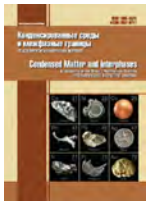

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Gender differences in lipid metabolism

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Abstract

The search for early markers of atherosclerosis is an effective method for providing personalized medicine allowing the prevention of the progression of this pathology. The aim of this study was the determination of the total indices of dyslipidemia and the identification of the gender indices of the extended lipid profile in the population of residents of the Southern and Central Federal Districts (Voronezh, Belgorod, Lipetsk, Kursk and Rostov regions) for the identification of early markers of atherogenicity. In a simultaneous clinical study, involving 339 patients (mean age 48 years), the concentrations of total cholesterol, triglycerides, LDL (low density lipoproteins), HDL (high density lipoproteins), apolipoproteins B and A1, the ApoB/ApoA1 ratio and the atherogenic coefficient were determined. For the identification of the relationship between changes in lipid profile indicators with cytolysis syndrome and indicators of carbohydrate metabolism, the activity of ALAT (alanine aminotransferase), GGTP (gamma-glutamyl transpeptidase) and glucose content were also studied. Analysis of the results of the lipid spectrum of the population sample of the middle age group revealed significant metabolic disorders of lipid metabolism with a predominance of atherogenic lipid fractions and a significant excess of indicators of atherogenic lipid fractions in middle-aged men in comparison with women. It has been shown that the apoB/apoA1 index can be used as an auxiliary marker for early assessment of the prevalence of atherogenic lipid fractions, allowing the identification of risk groups for the development of diseases associated with metabolic disorders.

Keywords: Lipid metabolism, Atherosclerosis, Metabolic syndrome, Cholesterol, Triglycerides, LDL, HDL, ApoV / ApoA1, Atherogenic coefficient

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1. Introduction

Cardiovascular diseases (CVD) associated with atherosclerosis represent a global medical and social problem and are the main cause of mortality and disability in the population [1]. The PESA study showed that worldwide 71 % of middle-aged men and 43 % of women have signs of subclinical atherosclerosis [2], mortality from CVD in the Russian Federation in 2017 amounted to 587.6 cases per 100 thousand population [3, 4].

The concept of high cardiovascular risk is associated primarily with dyslipidemia due to an increase in the concentration of atherogenic lipids. Under normal conditions, insulin limits lipolysis, however, with the development of insulin resistance it is unable to suppress this process [5]. The production of very-low-density lipoproteins (VLDL) and triglycerides in the liver and their retention in tissues increases with the development of insulin resistance and dyslipidemia is formed [6]. The nosological spectrum of diseases associated with dyslipidemia, has a similar pathogenesis, determined by laboratory markers of the disease: metabolic syndrome; obesity; diseases of the biliary tract and liver; steatohepatitis; arterial hypertension; hypothyroidism and adrenal gland pathology, thromboembolism, COVID-19 [7–13].

The studies using PCSK9 inhibitors [14] and the results of the ODYSSEY OUTCOMES study with alirocumab [15] have shown that lowering LDL cholesterol decreases the incidence of cardiovascular heart disease [14, 15]. Although LDL is recognized as the main source of intracellular lipid accumulation in plaque, native LDL does not induce significant lipid accumulation in cultured cells. The modification of LDL, which changes the physicochemical characteristics of the particles is atherogenic [16]. During the course of its modification, the LDL particle is first desialylated, followed by an increase in the particle density, a decrease in size, and the acquisition of a negative charge [17]. Modified LDL is utilized mainly by the non-specific phagocytosis, which leads to the accumulation of intracellular cholesterol and the formation of foam cells [18]. Foam cells are an important structural component of atherosclerotic plaque, and modified LDL forms immune complexes that have a damaging effect on the vascular wall, narrowing the vessel lumen and promoting thrombus formation [19].

Despite the leading role of LDL in the development of CVD, associated with atherosclerosis, the role of other lipoproteins, in particular apolipoprotein B (apoB), which is the main component of LDL was demonstrated [20]. It has been shown that the concentration of apoB can be considered a direct indicator of the total amount of atherogenic lipoproteins in the bloodstream [21]. The largest studies, INTERHEART [22] and AMORIS [23], showed that the determination of the levels of apoB and apoA1 in blood plasma seems to be the most informative indicator of the risk of developing CVD [22, 24].

Previously, the main role in the development of atherosclerosis was attributed to hypercholesterolemia, but recent clinical studies showed the participation of any hyperlipidemia in the onset and further development of atherosclerosis [25]. Thus, it was shown that although triglyceride levels above 1.7 mM/l are a factor of increased risk of CVD, the positive effect of lowering triglycerides has not been confirmed by evidence-based medicine [26]. The leading "pacemaker" of the pathological process and the degree of functional abnormalities which is not always determined by functional and visual diagnostic methods, are determined based on the presence and combination of biochemical abnormalities [27–29].

The role of dyslipidemic disorders in the etiopathogenesis of CVD, diabetes mellitus, hypertension, non-alcoholic steatohepatosis, diseases of the biliary tract, menopausal disorders determine the relevance of the search for early markers for predicting the risk of dyslipidemia in men and women [30,31].

Possible methods to search for biomarkers are:

1. In-depth/extended study of the lipid profile.

2. Inclusion in the analysis of new markers characterizing the functioning of the main metabolic systems and their disorders, which are involved in the pathogenesis of atherosclerosis in addition to the traditional factors of cardiovascular risk [32].

For the identification of the specificity and predictive value of apolipoproteins apoA1 and apoB in comparison with cholesterol, HDL,

LDL, and triglycerides we decided to analyse the extended lipid spectrum during the stage of transition of women to menopause and the indicators of men of a similar age group in order to determine the basic risks of development of atherogenic dyslipidemia. This approach determines the resources of health during the formative stage of risks associated with age, regardless of hormonal changes. The aim of this study was the determination of the total indices of dyslipidemia and the identification of the gender indices of the extended lipid profile in the population of residents of the Southern and Central Federal Districts (Voronezh, Belgorod, Lipetsk, Kursk and Rostov regions) in order to search for early markers of atherogenicity.

2. Experimental

The results of research obtained in the laboratory of OOO New Medical Technologies, Voronezh were used in the study.

For the identification of the relationship between changes in lipid profile parameters with cytolysis syndrome and indicators of carbohydrate metabolism, the activity of alanine aminotransferase (ALAT), gamma-glutamyl transpeptidase (GGTP), and glucose content was also studied in patients. The clinical study was carried out simultaneously, in the period from January to October 2019, the blood of 339 patients (242 women and 97 men) was examined, their average age was 48 years.

The participants were examined according to a unified scheme. A single blood sample with a volume of 10 ml on an empty stomach in the morning was carried out using a venipuncture of the superficial veins at the bend of the elbow for biochemical analysis. Serum was obtained from venous blood by standard methods.

Determination of total cholesterol, triglycerides, high density lipoprotein cholesterol was carried out by the colorimetric enzymatic method using Beckman Coulter AU analysers (USA) [33, 34, 35].

The determination of total cholesterol was carried out by the enzymatic method [33]. The reaction mixture included: 103 mM/l phosphate buffer (pH = 6.5), 0.31 mM/l 4-aminoantipyrine, 5.2 mM/l phenol, 3.3 μkat/l cholesterol esterase, 3.3 μkat/l cholesterol oxidase, 166.7 μkat/l peroxidase. The colour intensity of the reaction mixture, measured at 540/600 nm, is directly proportional to the total cholesterol concentration in the sample.

The method for measuring the concentration of triglycerides is based on the enzymatic method for the determination of glycerol [34]. Triglycerides present in the sample are hydrolysed to glycerol and fatty acids under the action of several bacterial lipases. The absorption intensity at 660/800 nm is proportional to the triglyceride content. The colorimetrised mixture contained: 50 mM/l PIPES buffer (pH = 7.5), 25 μkat /l lipase, 4.6 mM/l Mg^{2+}, 8.3 μkat/l glycerol kinase, 0.25 mM/l MADB, 16.3 μkat/l peroxidase, 0.5 mM/l 4-aminoantipyrine, 24.6 μkat/l ascorbic acid oxidase, 1.4 mM/l ATP, 24.6 μkat/l glycerol-3-phosphate oxidase.

The level of HDL was determined by the formation of a coloured product of the enzymatic reaction after antibodies against human β-lipoprotein, which are part of the reagent, bound to lipoproteins other than HDL (LDL, VLDL and chylomicrons), as a result, antigen-antibody complexes were formed, which are incapable of participating in enzymatic reactions [35]. The reaction mixture for determination of HDL-cholesterol contained: anti-human β-lipoprotein antibodies, 0.8 IU/ml cholesterol esterase, 4.4 IU/ml cholesterol oxidase, 1.7 IU/ml peroxidase, 2.0 IU/ml ascorbic acid oxidase, 30 mM/l Good's buffer (pH = 7.0), 0.20 mM/l N-ethyl-N- (2-hydroxy-3-sulfopropyl) -3,5-dimethoxy-4-fluoroaniline, 0.67 mM/l 4-aminoantipyrine.

The LDL concentration was calculated using the formula:

LDL = Total Cholesterol – (Triglycerides/2.2) – – HDL [36].

The atherogenic index (AI) was calculated using the following formula:

AI = (total cholesterol – HDL)/HDL [36].

Apoproteins: apo A1 and apo B were determined by the immunoturbidimetric method using Beckman Coulter reagents (USA). The method is based on measuring the absorption intensity of insoluble aggregates formed as a result of the immunological reaction of anti-apoproteins with antibodies. The concentration

of apoproteins was estimated based on the degree of turbidity development [37, 38, 39]. The compositions of the reaction mixtures for the determination of apoproteins A1 and B included the following components, respectively: 8 mM/l Tris buffer (pH = 7.4), 106 mM/l sodium chloride, 3.5 % polyethylene glycol 6000, goat anti-apoprotein A1 antibodies ≈ 0.14 g/l and 8.6 mM/l Tris buffer (pH = 7.4), 125 mM/l sodium chloride, 4 % polyethylene glycol 6000, goat anti-lipoproteins B antibodies ≈ 1.93 g/l.

ALAT activity (EC 2.6.1.2) was determined by the decrease in optical density at 340 nm caused by the oxidation of NADH in a coupled reaction in the presence of LDH [40]. The reaction mixture for the determination of ALAT contained: 100 mM/l Tris buffer (pH = 7.15), 500 mM/l L-alanine, 12 mM/l 2-oxoglutarate, 1.8 kU/l lactate dehydrogenase, 0.20 mM/l NADH, 0.1 mM/l pyridoxal phosphate.

GGTP activity (EC 2.3.2.2) was determined by the rate of formation of 5-amino-2-nitrobenzoate at 405 nm, in a reaction mixture containing: 150 mM/l glycylglycine (pH = 7.7), 6 mM/l L-γ-glutamyl-3-carboxy-4-nitroanilide [41].

For the quantitative determination of glucose, we used the hexokinase method based on an increase in optical density at 340 nm caused by the formation of NADH [42]. Determination of glucose concentration was carried out in a reaction mixture containing: 24 mM/l PIPES buffer (pH = 7.6), 2.0 mM/l ATP, 1.32 mM/l NAD^+, 2.37 mM/l Mg^{2+}, 0.59 kU/l hexokinase, 1.58 kU/l G6F-DG.

Statistical data processing: quantitative analysis data are presented as M ± m, where M is the mean, m is the standard error of the mean. For the identification of correlations between the studied indicators, the Pearson coefficient (*r*) was used. This study discusses the values of the average (0.30–0.50), significant (0.50–0.70), and high (0.70–0.90) degrees of correlation. The statistical processing was carried out using the Microsoft Excel program. Differences were considered significant at $p < 0.05$.

3. Results and discussion

As a result of the analysis, the presence of an average, significant, and high correlation of the total cholesterol (TC) concentration with the level of triglycerides (TG), LDL, HDL, apolipoproteins B and A1, ApoB/ApoA1 and the atherogenic index was revealed (Table 1). At the same time, there was no correlation of TC with the activities of ALAT, GGTP, or glucose concentration (data not shown). However, the average level of correlation between the TG level and these indicators was revealed (Table 2). For further research, the patients were divided into groups: a control group (patients with a normal TC level/or a normal TG level) and patients with an increased level of TC

Table 1. Values of lipid metabolism indicators and their correlation with blood cholesterol concentration

Indicators	Mean ± standard error of the mean (*M*±*m*)	Pearson's correlation coefficient r, $p < 0.05$
Total cholesterol, mM/l	5.54 ± 0.08	
Triglycerides, mM/l	1.52 ± 0.06	0.26
LDL cholesterol, mM/l	3.60 ± 0.07	0.94
HDL cholesterol, mM/l	1.28 ± 0.02	0.38
Apolipoprotein B, mg/dl	124.60 ± 2.02	0.87
Apolipoprotein 1, mg/dl	180.89 ± 1.81	0.26
ApoB/ApoA1	0.71 ± 0.01	0.64
Atherogenic index	3.55 ± 0.08	0.53

Table 2. The values of lipid metabolism indicators and their correlation with the concentration of blood triglycerides

Indicators	Mean ± standard error of the mean (*M*±*m*)	Pearson's correlation coefficient r, $p < 0.05$
Triglycerides, mM/l	1.52 ± 0.06	
ALAT, U/l	26.46 ± 1.30	0.22
GGTP, U/l	39.75 ± 3.86	0.22
Glucose, mM/l	5.85 ± 0.12	0.38

or TG. The comparison was made between the respective groups (normal TC-increased TC and normal TG-increased TG).

In the course of the study, it was revealed that 59.5 % of patients had an increased level of total cholesterol (TC, mean value – 6.51 mM/l, reference value – 3.63–5.20 mM/l) (Table 3). Elevated cholesterol levels were observed in 56.4 % of women (mean value – 6.69 mM/l) and 52.1 % of men (mean value – 6.29 mM/l) (Fig. 1).

The TG level in the group of patients with elevated TC was increased in 15 % of patients (3.68 mM/l, reference value <2.2 mM/l), in the group of patients with normal TC this indicator was 9 % (Table 3). Among patients with an increased TC level, an increase in TG was found in 17.3 % of women (mean value 3.22 mM/l) and 30.6 % of men (mean value – 3.55 mM/l, the number of men or women in the group with normal or increased TC was taken as 100 %). Among patients with a normal TC level, an increase was found in 7.9 % of women and 11.6 % of men (Fig. 2).

Among patients with an increased TC level, 61.4 % had an increase in the LDL content (on average 4.94 mM/l, reference value < 3.9 mM/l) (Table 3). In this group, an increase in LDL was detected in 66.1 % of women (mean value – 4.93 mM/l) and 63.6 % of men (mean value – 4.77 mM/l) (Fig. 3).

The blood concentration of apolipoprotein B contained in atherogenic lipoproteins correlates well with these data. Despite the fact that the mean value of the concentration of apolipoprotein in the group of patients with increased TC level

Table 3. Diagnostic indicators of the development of pathology in the control group and group with high cholesterol level

Indicators	Mean ± standard error of the mean ($M \pm m$) in patients with normal cholesterol	Percentage of patients with pathology	Mean ± standard error of the mean ($M \pm m$) in patients with normal cholesterol	Percentage of patients with pathology
Total cholesterol, mM/l	4.34 ± 0.05	0%	6.51 ± 0.09	100%
Triglycerides, mM/l	3.03 ± 0.26	9.0%	3.68 ± 0.23	15.9%
LDL cholesterol, mM/l	<3.9 мМ/л	0%	4.94 ± 0.10	61.4%
HDL cholesterol, mM/l	1.01 ± 0.02	69.3%	1.08 ± 0.02	49.7%
Apolipoprotein B, mg/dl	141.63 ± 5.82	4.6%	161.94 ± 3.14	64.0%
Apolipoprotein 1, mg/dl	227.01 ± 4.62	13.2%	230.46 ± 3.34	27.4%
ApoB/ApoA1	1.25 ± 0.21	1.3%	1.25 ± 0.04	11.8%
Atherogenic index	4.33 ± 0.12	24.0%	4.9 ± 0.11	60.4%
ALAT, U/l	46.12 ± 3.44	22.6%	48.84 ± 3.33	25.3%
GGTP, U/l	76.49 ± 16.15	36.0%	57.91 ± 5.34	52.4%
Glucose, mM/l	7.44 ± 0.54	21.6%	7.75 ± 0.53	25.9%

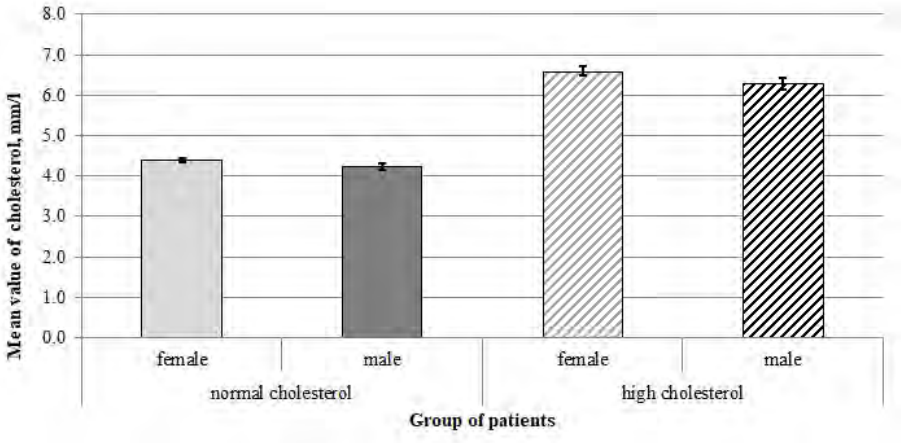

Fig. 1. Cholesterol level in the control group of patients and patients with increased cholesterol

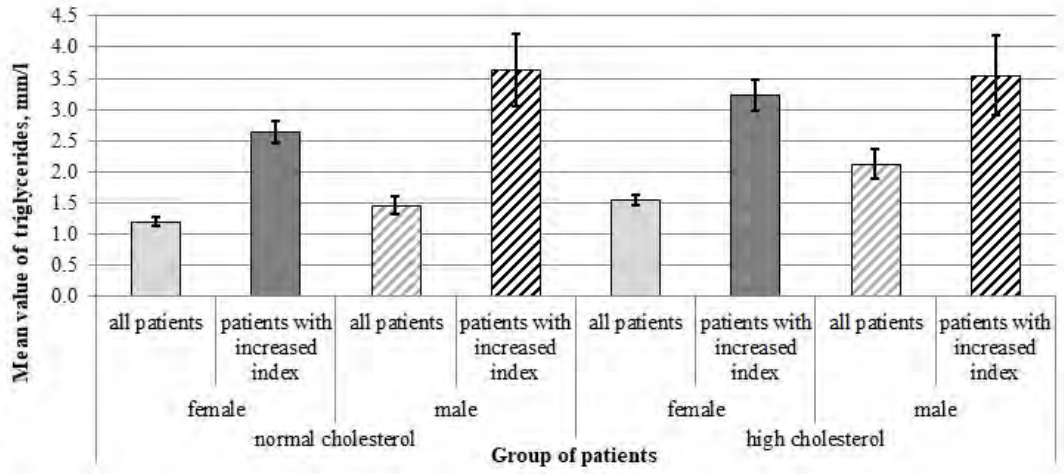

Fig. 2. Triglycerides level in the control group of patients and patients with increased cholesterol

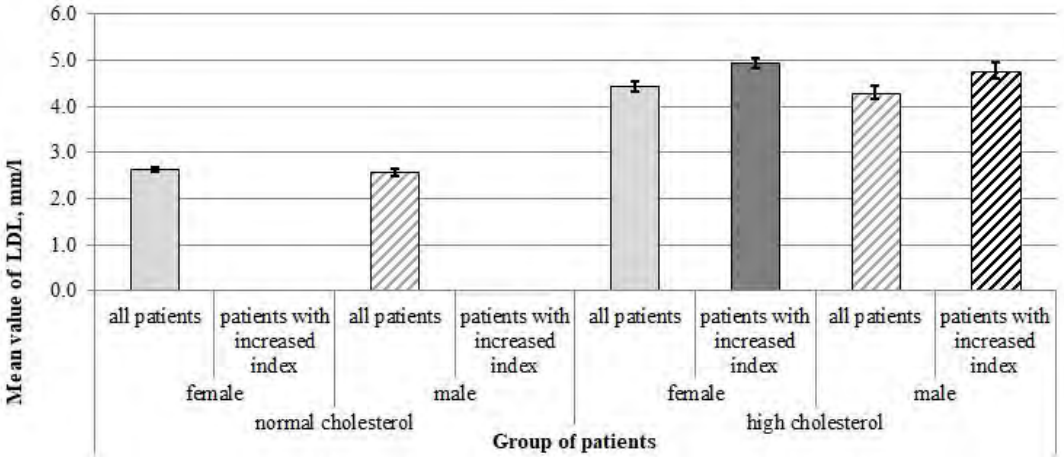

Fig. 3. LDL level in the control group of patients and patients with increased cholesterol

was 144.47 mg/dl with a reference value of 55–130 mg/dl, a significant increase to 161.4 mg/dl was found in 65.4 % of women and increase up to 169.6 mg/dl was revealed in 50 % of men (Fig. 4).

In some patients (13.2 %), with normal levels of total cholesterol, an increase in the level of apolipoproteins A1 to mean value of 227.0 mg/dl was observed (Table 3) (reference value – 105–205 mg/dl), which has a positive prognostic character, since these proteins are part of HDL and are responsible for receptor recognition of lipoproteins by cells. In patients with elevated TC levels, the average apoA1 value did not exceed the reference value and was 192.4 mg/dl. However, in 31.6 % of women and 16 % of men, the level of apoA1 was significantly increased and comprised 233.6 and 218.8 mg/dl, respectively. In the group of people with normal TC, an increase in the level of apoA1 was observed in 15.2 % of women and 8.7 % of men (Fig. 5).

The apoB/apoA1 ratio can be considered as an alternative assessment of the risk of complications of cardiovascular diseases. An increased risk of coronary artery disease was observed when the ratio was > 0.9 in men and > 0.8 in women. However, current clinical guidelines do not propose to consider the apoB/apoA1 ratio as a target when prescribing lipid-lowering therapy (LDL, HDL, and apoB cholesterol are used for therapeutic purposes). Our study showed that the apoB/apoA1 ratio was increased in 11.0 % of women (average value –1.29) and 14 % of men (average value – 1.14) in the group of patients with high TC (Fig. 6). In the group of patients with normal TC, an increase in this indicator was not detected in women and was observed only in 4.3 % of men (Fig. 6). The association of an increased risk of coronary artery disease with an increased apoB/apoA1 ratio has been shown in a number of studies [43, 44], and recent data have not confirmed

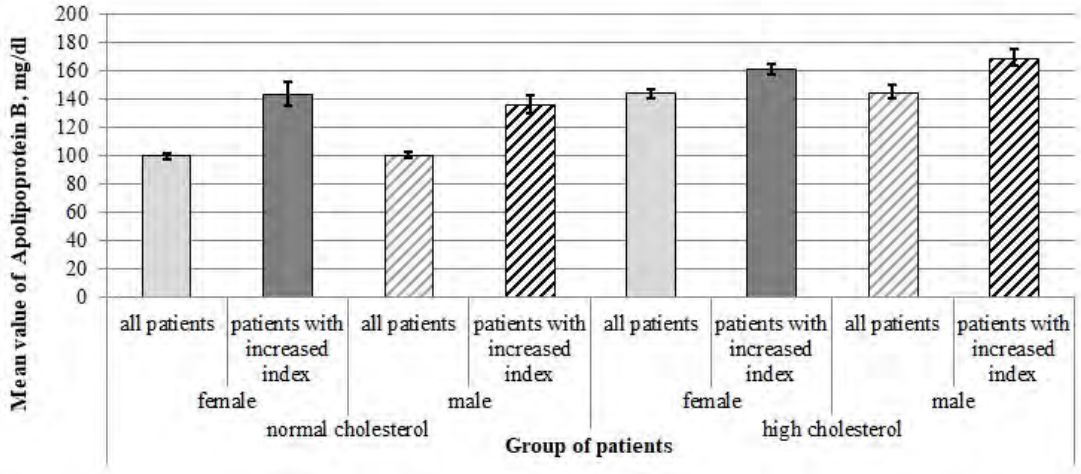

Fig. 4. Apolipoprotein B B level in the control group of patients and patients with increased cholesterol

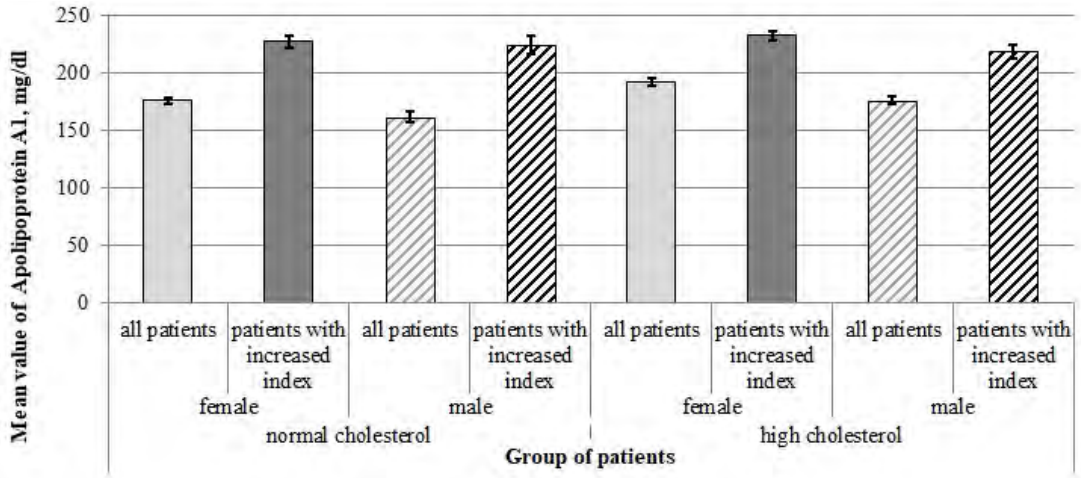

Fig. 5. Apolipoprotein A1 level in the control group of patients and patients with increased cholesterol

the role of isolated hypertriglyceridemia in the prediction of risk for cardiovascular diseases. As was noted by the authors, this criterion can only be valid in combination with LDL and HDL levels [45, 46]. The same diagnostic value of the value of the apoB/apoA1 ratio and the TG level for the diagnosis of metabolic syndrome was shown [47]. Also, some authors discuss the technical inconvenience associated with the requirement of fasting for 12 h before taking blood for analysis for TG and HDL cholesterol [48]. In contrast, the measurement of ApoB and ApoA1 does not require 12 hours of fasting. Thus, the ApoB/ApoA1 ratio appears to be more appropriate in the clinical setting than TG, LDL, and HDL levels for identifying patients with metabolic syndrome and CVD risk.

An increase in the atherogenic index of plasma, as a result of a decrease in HDL, was found in 24 % of patients with normal TC levels, which indicates the risk of developing atherosclerosis despite normal TC and LDL levels. HDL was decreased in 44.4 % of women (mean value – 1.12 mM/l, reference value > 1.3) and 63.8 % of men with high cholesterol (mean value – 1.01 mM/l) (Fig. 7). The AI was increased in 60.4 % of patients in the group with increased TC level (mean value – 4.90, reference value < 3.5) (Table 3). In the group of patients with normal cholesterol, a decrease was observed in 62.6 % of women and 90.2 % of men (Fig. 8). In the group of patients with normal TC levels, an increase in AI was found in 17.6 % of women and 39.5 % of men. A similar trend was found in the group of patients with increased TC levels: AI was increased in 55.2 % of women (mean value – 4.83) and 76.7 % of men (mean value – 4.99) (Fig. 8). The data obtained unambiguously indicate a greater predisposition of men to atherosclerosis.

The established gender differences in atherogenic indices in different nosoologies

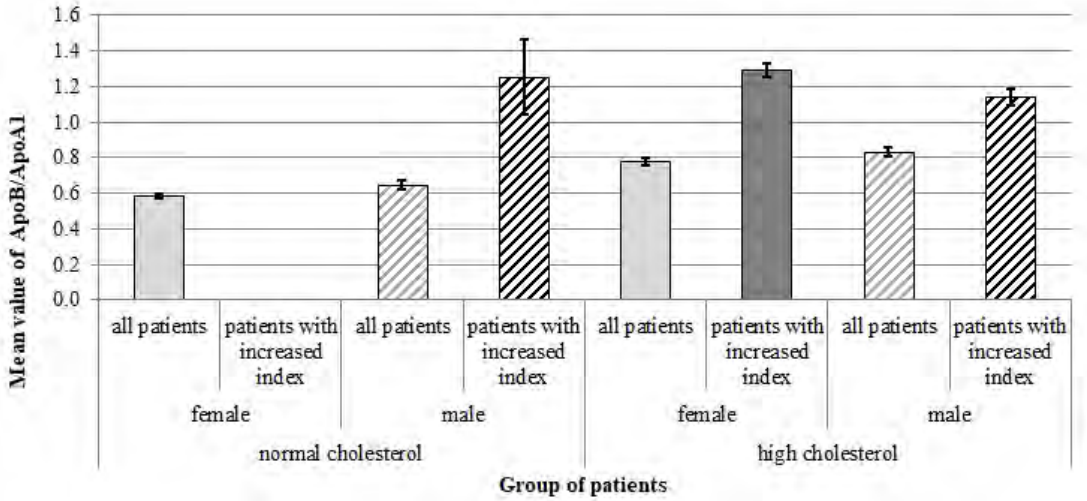

Fig. 6. ApoB/ApoA1 ratio in the control group of patients and patients with increased cholesterol

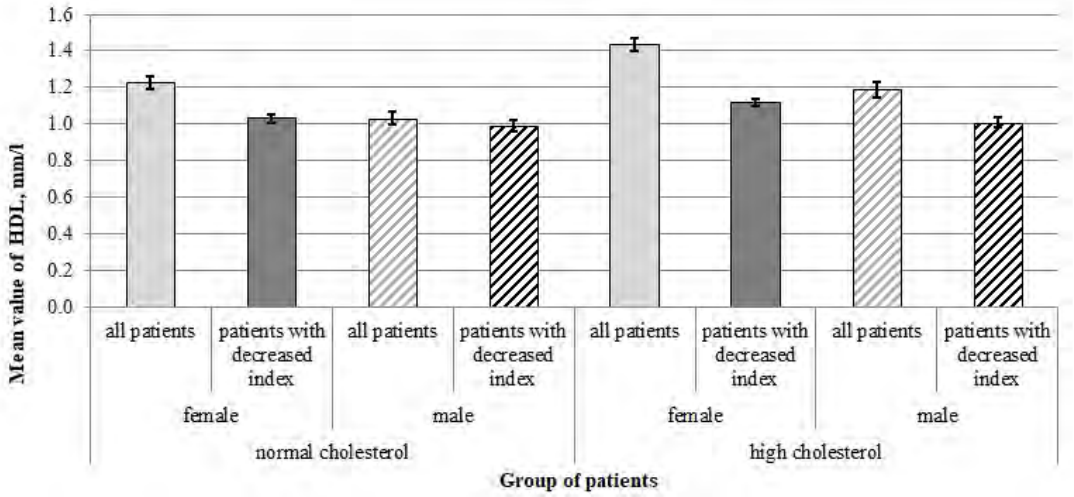

Fig. 7. HDL level in the control group of patients and patients with increased cholesterol

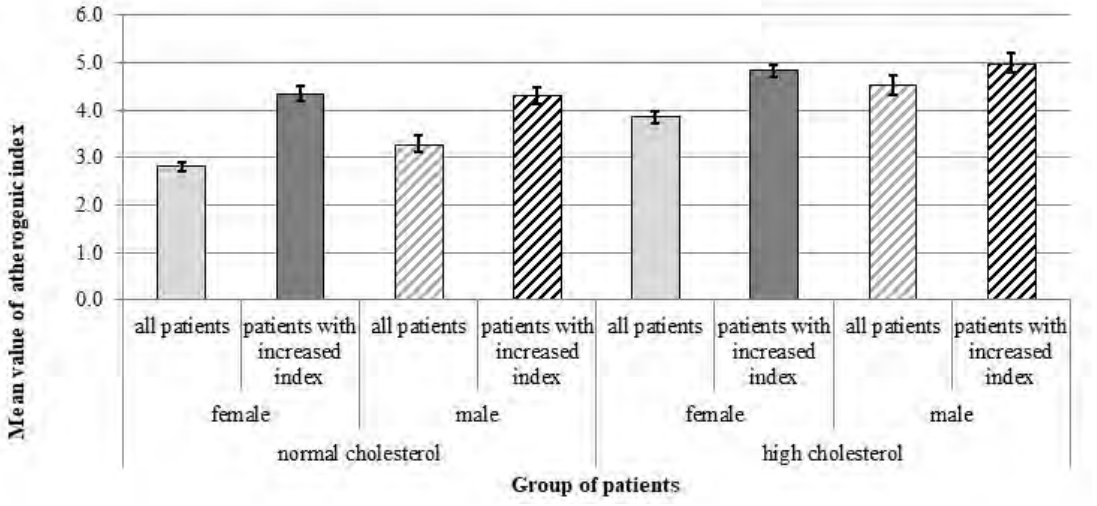

Fig. 8. Atherogenic index in the control group of patients and patients with increased cholesterol

and in different age subgroups characterize men as initially predisposed to the development of abdominal obesity in metabolic disorders, since abdominal obesity is androgen-dependent. In addition, with the formation of deposits of visceral fat due to metabolic syndrome, insulin sensitivity is impaired, which triggers a vicious circle and aggravates insulin resistance [49].

Interestingly, the role of the atherogenic lipid spectrum in the development of type 2 diabetes mellitus and hypertension in women over 60 is higher than in men. At the same time, the risk group is composed of women with early menarche, and the frequency and severity of cardiovascular events and thromboembolic complications correlates with the duration of the menopause. In women, the transition of the "silent" course of ischemic heart disease with the late appearance of clinical syndromes in the form of pain syndrome is recorded. Certain erasure of the clinical manifestations of diabetes mellitus, coronary artery disease, characteristic of women, contributes to a later detection of diseases in comparison with men. Ten years after the onset of menopause (postmenopause), the risk of cardiovascular disease in women is similar to that in men of the same age [50].

Statistically significant differences between men and women were not revealed in the study of the correlation between the level of TG and ALAT, GGTP and glucose, and, accordingly, patients were not divided according to gender.

In the group of patients with elevated TG levels, 29.2 % of patients showed an increase in ALAT levels (mean value – 46.12 U/l, reference value – up to 40 U/l for men and 35 U/l for women) (Fig. 9).

An increase in the indices of the enzymatic activity of ALAT, as an enzyme contained in liver cells, and to a lesser extent in the kidneys, muscles, heart and pancreas, reflect destructive damage in the above organs or secondary liver changes in metabolic disorders. It was shown that increased ALAT levels are clinically and histologically associated with steatohepatosis [51, 52].

In the same group, the GGTP activity was increased in 60 % of patients (the norm was up to 32 U/L). Among patients with normal TG levels, ALAT activity was increased in 14.6 % of patients, and GGTP activity increased in 38 % of patients (Fig. 10). An increase in GGTP indicates the destruction of parenchymal organs. Small increase in levels of GGTP and ALAT have been shown in patients with steatohepatosis [53].

Depending on the presence/absence of abdominal obesity, mild and moderate steatohepatosis was determined 11 times more often in women than in men, while cirrhosis, an extreme degree of damage to hepatocytes, prevailed in men. Clinical signs of steatohepatosis are an increase in the concentration of insulin (however, its numbers are not proportional to the degree of liver damage), C-peptide, hypertriglyceridemia, an increase in the activities of ALAT and aspartate amnotransferase (ASAT). It has been proven that an increase in liver function tests is less informative in women, which is probably due to the reaction of ALAT and ASAT as the ability of the liver to immediately respond

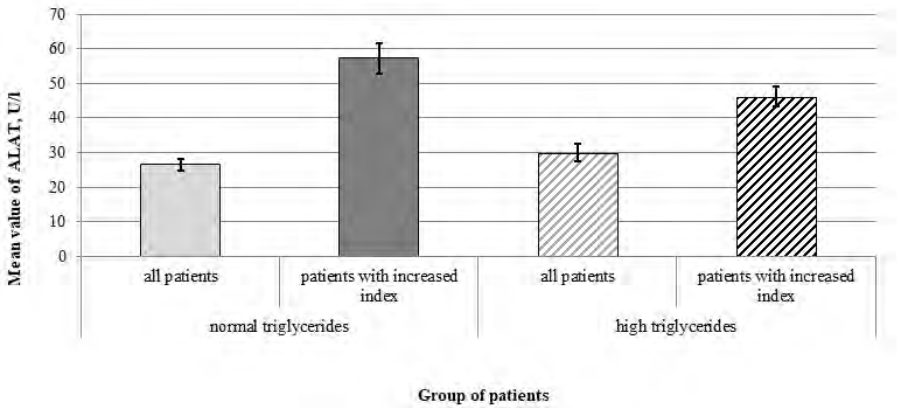

Fig. 9. ALAT activity in the control group of patients and patients with increased triglycerides

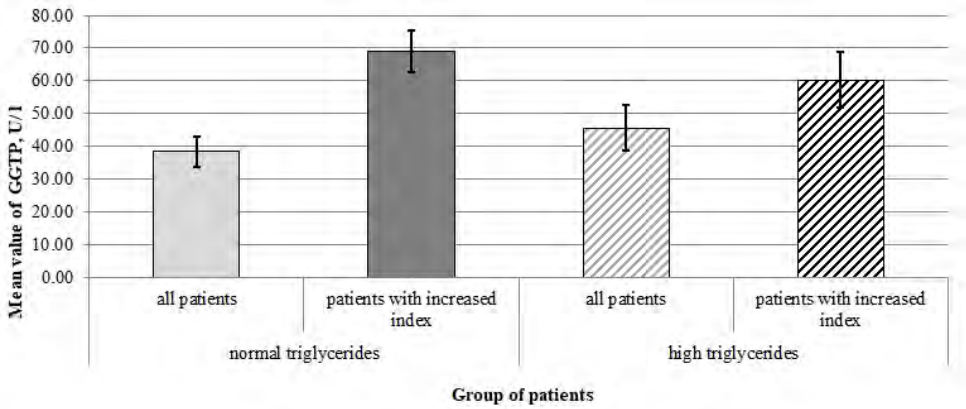

Fig. 10. GGTP activity in the control group of patients and patients with increased triglycerides

to hepatotoxic effects. In men, this potential is reduced under conditions of systematic damage to hepatocytes due to the systematic consumption of fried, spicy foods, heavy alcohol use, etc. A similar mechanism is triggered in women with abusive drinking behaviour, in this case, liver function tests can remain low for a long time.

In the group of patients with normal TG, an increase in glucose content was detected in 21.6 % (mean value – 7.43 mM/l, reference value – up to 6.2 mM/l), while in the group of patients with elevated TG an increase in glucose was more significant (mean value – 8.44 mM/l) and was detected in 42.3 % of patients (Fig. 11). This correlation reflects the need for the ABC strategy proposed by the National Diabetes Education Program: diabetologists and patients with diabetes should pay attention not only to the control of glycemia ("A" - HbA1c) and blood pressure ("B" - blood pressure), but also to the level of blood lipids ("C" - cholesterol) [54]. The main cause of hypertriglyceridemia in diabetes mellitus is the low sensitivity of visceral adipose tissue to the anti-lipolytic action of insulin, which leads to increased lipolysis, the entry of large amounts of free fatty acids into the portal bloodstream and, in combination with hyperinsulinemia, an increase in the synthesis of triglycerides and VLDL by the liver. In addition, in patients with type 2 diabetes with hyperglycemia, the activity of endothelial lipoprotein lipase, which is responsible for the catabolism of triglycerides and VLDL, is reduced, which aggravates this disorder.

4. Conclusions

Thus, as a result of the conducted studies of lipid metabolism indicators in middle-aged group (from 32 to 61 years) of Southern and Central Federal Districts of Russia (Voronezh, Belgorod, Lipetsk, Kursk and Rostov regions) the following distinguishing features were identified:

– significant metabolic disorders of lipid metabolism in the middle age group with a predominance of atherogenic lipid fractions,

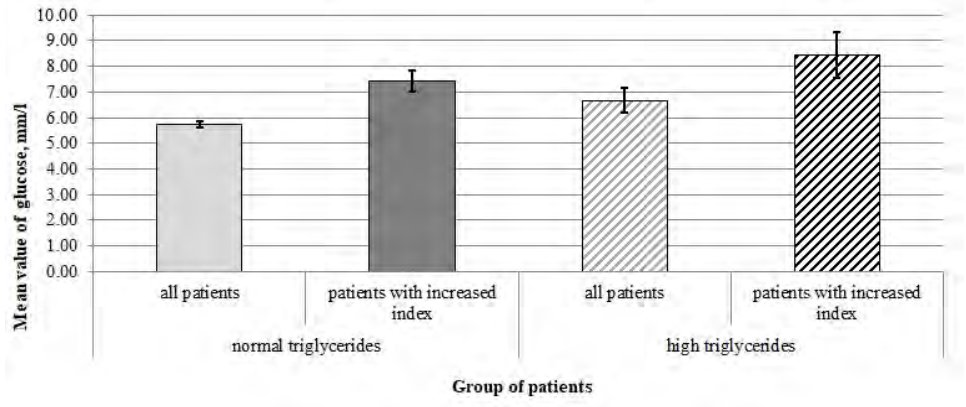

Fig. 11. Glucose content in the control group of patients and patients with increased triglycerides

which can serve as a negative indicator of the health status of the working-age population;

– in the absence of a universal marker of lipid atherogenicity for the early diagnosis of pathological changes in the body, a comprehensive screening of LDL fractions, triglycerides, glucose indicators for the isolation of risk groups in relation to the development of metabolic disorders leading to the development of atherogenic vascular lesions is justified. The feasibility of determination of insulin, conducting a glucose tolerance test, C-peptide is determined by the specialists in order to clarify the basic diagnosis, and their results do not always correlate with the severity of atherogenic changes;

– the results of the study showed that the apoB/apoA1 ratio can be used as an auxiliary marker for the early assessment of the prevalence of atherogenic lipid fractions, allowing to identify risk groups for the development of diseases associated with metabolic disorders;

– the revealed significant excess of atherogenic lipid fractions in men of the middle age group in comparison with women, at the stage of addition of natural menopausal changes in lipid metabolism, determines an almost two-fold increase in the risks of developing cardiovascular lesions in men in the age category up to 50 years;

– the revealed correlation of the TG level and the increase in glucose content shows the need for constant monitoring of the blood lipid profile in patients with diabetes;

– screening detection of indicators of hypertriglyceridemia and/or dyslipidemia, even in the absence of a somatic pathology, should be an indication for in-depth clinical and laboratory examination: exclusion of organic lesions of parenchymal organs (primarily of the liver and biliary tract).

Author contributions

Mittova V. O. – writing text; research design development. Khoroshikh A. O. – analysis of scientific literature, bibliography design. Zemchenkova O. V. – preparation and revision of the research part of the text. Ryazantsev S. V. - experimental research, data collection and analysis. Maslov O. V. – development of methodology, data processing. Corzh E. V. – interpretation of data, final conclusions, preparation of a literature review. Ryasnaya-Lokinskaya L. S. – writing of the clinical part of the discussion of the results, analysis of scientific literature. Alabovsky V. V. – scientific leadership, research concept.

Conflict of interests

The authors declare that they have no known financial conflicts of interest or personal relationships that might affect the work presented in this article.

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