following data can be obtained: clinical outcomes of the disease, symptoms and their severity, frequency of complications, rate of disease progression, and mortality rate. In recent years, the following phenotypes have been distinguished: emphysematous (cachectic), bronchitic (metabolic), COPD–asthma overlap, systemic inflammation, COPD in women, COPD in untreated patients, and COPD with frequent exacerbations. The bronchitic and emphysematous phenotypes are the most frequently registered.

Patients with the emphysematous phenotype are characterized by a low fat mass, osteoporosis, reduced body weight, low muscle mass, and emphysema. Patients with the bronchitic (metabolic) phenotype present with increased body weight, atherosclerosis, thickening of the bronchial walls, and high fat mass. Patients with the bronchitic phenotype of COPD exhibit a lesser degree of obstruction, but they more frequently suffer from cardiovascular diseases, among which arterial hypertension (AH) is most commonly registered, accounting for 57.5 % of cases. They present with characteristic features of coronary atherosclerosis [5, 6]. In another study, it was found that in the presence of COPD, a decrease in BMI is observed, due to a reduction in the proportion of patients with overweight and obesity [10, 12]. Thus, it is considered necessary to develop a comprehensive management strategy for COPD patients based on phenotype within primary health care [3]. An important fact is that frequent COPD exacerbations lead to significant economic costs, especially when treatment in the intensive care unit is required. In addition, frequent COPD exacerbations reduce the patient's quality of life and accelerate disease progression [4, 12]. All the above served as

the basis for further study of clinical parameters in a comparative aspect between patients with the bronchitic and emphysematous phenotypes of COPD.

The purpose of the study was to investigate the features of clinical manifestations of the bronchitic and emphysematous phenotypes of COPD in the population of the Republic of Azerbaijan.

Materials and methods. The study was conducted from 2020 to 2023 at the Department of Therapy of Azerbaijan State Institute of Advanced Medical Education named after A.Aliyev, and the Republican Clinical Hospital named after Academician M.A. Mirgasimov.

The examined persons were divided into three subgroups: one main group and two control groups:

– The main group included 120 patients with the bronchitic phenotype of COPD of different categories (A, B, E).

– Control group 1 consisted of 20 patients. They were diagnosed with the emphysematous phenotype of COPD.

– Control group 2 consisted of 20 apparently healthy persons. The age of the examined persons ranged from 30 to 65 years.

Blood pressure (BP) was measured by the Korotkoff method. Systolic and diastolic blood pressure (SBP, DBP) were determined. Body mass index (BMI) was calculated using the formula: BMI = weight, kg / height, m². Overweight corresponds to a BMI of 25.0–29.9 kg/m², obesity class I – 30.0–34.9

kg/m², class II – 35.0–39.9 kg/m², class III – 40.0–49.9 kg/m², class IV – 50.0–59.0 kg/m², class V – ≥ 60 kg/m², according to the recommendations of WHO [9]. In addition, the parameters of the main risk factor for COPD, tobacco smoking, were calculated in the patient groups: smoking duration (SD) and the pack-years index (PYI). PYI = SD × number of cigarettes smoked per day / 20, where 20 is the number of cigarettes in one pack. The unit of measurement for PYI is pack-years.

The study of the concentration of major plasma lipids was performed on an empty stomach after a 14-hour fast, using a Cobas-6000 analyzer by an enzymatic colorimetric method. The reference values for the major lipids were as follows: total cholesterol (TC) < 5.0 mmol/L (190 mg/dL), triglycerides (TG) < 1.7 mmol/L (150 mg/dL), high-density lipoproteins (HDL) > 1.0 mmol/L (40 mg/dL) for males, > 1.2 mmol/L (46 mg/dL) for females, low-density lipoproteins (LDL) < 3.0 mmol/L (115 mg/dL).

For statistical analysis, differences between groups were assessed using analysis of variance (ANOVA) and tests for homogeneity of variance (in particular, for cases of equal variances). For data with a non-normal distribution, the Mann-Whitney test was applied. A value of $p < 0.05$ was considered statistically significant.

Results of the study. Table 1 presents the age and gender characteristics of the examined patient groups.

Table 1

Age and gender characteristics of the examined groups of patients

Indicators	Groups		
	Main group, COPD, bronchitic phenotype (n=120)	Control group, apparently healthy persons (n=20)	Control group, COPD, emphysematous phenotype (n=20)
Mean age (years)	48.62±9.75	41.55±7.23	59.35±5.20
		$P_1 < 0.001$	$P_2 < 0.001$
Gender (%)			
Males	109 (90.83 %)	7 (35.00 %)	19 (95.50 %)
		$P_1 < 0.001$	$P_2 > 0.05$
Females	11 (9.16 %)	13 (65.00 %)	1 (5.00 %)
		$P_1 < 0.001$	$P_2 > 0.05$

Note: P_1 – significance between the main and control (healthy) groups; P_2 – significance between the main and control (emphysematous) groups.

Analysis of blood pressure indicators revealed that in persons with the bronchitic phenotype of COPD, the mean systolic blood pressure (SBP) was 128.33±13.32, and in those with the emphysematous phenotype – 126.00±11.88 mmHg, which was statistically significantly higher compared to the control group of apparently healthy persons – 110.75±8.47 mmHg ($p < 0.001$). However, the difference between SBP values in the bronchitic and emphysematous phenotypes was not statistically significant ($p > 0.05$).

The mean diastolic blood pressure (DBP) in persons with COPD with the bronchitic phenotype was 81.667±5.47 mmHg, and with the emphysematous phenotype – 81.00±6.46 mmHg, with no statistically significant difference ($p > 0.05$), but it was significantly higher compared to the group of apparently healthy persons – 71.95±6.46 mmHg ($p < 0.001$). Fig. 1 presents the main indicators of

plasma lipids in persons with the bronchitic and emphysematous phenotypes of COPD.

As can be seen from the diagram, in patients with the bronchitic phenotype of COPD, the mean plasma total cholesterol (TC) level was 241.31±47.83 mg/dL, and in those with the emphysematous phenotype – 196.9±34.01 mg/dL; however, the values did not significantly differ ($p > 0.05$) compared to the group of apparently healthy persons – 184.85±17.193 mg/dL ($p < 0.05$).

The mean plasma triglyceride (TG) level in persons with the bronchitic phenotype of COPD was 235.968±72.61 mg/dL, and in patients with the emphysematous phenotype – 220.1±51.76 mg/dL, with no statistically significant difference ($p > 0.05$), but it was significantly higher compared to the group of apparently healthy persons – 178.93±31.15 mg/dL ($p < 0.05$).

The mean plasma HDL level in patients with the bronchitic phenotype of COPD was 42.03 ± 6.24 mg/dL, in those with the emphysematous phenotype – 40.34 ± 2.68 mg/dL, and in apparently healthy persons – 41.70 ± 1.976 mg/dL, with no statistically significant difference ($p > 0.05$).

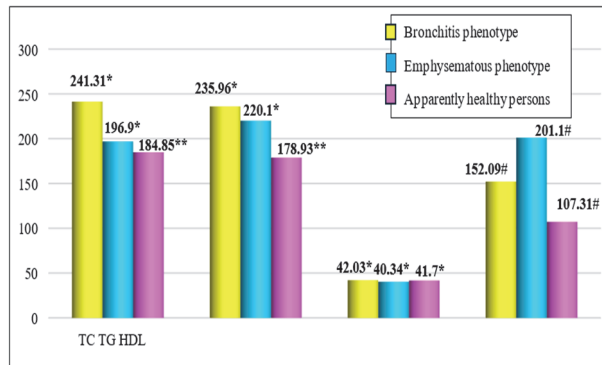


Fig. 1. Main indicators of plasma lipids in patients with bronchitic and emphysematous phenotypes of COPD. p – significance between groups: * – $p > 0.05$, ns; ** – $p < 0.05$; # – $p < 0.001$.

The mean plasma LDL level in patients with the bronchitic phenotype of COPD was 152.09 ± 45.81 mg/dL, and in those with the emphysematous phenotype – 201.10 ± 51.8 mg/dL, which was significantly higher with a high degree of significance ($p < 0.001$). In the group of apparently healthy persons, this parameter was 107.315 ± 16.67 mg/dL, which was significantly lower compared to the aforementioned groups and corresponded to the normal range ($p < 0.001$).

Discussion. Given the contradictory nature of certain results, we aimed to study the features of individual clinical parameters in patients with COPD with bronchitic and emphysematous phenotypes in the population of the Republic of Azerbaijan. Therefore, the first parameter discussed in our study was the Quetelet index, or body mass index (BMI).

It is known that patients with the bronchitic phenotype have excessive body weight, overly developed abdominal adipose tissue, and frequent dyslipidemia [1].

In our study, the finding was confirmed that in the presence of the bronchitic phenotype, the BMI value corresponded to the criterion of grade I obesity (30.97 ± 4.6 kg/m²), while in patients with the emphysematous phenotype of COPD, this parameter corresponded to the normal BMI range (21.64 ± 1.98 kg/m²), and the difference was statistically significant ($p < 0.001$).

Thus, discussing the obtained results, it should be noted that BMI assessment in the presence of the bronchitic phenotype of COPD predominantly reveals obesity. As for the parameters characterizing the state of lipid metabolism, it is necessary to note the presence of several significant differences, which is very important in terms of clinical application.

Studies from 2016–2024 have established that the bronchitic phenotype occurs against the background of pronounced atherogenic dyslipidemia, whereas for the emphysematous type, a normal or even reduced cholesterol level is more characteristic, but with signs of lipid peroxidation. It has been found

that patients with the bronchitic component and frequent exacerbations have significantly higher levels of TG and LDL, along with a reduced HDL level. This is associated with elevated levels of interleukin-8 (IL-8) and C-reactive protein (CRP) [1].

In another study, it was found that in patients with predominant emphysema, the TC and LDL levels were significantly lower than in patients with the bronchitic phenotype. However, the low cholesterol level in these patients directly correlated with a decrease in BMI and skeletal muscle wasting, acting as a marker of an unfavorable metabolic prognosis (the "energy-wasting" syndrome) [7].

In our study, the BMI in patients with the emphysematous phenotype, compared to the bronchitic (metabolic) phenotype, was within the normal range (21.64 ± 1.98 kg/m²), and no signs of wasting or a radiological picture of pronounced emphysema were observed in this group of patients.

Taking into account the influence of a long smoking history on the development of COPD, we also paid attention to this parameter. The study of the emphysematous phenotype of COPD against the background of a long smoking history over the past 10 years (2016–2026) has shifted to the subcellular level.

Studies have demonstrated that tobacco smoke toxins in combination with alveolar destruction trigger a unique "vicious cycle": lipid oxidative stress and membrane instability. In this case, in smokers with emphysema (unlike those with bronchitis), the total blood cholesterol level may remain normal, but its quality and structure are profoundly altered [8, 12, 15]. In another study, the effect of prolonged smoking on metabolic parameters was investigated. It was demonstrated that in smoking patients with COPD, chemical oxidative stress is observed (accompanied by a decrease in uric acid levels as an antioxidant). This directly induces a qualitative imbalance of lipids. In emphysematous lung damage, tobacco smoke enhances the modification of lipoproteins, which leads to damage of alveocyte membranes even at a borderline-normal level of total cholesterol [12, 16].

In our study, in the group of patients with the emphysematous phenotype, the smoking duration (SD) was 29.95 ± 6.0 years, and the pack-years were 44.57 ± 8.4 . Here, it would be appropriate to note that the development of metabolic and cardiovascular disorders, in particular dyslipidemia with high levels of atherogenic lipids, is also influenced by another risk factor – the atherogenic lipid status. Given that in the isolated emphysematous phenotype of COPD, the body undergoes so-called "metabolic wasting" due to oxidative stress, with low levels of TC and atherogenic lipid fractions, it can be assumed that in our study, the high values of the latter and the clinically unexpressed "cachectic/emphysematous" status of the patients suggest a mixed phenotype of COPD with the presence of two risk factors for atherogenesis – tobacco smoking and the corresponding nutritional behavioral status.

An analysis of international studies over the past 5 years reveals the so-called "lipid paradox" in COPD, concerning the key lipid profile parameters –

TC, TG, LDL, and HDL – across different disease phenotypes. These contradictions are attributed to the interplay of systemic inflammation, hypoxia, smoking, and the nutritional status of patients. The findings contain controversial and paradoxical conclusions. Thus, the classical concept regarding the metabolic phenotype of COPD, characterized by high levels of TG and LDL, which increases cardiovascular risk, contradicts the recent genetic and epidemiological data that question this concept [1].

In a large-scale study based on data utilizing Mendelian randomization, researchers discovered an unexpected protective role of hypercholesterolemia. It was demonstrated that genetically determined high levels of TC and LDL are causally associated with a reduced risk of severe COPD exacerbations and better lung function parameters (FEV1). This completely contradicts the standard cardiovascular paradigm regarding the detrimental effects of high TC levels in metabolic syndrome [1, 11, 16].

We have established that, contrary to the widely accepted notion that hyperlipidemia is characteristic of the bronchitic phenotype of COPD, this form of lipid metabolism disorder is also identified in the emphysematous phenotype and constitutes the basis

for the development of comorbid cardiovascular pathology in these patients. This is further supported by the fact that our study established a clear tendency toward the development of arterial hypertension in both the bronchitic and emphysematous phenotypes of COPD. The cause of this tendency lies in the development of atherosclerotic lesions of the vascular wall, which leads to a loss of its elasticity, the development of rigidity, and, as a consequence, an increase in total vascular resistance with the development of arterial hypertension. All the above may serve as a basis for revising the key characteristics of the emphysematous phenotype (especially the mixed phenotype) and for recognizing the presence of its metabolic component. In this regard, it is important to note that our study established a significantly high population level of atherogenic lipid fractions. This, in our view, also contributed to the high levels of atherogenic lipids in the examined patients with both the bronchitic and emphysematous phenotypes of COPD. This finding should undoubtedly be taken into account when developing preventive and therapeutic strategies for COPD patients with the bronchitic and emphysematous phenotypes.

Conclusions

1. Our study confirmed the presence of a BMI corresponding to the criterion of grade I obesity in patients with the bronchitic phenotype of COPD.
2. In patients with the bronchitic and emphysematous phenotypes of COPD, an increase in atherogenic lipid fractions was established, corresponding to the criteria of hyperlipidemia.
3. The study did not reveal any pathological changes in HDL parameters.
4. Patients with the emphysematous phenotype of COPD, as well as those with the bronchitic phenotype, are recommended to undergo periodic assessment of atherogenic lipid fractions, especially in the absence of clinical signs of "metabolic wasting."

Prospects for further research. The authors plan to continue the study in order to revise the key characteristics of the emphysematous/mixed phenotype and to recognize the presence of its metabolic component, taking into account the nutritional status and behavioral characteristics of the population across different regions of Azerbaijan.

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CHARACTERISTICS OF PUBERTAL DEVELOPMENT IN ADOLESCENT GIRLS BORN WITH LOW BIRTH WEIGHT

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Low birth weight is considered a significant risk factor for impaired physical, pubertal, and reproductive development in girls. This study aimed to investigate reproductive organ development during puberty in girls born with low birth weight. The study included 65 adolescent girls aged 14–17 years who were born at term with a birth weight of 1,900–2,500 g; the control group comprised 30 healthy age-matched girls. Anthropometric parameters, secondary sexual characteristics, and ultrasonographic measurements of the uterus and ovaries were assessed. Girls born with low birth weight had significantly lower height, body weight, and pelvic dimensions than controls ($p < 0.05$). Delayed breast development, more pronounced axillary and pubic hair growth, and moderate hirsutism were observed. Ultrasonography revealed significantly smaller uterine dimensions, reduced endometrial thickness, and lower bilateral ovarian volumes ($p < 0.05$). These findings indicate delayed physical and pubertal development and may suggest impaired reproductive system maturation in girls born with low birth weight.

Key words: low birth weight, puberty, adolescent girls, reproductive development, ultrasonography.

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ОСОБЛИВОСТІ ПЕРЕБІГУ ПЕРІОДУ СТАТЕВОГО ДОЗРІВАННЯ У ДІВЧАТОК З НИЗЬКОЮ МАСОЮ ТІЛА ПРИ НАРОДЖЕННІ

Низька маса тіла при народженні вважається значущим фактором ризику порушень фізичного, статевого та репродуктивного розвитку дівчаток. Метою дослідження було вивчення особливостей розвитку репродуктивних органів у період статевого дозрівання у дівчаток, які народилися з низькою масою тіла. Було обстежено 65 дівчат-підлітків віком 14–17 років, які народилися доношеними з масою тіла 1900–2500 г; контрольну групу склали 30 здорових однолітків. Оцінювали антропометричні показники, вторинні статеві ознаки та ультразвукові параметри матки й яєчників. У дівчаток із низькою масою тіла при народженні виявлено статистично значуще менші показники зросту, маси тіла та розмірів таза порівняно з контрольною групою ($p < 0.05$). Відзначалися затримка розвитку молочних залоз, більш виражене оволосіння в пахвових та лобкових ділянках та помірний гірсутизм. Під час ультразвукового дослідження було встановлено менші розміри матки, товщину ендометрія та об'єм обох яєчників ($p < 0.05$). Отримані результати свідчать про затримку фізичного та статевого розвитку та можливе порушення дозрівання репродуктивної системи у дівчаток, які народилися з низькою масою тіла.

Ключові слова: низька маса тіла при народженні, дівчата-підлітки, пубертатний період, репродуктивне здоров'я, гірсутизм, ультразвукове дослідження.

Preservation of reproductive health in adulthood largely depends on normal growth and maturation during childhood and adolescence. Fetal and early postnatal growth are increasingly recognized as important determinants of pubertal

timing and later endocrine and reproductive health [1–5].

Adverse intrauterine conditions may affect fetal growth and initiate long-term developmental adaptations. Current evidence links fetal growth