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АССОЦИАЦИИ АДИПОКИНОВОГО ПРОФИЛЯ КРОВИ И НАЛИЧИЯ ХРОНИЧЕСКОГО БРОНХИТА У МОЛОДЫХ ЛИЦ

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Associations Of Blood Adipokine Profile and The Presence of Chronic Bronchitis in Young Individuals

Резюме

Целью данного исследования является поиск ассоциации наличия хронического бронхита (ХБ) и уровня адипокинов крови у лиц 25-44 лет с абдоминальным ожирением (АО) и без него. Исследование выполнено на популяционной выборке жителей города Новосибирска (1415 человек). После исключения лиц с зафиксированной бронхообструкцией и с отсутствием данных спирометрии для анализа была сформирована подвыборка в размере 1086 человека, возраст обследованных составил 37,8 [32,0;41,9] года. Всем лицам произведена антропометрия, сбор анамнеза и забрана кровь из локтевой вены для определения показателей липидного профиля, уровня глюкозы и адипокинов. Диагноз ХБ выставлялся на основании стандартного эпидемиологического опросника при наличии кашля с мокротой не менее 3 месяцев в году или при наличии медицинской истории заболевания. Результаты. У лиц с ХБ и АО регистрировались более высокие значения систолического артериального давления (САД) ($p=0,001$) и диастолического артериального давления (ДАД) ($p=0,003$), наблюдались атерогенные изменения в липидном профиле (более высокие показатели холестерина липопротеинов низкой плотности (ХС-ЛНП), триглицеридов (ТГ), низкие холестерина липопротеинов высокой плотности (ХС-ЛВП)) и более высокие показатели глюкозы по сравнению с лицами без АО. Шанс наличия ХБ был ассоциирован с курением, АО и увеличением САД. При изучении концентрации адипокинов крови у лиц с ХБ и без него получено, что у лиц с ХБ и АО регистрировались более высокие уровни резистина ($p=0,023$), амилина ($p=0,041$), интерлейкина 6 (IL-6) ($p=0,002$), С-пептида ($0,0001$), инсулина ($p=0,035$), лептина ($p=0,0001$), фактора некроза опухоли альфа (TNF α) ($p=0,003$) и глюкагон-подобного пептида 1 (GLP-1) ($p=0,001$) по сравнению с лицами с ХБ и без АО. При проведении однофакторного логистического регрессионного анализа получено, что шанс наличия ХБ обратно ассоциирован с уровнем резистина (ОШ 0,998 ДИ 0,997-0,999) и пептида YY (РYY) (ОШ 0,994 ДИ 0,989-0,999), модели стандартизованы по полу, возрасту, окружности талии (ОТ) и статусу курения. При включении обеих молекул в модель многофакторного логистического регрессионного анализа вместе с АО, САД, курением, полом и возрастом ассоциации были получены только для резистина (ОШ 0,998 ДИ 0,997-0,999) и курения (ОШ 4,656 ДИ 2,802-7,738). Заключение. У лиц 25-44 лет шанс наличия ХБ прямо ассоциирован с курением и АО, обратно ассоциирован с концентрацией в крови резистина, независимо от пола и возраста.

Ключевые слова: хронический бронхит, абдоминальное ожирение, молодые лица, адипокины, резистин, РYY, курение

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования

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Соответствие принципам этики

Исследование одобрено локальным этическим комитетом НИИТПМ — филиал ИЦиГ СО РАН (Протокол № 71 от 27.02.2024). Исследование выполнено в соответствии с принципами Хельсинской декларации. Все лица, включенные в исследование лица, подписывали информированное согласие, одобренное локальным этическим комитетом.

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Abstract

The aim of this study was to investigate the association between the presence of chronic bronchitis (CB) and blood adipokine levels in individuals aged 25-44 years with and without abdominal obesity (AO). The study was conducted on a population-based sample of 1,415 residents of Novosibirsk. After excluding individuals with documented broncho-obstruction and missing spirometry data, a subsample of 1,086 individuals aged 37.8 [32.0; 41.9] years was formed for analysis. All individuals underwent anthropometry, anamnesis collection, and blood collection from the cubital vein to determine lipid profile, glucose, and adipokine levels. CB was diagnosed based on a standard epidemiological questionnaire in the presence of a cough with sputum for at least 3 months per year or with a medical history of the disease. Results. Individuals with chronic bronchitis and oxidative stress had higher systolic blood pressure (SBP) ($p=0.001$) and diastolic blood pressure (DBP) ($p=0.003$), atherogenic changes in the lipid profile (higher levels of low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and low levels of high-density lipoprotein cholesterol (HDL-C)) and higher glucose levels compared to individuals without oxidative stress. The likelihood of having chronic bronchitis was associated with smoking, oxidative stress, and increased SBP. When studying the concentration of blood adipokines in individuals with and without CB, it was found that individuals with CB and AO had higher levels of resistin ($p=0.023$), amylin ($p=0.041$), interleukin 6 (IL-6) ($p=0.002$), C-peptide (0.0001), insulin ($p=0.035$), leptin ($p=0.0001$), tumor necrosis factor alpha (TNF α) ($p=0.003$) and glucagon-like peptide 1 (GLP-1) ($p=0.001$) compared to individuals with CB and without AO. Univariate logistic regression analysis revealed that the odds of having CB were inversely associated with the levels of resistin (OR 0.998 CI 0.997-0.999) and peptide YY (PYY) (OR 0.994 CI 0.989-0.999); the models were adjusted for gender, age, waist circumference (WC), and smoking status. When both molecules were included in the multivariate logistic regression analysis model along with AO, SBP, smoking, gender, and age, associations were obtained only for resistin (OR 0.998 CI 0.997-0.999) and smoking (OR 4.656 CI 2.802-7.738). Conclusion. In individuals aged 25-44 years, the odds of having chronic kidney disease are directly associated with smoking and AO, and inversely associated with the blood concentration of resistin, regardless of gender and age.

Key words: chronic bronchitis, abdominal obesity, young people, adipokines, resistin, PYY, smoking

Conflict of Interest

The authors declare that this work, its topic, subject matter, and content do not affect any competing interests.

Funding Sources

The study was carried out within the framework of budget topic No. FWNR-2024-0002.

Compliance with the principles of ethics

The study was approved by the local ethics committee of the Research Institute of Therapeutic and Preventive Medicine, a branch of the Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences (Protocol No. 71, dated February 27, 2024). The study was conducted in accordance with the principles of the Declaration of Helsinki. All individuals included in the study signed informed consent, approved by the local ethics committee.

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ECRHS — European Community Respiratory Health Survey, EMD Millipore Corporation — diagnostic kit manufacturer (Germany), GIP — glucose-dependent insulinotropic polypeptide, GLP-1 — glucagon-like peptide-1, GOLD — Global Initiative for Chronic Obstructive Lung Disease, IL-6 — interleukin-6, MCP-1 — monocyte chemoattractant protein-1, PAI-1 — plasminogen activator inhibitor-1, PYY — peptide YY, BP — blood pressure, AO — abdominal obesity, WHO — World Health Organisation, BMI — body mass index, WC — waist circumference, TC — total cholesterol, TG — triglycerides, TNF- α — tumour necrosis factor alpha, CB — chronic bronchitis, COPD — chronic obstructive pulmonary disease, HDL cholesterol — high-density lipoprotein cholesterol, LDL cholesterol — low-density lipoprotein cholesterol, non-HDL cholesterol — non-high-density lipoprotein cholesterol

Introduction

The classical definition of chronic bronchitis (CB), i.e. wet cough for at least three months a year for at least two consecutive years in the absence of other causes, is used worldwide. However, recently the validity of CB as a separate diagnosis has been questioned. This is caused by a number of factors, the main one of which is the Global Initiative for Chronic Obstructive Lung Disease (GOLD) (global guidelines for chronic obstructive pulmonary disease (COPD)), where chronic bronchitis as a separate disease has been removed altogether; it is defined rather as a phenotype or COPD manifestation. This is because

the majority of patients with classical CB develop a form of obstruction, since the mechanisms of inflammation and bronchi remodelling are very similar to those in COPD patients (GOLD 2025) [1]. In Russia, the clinical guidelines for chronic bronchitis (2024) specify the classical criteria and describe algorithms for diagnosing and differential diagnosis [2]: US authors stick to the same concept; they rely on the classical clinical definition (wet cough for at least three times a year for at least two years), emphasising assessment of risk factors (smoking, occupational hazards) and identification of other causes of chronic cough [3]. However, it is hardly possible to

rule out all causes of bronchial inflammation; that is why numerous experts believe that the “pure” CB hardly exists, it is usually a part of another respiratory condition. The criteria of “three months and two years” have mostly historical meaning; however, they are useful for epidemiological studies [4].

Over the years, obesity has been studied as a contributing factor of chronic respiratory conditions, including CB. Higher body weight and excessive fat deposits are associated with systemic low-grade inflammation, which can facilitate inflammatory responses in bronchi and boost sputum production, creating conditions for CB [5].

A large population-based study reported an association between abdominal and general obesity and a high risk of chronic respiratory inflammation (including clinical manifestations resembling chronic bronchitis) and poorer outcomes. A prospective study of obese individuals showed a higher incidence of COPD, including manifestations resembling chronic bronchitis [6]. Besides, in patients with COPD, overweight modifies the clinical presentation: obesity affects symptom intensity, exacerbation frequency and overall disease severity, indirectly evidencing the role of adipose tissue and metabolic disorders in pathogenesis of chronic bronchopulmonary findings [7]. However, another large-scale cohort study demonstrates a dubious association between body mass index (BMI) and the risk of COPD: in some study arms, excessive body weight is associated with a higher risk of symptoms, while other subjects demonstrate protective effects, underlining the heterogeneity of effects from adipose tissue and its products on the respiratory system [8].

The objective of this study is to search for an association between presence of CB and blood adipokines in patients with AO.

Materials and methods

In 2013–2016, the Research Institute of Internal and Preventive Medicine, a branch of the Federal Research Centre at the Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, hosted a population-based study among the citizens of Novosibirsk aged 25 to 44 years. The study was performed under state-finance topic No. FWNR-2024-0002.

For population sampling, the database of the Territorial Federal Compulsory Medical Insurance Fund was used, which included subjects of 25 to 44 years of age in one district of Novosibirsk with the typical industrial, social, populational, demographic, and transport structures, as well as population migration levels. A random number generator was applied to form a random representative sample of 2,500 individuals. Younger age groups are known to be more reluctant to respond, that is why staggered epidemiological incentives were used: post

invitations, phone calls, mass media ads. 1,512 individuals were screened; the response rate was 60.5 %. After the exclusion of pregnant women and women on maternity leave, the study included 1,415 subjects (670 men, 47.3 %, and 745 women, 52.7 %). The mean age was 37.3 [31.8; 42.0] years. All subjects signed an informed consent form for personal data processing.

Respiratory symptoms were identified using the WHO respiratory disease detection tool and ECRHS (European Community Respiratory Health Survey) questionnaire [9]. The epidemiologic diagnosis of CB was made in the presence of wet cough for at least three months a year or a history of the disease. Besides, respiratory function was tested using spirometry under the spirometry guidelines with the use of Spiro USB Micro Medical Limited (UK) in order to rule out bronchial obstruction.

Exclusion criteria were: recorded bronchial obstruction and lack of spirometry results for the analysis.

Eventually, the sample comprised 1,086 subjects (517 men (45.4 %), and 569 women (54.6 %); the mean age was 37.8 [32.0; 41.9] years old).

Subjects receiving drug treatment accounted for under 1 % and did not affect the final results.

All patients had their height, weights, waist circumference, and blood pressure (BP) measured. Subjects' height was measured using a vertical height meter in the upright position without shoes, with the accuracy of 0.5 cm. For weighing, calibrated electronic hospital scales were used; and the measurement accuracy was 100 grams. BMI was calculated as follows: $BMI = \text{body weight (kg)} / \text{height (m)}^2$. Overweight was reported as $BMI \geq 25 \text{ kg/m}^2$, obesity was diagnosed at $BMI \geq 30 \text{ kg/m}^2$ [10].

Waist circumference (WC) was measured using a measuring tape, placed horizontally strictly between the lower costal arch and sacral section of the iliac bone. Abdominal obesity (AO) was reported as waist circumference of $\geq 94 \text{ cm}$ in men and $\geq 80 \text{ cm}$ in women [10].

BP was measured three times at a 2-minute interval on both arms seated after 5-minute rest, using Omron M5-I (Japan) blood pressure sensor; the mean of the three measurements was recorded. AH was reported using the epidemiological criteria, where SBP was $\geq 140 \text{ mm Hg}$ and/or DBP was $\geq 90 \text{ mm Hg}$ [11].

All subjects underwent a one-off fasting blood draw from their ulnar vein (12 hours after meal). Lipid profile, i.e. triglycerides (TG), high-density lipoprotein cholesterol (HDL cholesterol) and total cholesterol (TC), as well as serum glucose levels, were measured using enzymic methods with standard Termofisher reagents (Finland) and Konelab 30i analyser (Finland).

Serum glucose was converted into plasma glucose using the following formula: $\text{Plasma Glucose (mmol/L)} = -0.137 + 1.047 \times \text{serum glucose (mmol/L)}$. An elevated fasting plasma glucose level was reported at $\geq 7 \text{ mmol/L}$ [12].

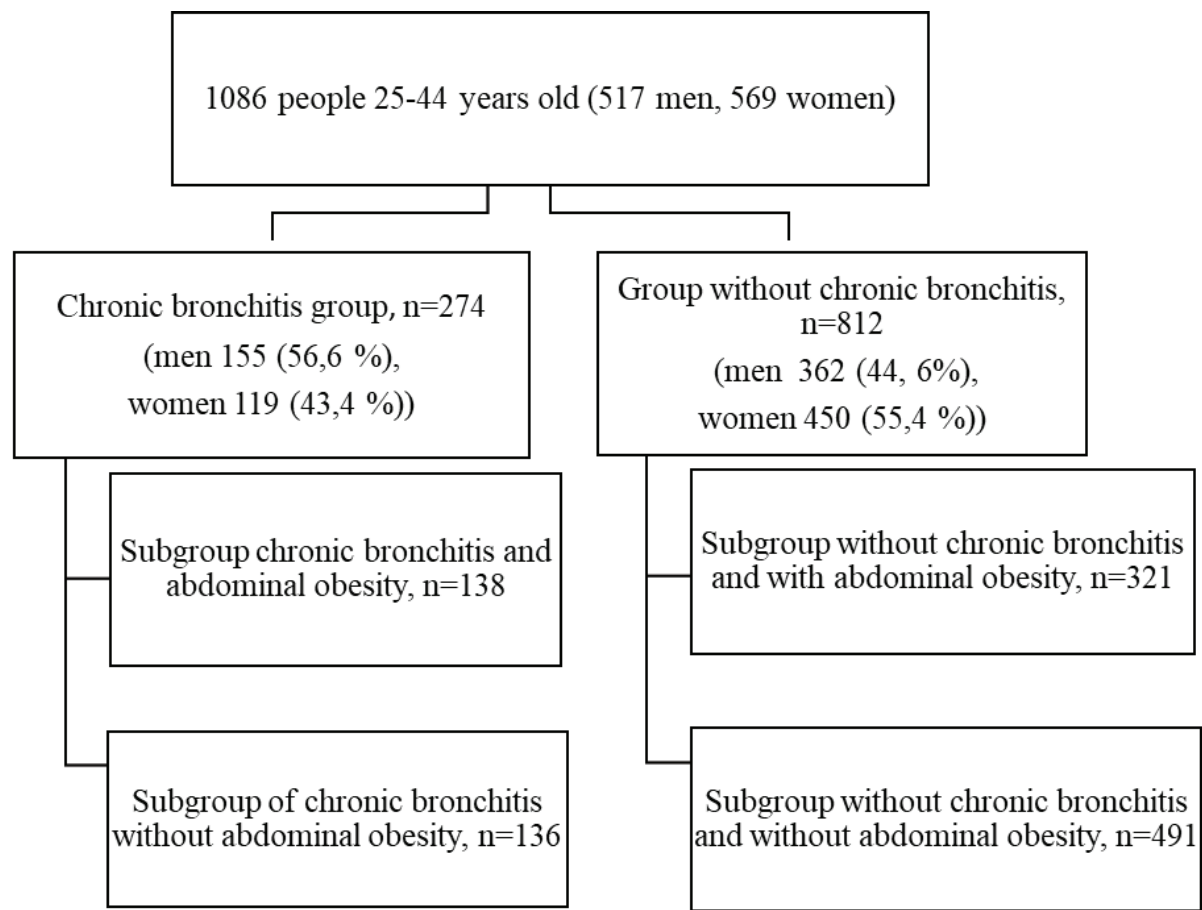


Figure 1. Study design

Low-density lipoprotein cholesterol (LDL cholesterol) was calculated using Friedewald formula: $\text{LDL cholesterol} = \text{TC} - (\text{TG} / 2.2) - \text{HDL cholesterol}$. According to epidemiological criteria, elevated blood LDL cholesterol levels were reported at LDL cholesterol and TG of ≥ 3.0 mmol/L and ≥ 1.7 mmol/L, respectively [13].

Non-high-density lipoprotein cholesterol (non-HDL cholesterol) values were calculated as follows: $\text{non-HDL cholesterol (mmol/L)} = \text{TC (mmol/L)} - \text{HDL cholesterol (mmol/L)}$.

Characteristics of the subjects with and without CB are presented in Table 1.

A multiplex assay using Luminex 20 MAGPIX flow cytometer was utilised to measure the blood levels of biomolecules associated with secretory activity of visceral fat cells:

- a) using Human Adipokine Magnetic Bead Panel 1 kit (EMDMillipore Corporation, Germany): adiponectin, adipisin, lipocalin-2, resistin, plasminogen activator inhibitor 1 (PAI-1);
- b) using Human Metabolic Hormone V3 kit (EMDMillipore Corporation, Germany): amylin, C-peptide, ghrelin, glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide-1

(GLP-1), glucagon, insulin, pancreatic polypeptide (PP), peptide YY (PYY), interleukin 6 (IL-6), leptin, monocyte chemoattractant protein 1 (MCP-1), tumour necrosis factor alpha (TNF- α), secretin.

SPSS package (version 13.0) was used for statistical processing of results. The normality of distribution was tested using the Kolmogorov-Smirnov test. Since the distribution of the majority of tested parameters was not normal, the data for continuous variables are presented as Me [25%; 75%], where Me is the median, 25% and 75% are the 1st and 3rd quartiles; categorical variables are presented as absolute and relative values — n (%). Two independent samples were compared using the Mann-Whitney U test. For ratio comparison, the Pearson's chi-square test was utilised. Associations were evaluated with the help of the multivariate logistic regression analysis under the following conditions: a dependent variable, dichotomic: presence/absence of CB; independent observations; absence of multicollinearity; linear dependance between each independent variable and log odds (logarithm factors); tail independence. Results of the multivariate logistic regression analysis are presented as odds ratio (OR) and 95% confidence interval (CI) for OR. The zero hypothesis significance level (p) was set at 0.05.

Table 1. Clinical and anamnestic data of individuals with and without CB

Indicators		CB group (+), n=274	CB group (-), n=812	p
Age, years				
Me [25 %;75 %]		38.5 [32.6;42.0]	37.2 [31.8;41.9]	0.057
Sex, n %	Men	155 (56.6 %)	362 (44.6 %)	0.001
	Women	119 (43.4 %)	450 (55.4 %)	
BMI, kg/m ²				
Me [25 %;75 %]		26.2 [22.6;29.9]	24.8 [21.9;28.5]	0.002
WC, cm				
Me [25 %;75 %]		89.0 [80.0;98.1]	84.0 [74.0;94.2]	<0.001
AO, n %		138 (50.4 %)	321 (39.5 %)	0.002
SBP, mmHg				
Me [25 %;75 %]		123.0 [113.4;132.1]	118.5 [109.5;129,0]	<0.001
DBP, mmHg				
Me [25 %;75 %]		80.5 [74.0;89.5]	78.0 [71.0;85.6]	<0.001
HR, beats/min				
Me [25 %;75 %]		74.0 [67.0;80.0]	72.0 [66.0;79.0]	0.102
TCH, mmol/l				
Me [25 %;75 %]		5.2 [4.5;5.8]	4.9 [4.2;5.6]	0.004
LDL-C, mmol/L				
Me [25 %;75 %]		3.3 [2.7;3.9]	3.1 [2.5;3.7]	0.002
HDL-C, mmol/L				
Me [25 %;75 %]		12 [11;15]	13 [11;15]	0.009
NonHDL-C, mmol/L				
Me [25 %;75 %]		38 [32;46]	36 [29;42]	<0.001
TG, mmol/L				
Me [25 %;75 %]		1.0 [0.7;1.6]	0.9 [0.7;1.4]	0.006
Glucose, mmol/l				
Me [25 %;75 %]		5.8 [5.4;6.2]	5.6 [5.3;6.0]	0.001
Smoking, n (%)	Never smoked	56 (20.4 %)	356 (43.8 %)	0.0001
	Smokes	173 (63.1 %)	207 (25.5 %)	
	Smoked, but quit	45 (16.4 %)	249 (30.7 %)	
Hypertension, n (%)		70 (25.5 %)	143 (17.7 %)	0.004
TG≥1,7 mmol/L, n (%)		60 (21.9 %)	128 (15.8 %)	0.020
LDL-C≥3,0 mmol/L, n (%)		172 (62.8 %)	429 (52.9 %)	0.004
Glucose ≥7 mmol/l, n (%)		13 (4.7 %)	16 (2.0 %)	0.014

Note: CB — chronic bronchitis, SBP — systolic blood pressure, DBP — diastolic blood pressure, AG — arterial hypertension, HR — heart rate, BMI — body mass index, WC — waist circumference, TC — cholesterol, LDL-C — low-density lipoprotein cholesterol, HDL-C — high-density lipoprotein cholesterol, non-HDL-C — non-high-density lipoprotein cholesterol, TG — triglycerides, Me — median, 25 % and 75 % — 1st and 3rd quartiles

Study results

The study group included subjects with CB: 274 patients (25.2 %).

Individuals with CB and AO had higher systolic blood pressure (SPB) (p=0.001) and diastolic blood pressure (DBP) (p=0.003) vs. individuals without AO. Besides, subjects with CB and AO demonstrated atherogenic changes in their lipid profile (higher LDL cholesterol, TGs and lower HDL cholesterol values) as well as higher glucose levels vs. subjects without AO (Table 2).

Subjects with CB and AO more frequently had a history of smoking, but currently smoked less (p=0.001) than patients with CB who did not have AO. They also

had a higher incidence of AH (p=0.007) and hypertriglyceridemia (p=0.002). Of note, despite the fact that subjects with CB and AO had higher absolute values of LDL cholesterol vs. subjects without AO, there were no differences between the incidence of hyper-LDL cholesterol values between these arms (p=0.278) (Figure 2).

Male subjects with CB and AO had more differences in their smoking status (p=0.023): used to smoke (15 (20.0 %) vs. 5 (6.3 %)), smoked less at present (50 (66.7 %) vs. 67 (83.8 %)); approximately the equal number of men mentioned that they had never smoked (10 (13.3 %) vs. 8 (10.0 %)) vs. subjects with CB and AO. Men with AO also had higher incidences of AH

($p=0.007$) and hypertriglyceridemia ($p=0.0001$) vs. men without AO (Figure 3).

Female subjects with CB and AO also differed in their smoking status ($p=0.017$): used to smoke more (19 (30.2 %) vs. 6 (10.7 %)) and mentioned that they had never smoked before (15 (20.0 %) vs. 5 (6.3 %)); approximately the equal number of women shared that they currently were smokers (29 (46.0 %) vs. 27 (48.2 %)) vs. individuals with CB without AO. Women with AO had a high rate of AH ($p=0.007$) vs. women without AO. Hyperglycaemia was reported more often in women with CB who also had AO (2 (3.2 %)) (Figure 4).

The logistic regression analysis showed that the odds of CB increases more than 5-fold in smokers, 1.5-fold in the presence of AO, and is associated with higher SBP values (Table 3).

Blood adipokine tests showed that individuals with CB had higher values of adipsin (1.1 times higher), IL-6 (1.4 times higher), C-peptide (1.1 times higher), GIP (1.1 times higher), PP (1.2 times higher), PYY was 1.2 times lower than in subjects without CB (Table 4).

Patients with CB and AO had higher levels of resistin, amylin, IL-6, C-peptide, insulin, leptin, TNF α , and GLP-1 vs. patients with CB, but without AO (Table 5).

Table 2. Quantitative indicators of metabolic risk factors in individuals with CB in subgroups with and without AO

Subgroups Indicator	CB /AO (-), n=136		CB /AO (+), n=138		P
	Me	[25 %;75 %]	Me	[25 %;75 %]	
Age, years	37.9	31.8;41.4	39.8	33.9;42.5	0.019
BMI, kg/m ²	22.6	20.7;25.1	29.8	27.3;32.9	0.0001
WC, cm	80.0	74.1;87.9	98.0	90.8;105.9	0.0001
SBP, mmHg	120.0	110.1;128.9	125.0	115.4;137.0	0.001
DBP, mmHg	78.5	71.6;86.8	83.0	75.4;91.5	0.003
HR, beats/min	73.0	66.0;79.0	74.0	67.3;82.8	0.110
TCH, mmol/l	5.0	4.3;5.7	5.2	4.6;5.9	0.141
HDL-C, mmol/L	1.3	1.1;1.5	1.2	1.0;1.4	0.0001
LDL-C, mmol/L	3.2	2.6;3.8	3.4	2.7;4.0	0.315
NonHDL-C, mmol/L	3.6	3.0;4.4	4.1	3.3;4.8	0.018
TG, mmol/L	0.8	0.6;1.4	1.3	0.9;1.9	0.0001
Glucose, mmol/L	5.7	5.3;6.1	5.9	5.5;6.2	0.027

Note: CB — chronic bronchitis, AO — abdominal obesity, SBP — systolic blood pressure, DBP — diastolic blood pressure, AG — arterial hypertension, HR — heart rate, BMI — body mass index, WC — waist circumference, TC — cholesterol, LDL-C — low-density lipoprotein cholesterol, HDL-C — high-density lipoprotein cholesterol, non-HDL-C — non-high-density lipoprotein cholesterol, TG — triglycerides, Me — median, 25 % and 75 % — 1st and 3rd quartiles

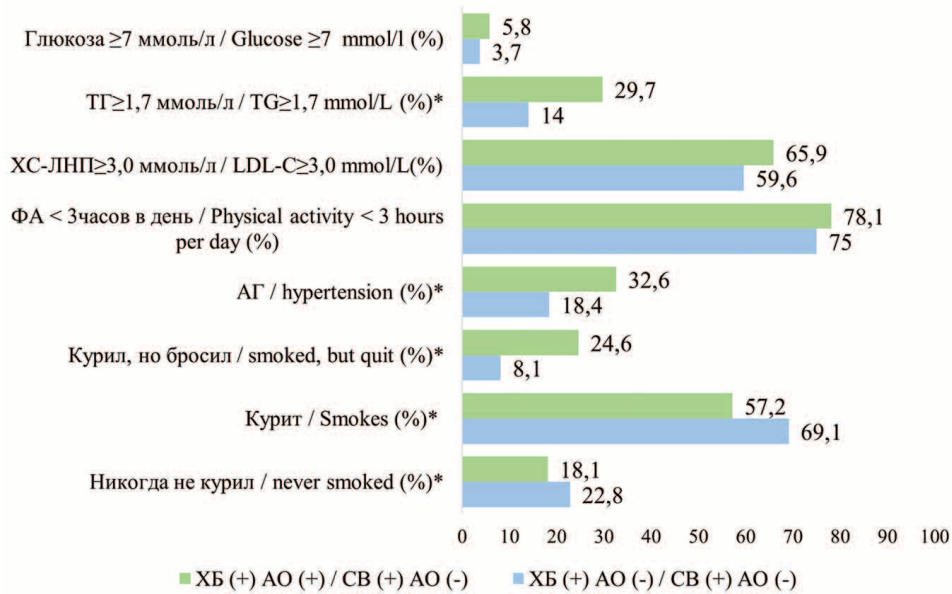


Figure 2. Frequency of metabolic risk factors in individuals with CB depending on the presence of AO

Note: CB — chronic bronchitis, AO — abdominal obesity, TG — triglycerides, LDL-C — low-density lipoprotein cholesterol, PA — physical activity, AG — arterial hypertension.

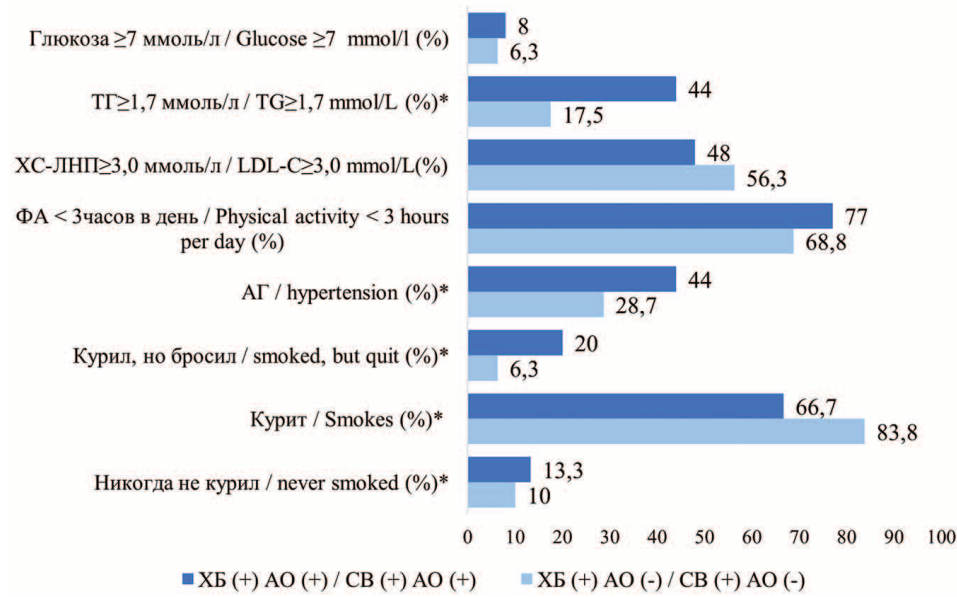


Figure 3. Frequency of metabolic risk factors in men with CB depending on the presence of AO
Note: CB — chronic bronchitis, AO — abdominal obesity, TG — triglycerides, LDL-C — low-density lipoprotein cholesterol, PA — physical activity, AG — arterial hypertension

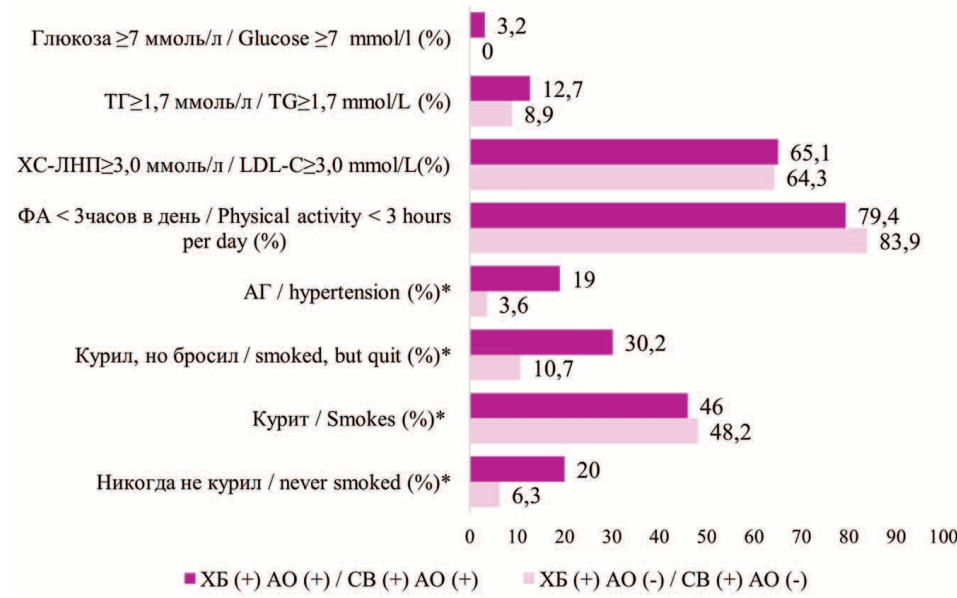


Figure 4. Frequency of metabolic risk factors in women with CB depending on the presence of AO
Note: CB — chronic bronchitis, AO — abdominal obesity, TG — triglycerides, LDL-C — low-density lipoprotein cholesterol, PA — physical activity, AG — arterial hypertension

Table 3. Univariate logistic regression analysis of the odds of having CB depending on metabolic risk factors (standardized by gender, age)

Indicator	OR	95 % confidence interval (CI)		P
		Lower limit	Upper limit	
Smoking,				
Smokes vs never smoked	5.187	3.629	7.415	0.0001
Smoked but quit vs never smoked	1.084	0.705	1.667	0.712
AO, yes vs no	1.480	1.117	1.962	0.006
SBP, per 1 mm Hg.	1.013	1.003	1.022	0.010
TG per 1 mmol/l	1.148	0.981	1.342	0.085
Glucose, per 1 mmol/l	1.144	0.983	1.331	0.083

Note: AO — abdominal obesity, AG — arterial hypertension, PA — physical activity, LDL-C — low-density lipoprotein cholesterol, Non-HDL-C — non-high-density lipoprotein cholesterol, TG — triglycerides, OR — odds ratio.

Table 4. Levels of the studied human adipokines (Me [25 %;75 %])

Adipokines	Group CB (+), n=274	Group CB (-), n=812	P
Adiponectin, µg/ml	42.3 [28.1;115.2]	37.2 [23.9;120.1]	0.233
Adipsin, µg/ml	12.5 [9.0;14.9]	11.0 [6.9;13.9]	0.001
Lipoclin-2, ng/ml	458.7 [274.0;945.3]	378.1 [190.0;1214.7]	0.304
Resistin, ng/ml	22.6 [12.6;31.6]	21.2 [13.4;31.5]	0.902
Amylin, pg/ml	170.8 [38.3;536.2]	132.2 [22.3;619.3]	0.954
IL-6, pg/ml	6.2 [3.5;13.9]	6.3 [5.0;14.2]	0.741
PAI-1, ng/ml	1.4 [0.7;3.8]	1.0 [0.6;2.0]	0.001
C-peptide, ng/ml	0.8 [0.4;1.4]	0.7 [0.2;1.2]	0.027
Insulin, pmol/L	438.6 [277.6;646.6]	463.9 [277.6;675.4]	0.749
Leptin, ng/ml	4.3 [1.5;8.5]	4.1 [1.6;7.8]	0.770
MCP-1, pg/ml	243.7 [144.9;328.0]	230.6 [158.2;313.2]	0.440
Ghrelin, pg/ml	29.3 [18.6;56.2]	36.4 [18.1;95.4]	0.258
TNFa, pg/ml	4.6 [2.9;7.4]	4.5 [2.9;7.0]	0.294
GIP, pg/ml	27.9 [169.8;448.7]	25.2 [15.7;50.5]	0.032
Glucagon, pg/ml	266.9 [169.8;448.7]	267.8 [169.3;492.2]	0.495
PP, pg/ml	11.1 [6.0;23.8]	12.4 [8.3;23.4]	0.178
GLP1, pg/ml	43.2 [26.5;85.8]	37.0 [20.5;74.5]	0.001
PYY, pg/ml	48.2 [36.0;66.2]	58.0 [37.8;79.2]	0.008
Secretin, pg/ml	22.4 [14.1;68.3]	22.5 [15.6;69.0]	0.831

Note: CB — chronic bronchitis, PAI-1 — plasminogen activator inhibitor type 1, IL-6 — interleukin 6, MCP-1 — monocyte chemoattractant protein-1, TNFa — tumor necrosis factor-alpha, GIP — glucose-dependent insulintropic polypeptide, PP — pancreatic polypeptide, GLP1 — glucagon-like peptide type 1, PYY — peptide YY, Me — median, 25 % and 75 % — 1st and 3rd quartiles

Table 5. Levels of the studied blood adipokines in individuals with CB with AO and without it (Me [25 %; 75 %])

Adipokines	People with CB (n=274)		P
	No AO (n=136)	Yes AO (n=138)	
Adipokines	40.5 [30.0;101.1]	47.9 [27.1;121.7]	0.682
Adiponectin, µg/ml	12.1 [8.2;14.6]	12.7 [9.7;15.4]	0.079
Adipsin, µg/ml	407.6 [227.6;781.9]	484.8 [328.8;1066.0]	0.065
Lipoclin-2, ng/ml	21.5 [10.7;30.1]	24.2 [16.0;32.0]	0.092
Resistin, ng/ml	130.7 [23.5;502.8]	189.8 [103.4;547.5]	0.023
Amylin, pg/ml	6.0 [1.4;10.4]	6.5 [4.0;14.2]	0.041
IL-6, pg/ml	1.2 [0.6;1.9]	1.7 [0.8;5.7]	0.002
PAI-1, ng/ml	0.6 [0.2;0.9]	1.2 [0.5;1.7]	0.0001
C-peptide, ng/ml	404.4 [277.4;549.7]	483.2 [322.9;719.1]	0.035
Insulin, pmol/L	1.8 [0.7;4.5]	6.8 [4.0;11.8]	0.0001
Leptin, ng/ml	232.0 [141.0;322.9]	256.6 [145.4;331.6]	0.652
MCP-1, pg/ml	29.3 [17.9;61.0]	29.3 [18.8;50.3]	0.656
Ghrelin, pg/ml	4.1 [2.7;6.5]	5.6 [3.4;7.8]	0.003
TNFa, pg/ml	27.5 [16.9;49.5]	29.5 [20.2;55.7]	0.225
GIP, pg/ml	228.2 [155.4;413.3]	323.1 [206.2;506.4]	0.001
Glucagon, pg/ml	11.1 [6.7;23.3]	11.1 [5.5;25.9]	0.912
PP, pg/ml	41.8 [25.1;80.6]	52.1 [31.7;89.0]	0.072
GLP1, pg/ml	48.2 [36.0;67.7]	48.2 [35.3;65.5]	0.886
PYY, pg/ml	20.3 [11.9;36.5]	23.5 [17.4;80.4]	0.169

Note: CB — chronic bronchitis, AO — PAI-1 — plasminogen activator inhibitor type 1, IL-6 — interleukin 6, MCP-1 — monocyte chemoattractant protein-1, TNFa — tumor necrosis factor-alpha, GIP — glucose-dependent insulintropic polypeptide, PP — pancreatic polypeptide, GLP1 — glucagon-like peptide type 1, PYY — peptide YY, Me — median, 25 % and 75 % — 1st and 3rd quartiles.

Table 6. Logistic regression analysis of associations of adipokines with the odds of having chronic kidney disease, standardized for gender, age, smoking status, and WC

Indicators	Univariate regression analysis			
	OR	95 % confidence interval (CI)		p
		Lower limit	Upper limit	
Adipsin at 1 µg/ml	1.008	0.995	1.021	0.227
IL-6 at 1 pg/ml	0.997	0.983	1.011	0.664
C-peptide at 1 pg/ml	1.121	0.901	1.396	0.306
GIP at 1 pg/ml	1.000	0.997	1.004	0.914
PP at 1 pg/ml	1.002	0.998	1.005	0.310
PYY at 1 pg/ml	0.994	0.989	0.999	0.030
GLP-1 at 1 pg/ml	0.999	0.999	1.000	0.082
Resistin at 1 mcg/ml	0.998	0.997	0.999	0.020
Amylin at 1 pg/ml	0.989	0.972	1.007	0.218
Insulin at 1 pg/ml	1.0001	1.000	1.0002	0.285
Leptin at 1 ng/ml	1.0001	1.000	1.0002	0.537
TNFα at 1 pg/ml	1.009	0.963	1.056	0.714

Note: PAI-1 — plasminogen activator inhibitor type 1, IL-6 — interleukin 6, MCP-1 — monocyte chemoattractant protein-1, TNFα — tumor necrosis factor-alpha, GIP — glucose-dependent insulinotropic polypeptide, PP — pancreatic polypeptide, GLP1 — glucagon-like peptide type 1, PYY — peptide YY, OR — odds ratio.

Table 7. Results of multivariate logistic regression analysis of the relationship between adipokines and the chance of having CB

Indicators	Multivariate regression analysis			
	OR	95 % confidence interval (CI)		p
		Lower limit	Upper limit	
Age by 1 year	1.043	0.998	1.090	0.062
Sex, men vs women	1.268	0.764	2.107	0.358
Smokes vs. doesn't smoke	4.656	2.802	7.738	0.0001
AO, yes vs no	2.300	1.402	3.774	0.001
PYY at 1 pg/ml	0.998	0.992	1.004	0.420
Resistin 1 mcg/ml	0.998	0.997	0.999	0.0001

Note: AO — abdominal obesity, PYY — peptide YY, OR — odds ratio

When the logistic regression analysis included adipokines, which demonstrated significant differences at previous stages of the study, it was established that the odds of CH were directly correlated with resistin levels and had inverse relationship with PYY levels (Table 6). Where the model included both molecules, which demonstrated associations with the odds of CB in the univariate regression analysis (resistin and PYY), age, gender, smoking status, and presence/absence of AO, it was found out that the odds of CB in younger population is over 4.5-times higher in smokers and is 2.3 higher with AO; it is directly associated with age and has inverse relationship with resistin levels, irrespective of gender (Table 6).

Discussion

We have demonstrated in a group of subjects of 25 to 44 years of age that the presence of CB is associated with active smoking status, higher SBP values and AO. These

results confirm and supplement the existing knowledge about the multi-factor nature of early manifestations of chronic respiratory diseases and are of practical significance for early prevention and screening. The leading role of smoking in forecasting CB development is in line with the extensive epidemiological data on tobacco smoking as the main risk factor of bronchitis and COPD. Current reviews and guidelines emphasise that, even in young people, prolonged smoking significantly increases the odds of chronical bronchi inflammation and subsequent progression of obstructive changes [14]. Association between CB and AO in young people correlates with recent studies, which show that abdominal obesity is associated with a higher risk of chronic inflammatory respiratory conditions and reduced pulmonary function irrespective of BMI. Mechanisms trigger impairment of respiratory function (diaphragm limitations, reduced lung capacity), as well as metabolic inflammatory changes linked to the biochemical activity

of adipose tissue, which worsen cough and facilitate chronic inflammation in bronchi [15].

Resistin activates transcription factor NF- κ B and signal cascades via TLR4/CAP1 receptors in monocytes and macrophages, inducing production of pro-inflammatory cytokines (TNF- α , IL-6, etc.). In such settings, higher resistin levels correlate with systemic and local inflammation in lungs, and a number of studies demonstrated an association with impaired pulmonary function and COPD severity [16]. At the same time, despite the fact that the majority of studies report direct association between blood resistin levels and development of bronchopulmonary diseases [17], Wang et al. demonstrated reduced serum resistin and leptin levels in COPD patients, which was most prominent in patients with cachexia [18]. In this study, we have also observed inverse association between resistin levels and CB; in subjects with CB and AO, its levels were higher than in subjects without AO. It can evidence that resistin can be a marker of chronic inflammation in bronchi also in individuals with normal BMI levels.

PYY is an intestinal peptide (it is mostly secreted by L-cells of distal segment of the bowels); it is primarily known as a regulator of appetite and energy exchange (through Y-receptors, including Y2). Nevertheless, PYY can also modify systemic metabolic and inflammation responses, and can affect respiratory system via the intestine — lungs axis [19]. Another possible association of PYY — bronchopulmonary system can be the fact that PYY suppresses appetite and impacts energy distribution, while changes in PYY levels are associated with changes in the body fat mass. Since AO impairs respiratory function and worsens systemic inflammation, changes in PYY concentrations can indirectly alter the risk of respiratory symptoms. In other words, a higher PYY level is associated with lower fat tissue deposits; therefore, the load on the bronchopulmonary system drops [20]. We have observed the inverse association between the PYY level and CB, and there was no correlation when resistin was included in the model.

Conclusion

In individuals of 25 to 44 years of age, the odds of CB are associated with active smoking status, SBP and AO. The odds of CB in individuals of 25 to 44 years old have inverse association with blood PYY and resistin levels; however, when age, gender, smoking status, AO status, PYY, and resistin were included in the model, the association remained only with smoking status, AO, and blood resistin. The results confirm the available data on the presence of cause-effect relation between development of CB and AO; they also add to the understanding of the pathogenetic patterns of bronchopulmonary inflammations.

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All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

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