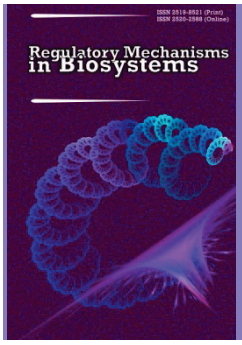

Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.,
2023, 14(1), 23–27
doi: 10.15421/022304

Gender characteristics of lipid metabolism in patients with coronary heart disease and type 2 diabetes mellitus

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Article info

Received 10.01.2023
Received in revised form 02.02.2023
Accepted 03.02.2023

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Yakovleva, Y. S., Ostanina, T. H., Voronkova, Y. S., Snisar, O. S., & Voronkova, O. S. (2023). Gender characteristics of lipid metabolism in patients with coronary heart disease and type 2 diabetes mellitus. Regulatory Mechanisms in Biosystems, 14(1), 23–27. doi:10.15421/022304

Heart and metabolic diseases are very common in society today. There are many special features in their manifestation that have influence on prognosis and therapy approaches. Among them are gender characteristics. The aim of the research was to determine the gender peculiarities of disorders of lipid metabolism in patients with coronary heart disease and type 2 diabetes mellitus (T2DM). The study of the blood lipid spectrum in patients with coronary heart disease and T2DM was conducted in 72 patients aged 37 to 85 years old. The patients with coronary heart disease were divided into 2 groups depending on the presence or absence of T2DM: 1 group (n = 40) – patients with coronary heart disease only (Stable Angina Pectoris); group 2 (n = 32) – patients with coronary heart disease and T2DM. Each group was divided into subgroups depending on the gender of the patients: 1A and 2A – males, 1B and 2B – females. Despite the presence of T2DM, a majority of patients with coronary heart disease were overweight and obese. At the same time, obesity was more common in the female subgroups (1B – 45.0%, 2B – 64.7%) than in the male subgroups (1A – 35.0% and 2A – 33.3% respectively). There was an increase in the levels of total cholesterol, triglycerides and low-density lipoproteins for impaired lipid metabolism in patients with coronary heart disease. There was a slightly higher level of total cholesterol (6.12 ± 2.06 mmol/L) and low-density lipoproteins (4.24 ± 1.79 mmol/L) and a lower level of triglycerides (1.63 ± 0.65 mmol/L) in females than in males (5.15 ± 1.29, 3.71 ± 1.14 and 2.40 ± 1.06 mmol/l, respectively). Disruption of lipid metabolism was characterized predominantly by an increase in levels of triglycerides and low-density lipoproteins in blood in patients with coronary heart disease and T2DM regardless of gender. About a quarter of males (25.0% with coronary heart disease and 26.7% with coronary heart disease with T2DM) and females with T2DM (23.5%) reached the target total cholesterol level (<4.0 mmol/L), less frequently females with coronary heart disease (15.0%). The incidence of low-density lipoproteins target (<1.8 mmol/L) was significantly lower than total cholesterol: about 5.0% in males (regardless of the presence of T2DM) and 10.0% in females with coronary heart disease. Women with coronary heart disease and T2DM did not reach the target low-density lipoproteins level (<1.8 mmol/L). In most patients with coronary heart disease dyslipidemia grade II by Fredrickson was observed regardless of the presence of T2DM: in 100% of patients with coronary heart disease and 81.1% of patients with coronary heart disease and T2DM. A distinctive feature of impaired lipid metabolism in patients with coronary heart disease and T2DM is the presence in some of patients of Dyslipidemia grade IV by Fredrickson (6.7% of males and 5.9% of females) and the absence of Dyslipidemia class IIa in males in this group. Analysis of the achievement of the target levels of total cholesterol and low-density lipoproteins indicates insufficient prescribing of adequate hypolipidemic therapy for patients with coronary heart disease and T2DM.

Keywords: heart disease diabetes; obesity; risk factors; total cholesterol; triglycerides; low-density lipoproteins; high-density lipoproteins; gender.

Introduction

Over the past decades, cardiovascular diseases have maintained a leading place in the overall structure of the causes of mortality and disability of the working population in the developed countries of the world, and in recent years this indicator has had a clear tendency to increase (Garkusha & Korzun, 2015; Mankovsky, 2018; Rosoff et al., 2020). According to data of the World Health Organization (WHO), cardiovascular diseases led to the death of 17.5 million people in 2018 and rank first among the causes of mortality both in the world and in Ukraine – more than 50% in the structure of causes of death of the population. According to the data of the State Statistics Service of Ukraine, in 2019, 265,628 people died from diseases of the circulatory system, which is 67.3% in the mortality structure. In the modern world, the relevance of a multifactorial approach to the implementation of measures for primary and secondary prevention of cardiovascular diseases is gaining particular importance (Garkusha & Korzun, 2015).

In recent years, another important medical and social problem has gained an increasingly "epidemic" character – diabetes (Sypalo et al., 2017), which correlates with higher risk of development of cardiovascular diseases (Penna et al., 2020). After cancer and cardiovascular diseases, diabetes mellitus (DM) is one of the leading cause of death in the world (Tomic et al., 2022). WHO recognized DM as an epidemic of non-infectious origin (Aschner et al., 2016). The predicted number of patients with type 2 diabetes mellitus (T2DM) will be about 642 million by 2040 (Sypalo et al., 2017).

Diabetes is one of the most significant risk factors for cardiovascular diseases (American Diabetes Association, 2018; Mankovsky, 2018). Coronary heart disease and T2DM are often combined, thus increasing the negative course of each of these diseases. At the same time, due to the

frequent late diagnosis of diabetes, the true frequency of metabolism disorders in persons with confirmed atherosclerotic lesions of coronary heart vessels both in the world and in Ukraine has not been sufficiently studied (Fox et al., 2015; Rosenblit, 2019; Lehto et al., 2020).

The high risk of vascular problems against the background of DM gave the American Heart Association reason to classify this disease as a cardiovascular disease. It has been proven that 6–7 patients out of 10 with DM die from cardiovascular diseases, which is 2–4 times higher than in the general population (Rosul, 2002; Nathan et al., 2009; Stamler et al., 2012; Raghavan et al., 2019). DM is equated with coronary heart disease not only because of the high probability of primary disease in patients with coronary heart disease, but also because of its typical association with multiple risk factors of atherosclerosis and coronary heart disease: dyslipidemia in T2DM occurs two times more often than without it (Rosul, 2002). It is also believed that the influence of any risk factor on the level of cardiovascular mortality in patients with diabetes is three times higher than in people without diabetes (Rosul, 2002; Nathan et al., 2009; Sypalo et al., 2017).

The aim of the research was to determine the gender characteristics of lipid metabolism disorders in patients with coronary heart disease and type 2 diabetes mellitus.

Materials and methods

To solve the problem, the data of examinations of patients with coronary heart disease and T2DM for the period from September, 2019 to November, 2019 in the Dnipropetrovsk Regional Center of Cardiology and Cardiosurgery, Dnipro, were processed. For the analysis, data from archival patient histories were used in accordance with the norms of medical ethics. The analysis includes only data on age, gender, and anthropometric examinations of patients with coronary heart disease and T2DM. For further analysis, 72 patients with coronary heart disease and T2DM, aged from 37 to 85 years, were selected by the continuous sampling method.

The blood serum of patients was used as the research material for biochemical blood analysis, the research of which was carried out on an automatic biochemical analyzer "Beckman Coulter AU480" (Beckman Coulter, USA) with the determination of the following indicators of the lipid spectrum: total cholesterol, low and high density lipoproteins, triglycerides.

Depending on the presence or absence of T2DM, all patients with coronary heart disease were divided into two groups: group 1 (n = 40) – patients with coronary heart disease (stable angina); group 2 (n = 32) – patients with coronary heart disease and T2DM. Each group, depending on the gender of the patients, was divided into subgroups:

1A group (n = 20) – men with coronary heart disease (stable angina);

1B group (n = 20) – women with coronary heart disease (stable angina);

2A group (n = 15) – men with coronary heart disease and T2DM;

2B group (n = 17) – women with coronary heart disease and T2DM.

The results of the study were statistically analyzed using ANOVA. Differences between the groups were considered statistically significant at $P < 0.05$. The data in the tables are presented as x ± SD (mean value ± standard deviation).

Results

The obtained results showed that the groups of examined patients did not differ significantly in most of the investigated indicators (Table 1). The only exception was the average blood glucose level, which was significantly higher in group 2 (9.08 ± 3.46 mmol/L) due to the presence of type 2 diabetes in patients.

The gender analysis revealed that female groups with coronary heart disease are on average older than male groups. The average age of female patients is 68.15 ± 11.26 and 70.41 ± 8.96 years (in subgroups 1B and 2B, respectively); in male subgroups – 65.40 ± 13.12 and 64.93 ± 12.28 years (in subgroups 1A and 2A, respectively).

Coronary heart disease in 75.0% of cases occurred in patients with an increased value of body mass index (>25 kg/m^2); the average body mass index in group 1 was 29.97 ± 4.33 kg/m^2. In the patients of the second group, the average body mass index was slightly higher (31.74 ± 6.15 kg/m^2), and a significant majority of patients also had an increase in body mass index (87.5%). The average body mass index in all examined subgroups exceeded normal values. Its higher values were determined in the group of women, regardless of the presence of T2DM: 1A subgroup – 28.77 ± 3.61 kg/m^2, 1B subgroup – 31.49 ± 4.79 kg/m^2, 2A subgroup – 30.97 ± 6.44 kg/m^2, 2B subgroup – 32.41 ± 6.00 kg/m^2. The majority of women in both subgroups were obese (45.0% and 64.7% in 1B and 2B subgroups, respectively), while obesity was slightly less common in groups of men (35.0% and 33.3% in 1A and 2A subgroups, respectively).

Table 1
General characteristics of groups of patients (x ± SD)

Indexes	Group 1 (n = 40)	Group 2 (n = 32)
Average age, years	66.78 ± 12.15	67.84 ± 10.83
Body mass index, kg/m^2	29.97 ± 4.33	31.74 ± 6.15
Glucose, mmol/L	4.89 ± 0.81	9.08 ± 3.46*
Total cholesterol, mmol/L	5.64 ± 1.77	5.35 ± 1.85
High-density lipoproteins, mmol/L	1.48 ± 0.38	1.48 ± 0.50
Triglycerides, mmol/L	2.02 ± 1.24	2.20 ± 1.49
Low-density lipoproteins, mmol/L	3.98 ± 1.50	3.75 ± 1.44

Note: * – $P < 0.05$.

Biochemical indicators of lipid metabolism by subgroups are presented in the Table 2. The average level of total cholesterol in all studied subgroups, with the exception of subgroup 1B (women with coronary heart disease), was at the level of the upper limit of the norm. In subgroup 1B, the level of total cholesterol was 6.12 ± 2.06 mmol/L, which is an excess of the norm.

Table 2
Gender features of lipid metabolism in patients with coronary heart disease and T2DM (x ± SD)

Indexes	Group 1 (n = 40)		Group 2 (n = 32)	
	1A (n = 20)	1B (n = 20)	2A (n = 15)	2B (n = 17)
Total cholesterol, mmol/L	5.15 ± 1.29	6.12 ± 2.06*	5.24 ± 2.05	5.45 ± 1.71
High-density lipoproteins, mmol/L	1.23 ± 0.21	1.75 ± 0.34*	1.28 ± 0.63	1.67 ± 0.31*
Triglycerides, mmol/L	2.40 ± 1.06	1.63 ± 0.65*	2.16 ± 0.73	2.23 ± 0.84
Low-density lipoproteins, mmol/L	3.71 ± 1.14	4.24 ± 1.79*	3.77 ± 1.57	3.72 ± 1.37

Note: * – $P < 0.05$ (between 1A and 1B and between 2A and 2B).

When analyzing the average level of high-density lipoproteins, it was found that in all subgroups their level was inside the norm, but in women there is a tendency to increase to the upper limit. In subgroup 1B – 1.75 ± 0.34 mmol/L, in 2B – 1.67 ± 0.31 mmol/L. In the male groups, these values were closer to the normal average: in subgroup 1A – 1.23 ± 0.21 mmol/L, in 2A – 1.28 ± 0.63 mmol/L. The average level of triglycerides in patients with coronary heart disease and T2DM, regardless of gender, was compared and exceeded normal values. In subgroup 2A – 2.16 ± 0.73 mmol/L, in 2B – 2.23 ± 0.84 mmol/L. In the group of men with coronary heart disease, the average triglycerides level was significantly higher (1A – 2.40 ± 1.06 mmol/L) than in the group of women with coronary heart disease (1B – 1.63 ± 0.65 mmol/L). The average level of low-density lipoproteins was the highest in women with coronary artery disease (1B – 4.24 ± 1.79 mmol/L). In all other subgroups, the level of increased low-density lipoproteins was also higher than normal, but in the second group there were no gender differences (2A –3.77 ± 1.57 mmol/L, 2B –3.72 ± 1.37 mmol/L).

The analysis of the frequency of cases of pathological levels of blood lipid metabolism indexes in all examined subgroups showed that, on average, in half of the patients, regardless of the presence of coronary heart disease and T2DM, the blood cholesterol exceeded the norm (1A – 55.0%, 1B – 65.0%, 2A – 46.7%, 2B – 41.2%). At the same time, an increase in blood sugar (both in men and in women) was more often registered in the absence of diabetes (Table 3). Also, in the majority of patients of the first group, an increase in the level of low-density lipoproteins was found (1A – 80.0%, 1B – 75.0%). An increase in this index was less common in patients with coronary heart disease and T2DM (2A – 66.7%; 2B – 70.6%). In all observed women, the level of high-density

lipoproteins was normal, while the proportion of high-density lipoproteins in men was reduced (1A – 5.0%, 2A – 6.7%). In the presence of coronary heart disease, an increase in triglycerides level was recorded 1.5 times more often in men than in women (1A subgroup – 60.0% and 1B subgroup – 40.0%), while the frequency of detection of increased triglycerides in patients with coronary heart disease and T2DM did not differ significantly (2A subgroup – 46.7% and 2B subgroup – 41.2%).

Table 3
The frequency of pathological levels
of blood lipid spectrum indicators in the studied groups (%)

Indexes	Group 1 (n = 40)		Group 2 (n = 32)	
	1A (n = 20)	1B (n = 20)	2A (n = 15)	2B (n = 17)
Total cholesterol >5.2 mmol/L	55.0	65.0	46.7	41.2
High-density lipoproteins: men: ≤1.0 mmol/L; woman: ≤1.2 mmol/L	5.0	0.0	6.7	0.0
Triglycerides >1.7 mmol/L	60.0	40.0	46.7	41.2
Low-density lipoproteins >3.0 mmol/L	80.0	75.0	66.7	70.6

For a comprehensive assessment of changes in lipid metabolism in surveyed patients, the classification of dyslipidemias according to Fredrickson, which is recommended by the WHO, was used. Class II dyslipidemia was most often detected in the examined patients of both groups: 100% in group 1 and 81.1% in group 2 (Table 4).

Table 4
Frequency of detection of different classes of dyslipidemias
by D. Fredrickson classification in surveyed patients (%)

Type of dyslipidemia	Group 1 (n = 40)		Group 2 (n = 32)	
	1A (n = 20)	1B (n = 20)	1A (n = 15)	1B (n = 17)
IIa	15.0	35.0	0.0	17.6
IIb	30.0	25.0	40.0	23.5
IV	0.0	0.0	6.7	5.9

Note: group 1 – $\chi^2 = 0.6934$; group 2 – $\chi^2 = 0.6459$.

In the group of patients exclusively with coronary heart disease, dyslipidemia of IIa class was observed 20.0% more often in women. There were no gender differences in the frequency of detection of IIb dyslipidemia (30.0% and 25.0% in 1A and 1B subgroups, respectively). In the group of patients with coronary heart disease and T2DM, IIa class dyslipidemia was registered only in women (2B subgroup) – 17.6%, while IIb class was much more common in men (40.0%) than in women (23.5%). A feature of lipid metabolism disorders in patients with coronary heart disease and T2DM is the presence of class IV dyslipidemia in a proportion of patients: 6.7% and 5.9% in 2A and 2B subgroups, respectively.

When analyzing the frequency of reaching the target level of total cholesterol by the examined patients, it was noted that in the presence of coronary heart disease and T2DM, about a quarter of patients, regardless of gender, reach a level of total cholesterol < 4.0 mmol/L: 26.7% and 23.5% in 2A and 2B subgroups, respectively (Table 5).

Table 5
Achieving target levels of cholesterol and low-density lipoproteins
in patients with coronary heart disease and T2DM (%)

Type of dyslipidemia	Group 1 (n = 40)		Group 2 (n = 32)	
	1A (n = 20)	1B (n = 20)	1A (n = 20)	1B (n = 20)
Total cholesterol < 4.0 mmol/L	25.0	15.0	26.7	23.5
Low-density lipoproteins < 4.0 mmol/L	5.0	10.0	6.7	0.0

Note: $\chi^2 = 1.00$ for total cholesterol; $\chi^2 = -1.00$ for low-density lipoproteins.

Men with coronary heart disease reach the target level of total cholesterol 10% more often (1A subgroup – 25.0%) than women (1B subgroup – 15.0%). The examined patients reached the target low-density lipoproteins level much less frequently: only 6.7% of men with coronary heart disease and T2DM had a low-density lipoproteins level <1.8 mmol/L, and 100% of men with coronary heart disease and T2DM had a low-density lipoproteins level >1.8 mmol/L. Among patients with coronary heart disease, there was also a rather low percentage of patients with the target level of low-density lipoproteins, while women of this group had a level of low-density lipoproteins <1.8 mmol/L two times more often than men (1A subgroup – 5.0%, 1B subgroup – 10.0%).

Discussion

The analysis of the results of laboratory tests of different groups of patients showed that they were not significantly different in all applied indicators, except for the average blood glucose, which was much higher in the group of patients with T2DM. The majority of surveyed patients (75%) with coronary heart disease had increased body mass index values, which agrees with other researcher's data (Held et al., 2022). Increased body mass index, even in childhood, may be associated with the risk of cardiovascular diseases in middle age (Kindblom et al., 2021). In particular, it is indicated that patients with body mass index > 25 kg/m^2 have moderate changes in lipid metabolism markers, and at body mass index > 35 kg/m^2 they have unfavourable prognosis for the development of the disease (Held et al., 2022). The average levels of total cholesterol, low-density lipoproteins and triglycerides in both groups exceeded several thresholds, and the average level of high-density lipoproteins in both groups of patients was within the norm, which agrees with data (Wang et al., 2022). Changes in these biomarkers are often associated with an increased risk of mortality from cardiovascular diseases (Cai et al., 2016; Held et al., 2022; Wang et al., 2022).

The analysis of the obtained results, depending on the gender of patients, showed that the average age of patients in the female subgroups was slightly higher than in subgroups of men, which coincides with the data obtained by many studies on the development of cardiovascular diseases and diabetes in men at an earlier age than women (Barrett-Connor, 2013; Rosenblit, 2019; Bays et al., 2022). In addition to age, other risk factors, including smoking, nutrition, are also of particular importance (Barrett-Connor, 2013; Kautzky-Willer et al., 2016; Bays et al., 2022).

The average body mass index in all subgroups exceeded normal values and was higher in women, regardless of T2DM. Most women of both subgroups had obesity, while it was less common in men. Similar trends are also indicated in the analysis (Regitz-Zagrosek & Gebhard, 2022). The average level of total cholesterol in all the subgroups under study had thresholds, except for the subgroup of women with coronary heart disease, where the level of total cholesterol exceeded the norm, which is typical for this pathology (Sethi et al., 2021; Yubero-Serrano et al., 2021; Wang et al., 2022).

In all subgroups, the level of high-density lipoproteins was within normal limits, but in women this index approached the upper limit, which exceeds similar indicators specified in other research (Qin et al., 2019). The average level of triglycerides in patients with coronary heart disease and T2DM, regardless of gender, was compared and exceeded normal values, with the average values being higher in the male groups. The average level of low-density lipoproteins in all subgroups exceeded normal levels and was of the highest importance in women with coronary heart disease. In all other subgroups, the level of increase in low-density lipoproteins was compared and in the groups of persons with diabetes had no gender differences.

A typical tendency is that the majority of patients of the first group revealed an increase in low-density lipoproteins levels, which coincides with other studies (Cai et al., 2016; Liu et al., 2016) and indicates the risks of deterioration of coronary heart disease. In patients with coronary heart disease and T2DM, this index was slightly less elevated, and in other groups the increase was not so significant. The high-density lipoproteins indicator in women's groups corresponded to the norm, and in men, high-density lipoproteins were reduced, which is an unfavourable prognostic marker (Liu et al., 2016). Only coronary heart disease is distinguished by the increase in triglycerides levels, while the frequency of detection of increases in triglycerides in patients with coronary heart disease and T2DM did not differ significantly in the gender subgroup cardiovascular diseases, although it is believed that an increase in this indicator is a poor prognostic sign (Ye et al., 2019). According to the classification of Fredrickson dyslipidemia (Fredrickson & Lees, 1965), which has been introduced into clinical practice since 1970, for patients of both groups, second class dyslipidemia was typical. Moreover, in patients with coronary heart

disease IIa class was more common in women, while the frequency of detection of IIb dyslipidemia on a gender feature was not significantly different. The higher risks of dyslipidemia in women due to the development of high levels of Non- high-density lipoproteins-C are shown in the study (Lokpo et al., 2022).

According to European recommendations for the prevention of cardiovascular diseases (2016), the target for the selection and control of hypolipidemic therapy is the level of low-density lipoproteins, and if it is inaccessible to its determination – the level of total cholesterol (Piepoli et al., 2016). Low-density lipoproteins are basic for assessing the prognosis for the progression of cardiovascular diseases and complications. According to these recommendations and recommendations of the Association of Cardiologists of Ukraine for the prevention of cardiovascular diseases (2013), all patients with diagnosed coronary heart disease and T2DM belong to the group of very high cardiovascular risk for which the target level of low-density lipoproteins should be <1.8 mmol/L (<70 mg/dL), and total cholesterol – <4.0 mmol/L (<155 mg/dL). Our research has shown that in the presence of coronary heart disease and T2DM, about a quarter of patients, regardless of gender, reached the level of <4.0 mmol/L. It was mostly in groups of men. Much less frequently, examined patients reached the target level of low-density lipoproteins <1.8 mmol/L, and in all patients with coronary heart disease and T2DM, the level of low-density lipoproteins was >1.8 mmol/L. These data indicate insufficient prescription of adequate hypolipidemic therapy for patients with coronary heart disease and T2DM.

Conclusions

A larger proportion of patients with coronary heart disease, regardless of T2DM, had overweight and obesity, with women more often (without diabetes – 45.0%, with diabetes, 64.7%) than men (35.0% and 33.3% in the absence or presence of T2DM respectively).

Disturbance of lipid metabolism in patients with coronary heart disease consists in an increase in the levels of total cholesterol, triglycerides and low-density lipoproteins, while women had slightly higher levels of total cholesterol and low-density lipoproteins and a lower level of blood triglycerides than men. In patients with coronary heart disease and T2DM, regardless of gender, lipid metabolism disorder was characterized predominantly by an increase in the blood levels of triglycerides and low-density lipoproteins.

The majority of patients with coronary heart disease, regardless of the presence of D2TM, had Fredrickson class II dyslipidemia: 100% of patients with coronary heart disease and 81.1% of patients with coronary heart disease and T2DM. Class IIb dyslipidemia occurred twice as often (in 30.0%) in men with coronary heart disease than class IIa (in 15.0%), and in women, class IIa dyslipidemia occurred more often (class IIa and IIb in 35.0% and 25.0%, respectively).

A distinctive feature of lipid metabolism disorders in patients with coronary heart disease and T2DM was the presence of class IV dyslipidemia according to Fredrickson (in 6.7% of men and 5.9% of women) and the absence of class IIa dyslipidemia in men of this group.

The analysis of the achievement of the target levels of total cholesterol and low-density lipoproteins indicates insufficient prescription of adequate hypolipidemic therapy for patients with coronary heart disease and T2DM.

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