



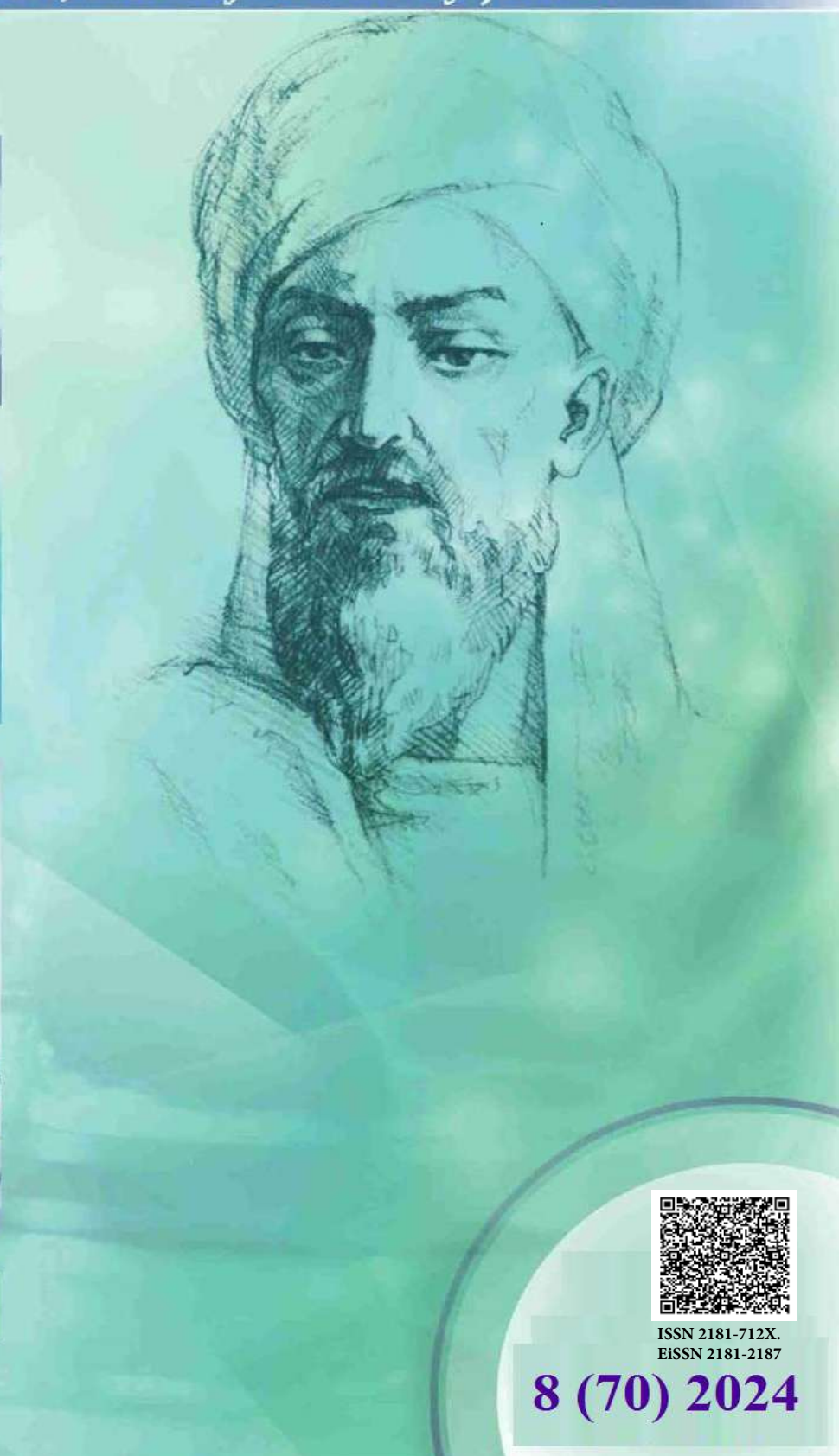
New Day in Medicine
Новый День в Медицине

NDM



TIBBIOVIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal



AVICENNA-MED.UZ



ISSN 2181-712X.
EiSSN 2181-2187

8 (70) 2024

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ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE

*Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал*

УЧРЕДИТЕЛИ:

**БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ
МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»**

Национальный медицинский
исследовательский центр хирургии имени
А.В. Вишневского является генеральным
научно-практическим
консультантом редакции

Журнал был включен в список журнальных
изданий, рецензируемых Высшей
Аттестационной Комиссией
Республики Узбекистан
(Протокол № 201/03 от 30.12.2013 г.)

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8 (70)

2024

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UDK 616-056.5

CARBOHYDRATE METABOLISM DISORDERS AS A CARDIOVASCULAR RISK FACTOR

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✓ Resume

One of the most significant risk factors for ischemic heart disease is diabetes. However, the literature on the role of IGT as a risk factor for coronary artery disease varies significantly. Meanwhile, in some cases, IGT may precede the development of diabetes and, in a certain sense, it can be considered as a "pre-illness" state in relation to diabetes. Hyperglycemia, including hidden ones, often occurs with hyperinsulinemia, which is considered one of the components of the "metabolic" syndrome, which plays an important role in the formation of cardiovascular diseases, including coronary artery disease.

Key words: Blood pressure, hyperlipidemia, obesity, diabetes mellitus.

НАРУШЕНИЯ УГЛЕВОДНОГО ОБМЕНА КАК ФАКТОР СЕРДЕЧНО-СОСУДИСТОГО РИСКА

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✓ Резюме

Одним из наиболее значимых факторов риска развития ишемической болезни сердца является сахарный диабет. Однако литература о роли IGT как фактора риска развития ишемической болезни сердца существенно различается. Между тем в ряде случаев НТГ может предшествовать развитию СД и в определенном смысле может рассматриваться как «предболезненное» состояние по отношению к СД. Гипергликемия, в том числе скрытая, часто возникает при гиперинсулинемии, которую считают одним из компонентов «метаболического» синдрома, играющего важную роль в формировании сердечно-сосудистых заболеваний, в том числе ишемической болезни сердца.

Ключевые слова: Артериальное давление, гиперлипидемия, ожирение, сахарный диабет.

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✓ Rezyume

Ishemik yurak kasalligi uchun eng muhim xavf omillaridan biri diabetdir. Biroq, IGT ning koronar arter kasalligi uchun xavf omili sifatidagi roli bo'yicha adabiyotlar sezilarli darajada farq qiladi. Ayni paytda, ba'zi hollarda, IGT diabet rivojlanishidan oldin bo'lishi mumkin va ma'lum ma'noda diabetga nisbatan "kasallikdan oldingi" holat sifatida qaralishi mumkin. Giperglikemiya, shu jumladan yashirin, ko'pincha "metabolik" sindromning tarkibiy qismlaridan biri hisoblangan giperinsulinemiya bilan yuzaga keladi, bu yurak-qon tomir kasalliklari, shu jumladan koronar arteriya kasalliklarining shakllanishida muhim rol o'ynaydi.

Kalit so'zlar: Qon bosimi, giperlipidemiya, semizlik, qandli diabet.

Relevance

The epidemiological situation regarding coronary heart disease (CHD) in different regions of the world and in certain populations is very ambiguous. More than 1 million Americans experienced new cases of CHD or exacerbations of CHD (qualified as myocardial infarction or fatal CHD). Moreover, 650,000 of them had newly diagnosed IHD, and 350,000 had an exacerbation of chronic IHD. About 250,000 patients died before hospitalization. Most of them had ventricular fibrillation. The value of the standardized indicator of the prevalence of coronary heart disease in different cities differed significantly. Thus, the highest value of this indicator was noted in Baku, Kyiv and Moscow (19.5%, 16.4% and 14.5%), and the lowest it was in Nalchik (6.9%). In Tashkent, the prevalence of IHD was 9.3%. The most common type of angina among the surveyed populations was angina pectoris (4.5%), while “possible” ischemic changes on the ECG were somewhat less common (3.8%).

Previous myocardial infarction and painless forms of coronary artery disease are even less common (in 1.3% and 1.5%, respectively), and a possible history of myocardial infarction (not confirmed by ECG changes) was identified in 1.0%. Factors contributing to the increase in sudden death, along with such generally accepted risk factors as high blood pressure, hyperlipidemia, obesity, diabetes mellitus, etc. also include non-painful myocardial ischemia [9] and untimely establishment (or failure to establish) diagnosis [16]. In France, a 20-year study of the causes of death of the population was conducted, which showed a decrease in mortality from cardiovascular diseases (CVD) by more than 30% [8]. In this regard, the issue of determining the range of risk factors for mortality from coronary artery disease and the development of adequate methods for preventing this disease is of particular importance. Summary data from studies conducted in three regions of France, two regions of Italy, two regions of Sweden, Barcelona, Belfast and Glasgow covered the population aged 35-64 years [10]. The authors concluded that mortality rates are influenced by both geographic location and lifestyle, diet and other factors. It has been shown that one of the most important factors in increasing mortality from coronary heart disease is the very low coverage of treatment for both patients suffering from coronary artery disease and those with high blood pressure.

Large population studies conducted by the Center for Cardiology of the Ministry of Health of the Republic of Uzbekistan indicate the importance and fairly high effectiveness of preventive measures against cardiovascular diseases [3, 2, 15]. Preventive programs implemented in production teams made it possible to increase the effectiveness of drug control of hypertension by 7 times, reduce the frequency of hypertension by 10%, and up to 25% of men quit smoking [2]. Multifactorial prevention has generally been effective in both men and women [3]. However, it should be noted that the effectiveness of preventing hypertension and smoking was more pronounced among men than among women. Among men 30-59 years old in Samarkand, the incidence of coronary heart disease with normal blood pressure was 3.4%, with borderline hypertension - 7.5%, and with hypertension - 16.7%, respectively [3,4]. Studies in Tomsk were conducted among 647 patients with coronary artery disease whose average age was 53.1 ± 2.36 years, showing that HDL-C has a stabilizing effect on atherosclerotic plaque and has a positive effect on the course of coronary artery disease, and also to a certain extent prevents the development of myocardial infarction [9]. Dyslipoproteinemia in some cases may be a manifestation of a common hereditary syndrome. In individuals with a family history of cardiovascular diseases, hypertension was significantly more common among individuals with dyslipoproteinemia than with normolipidemia (20.2% and 12.5%, respectively). At the same time, the authors support the opinion that excess fat consumption increases blood cholesterol, and this, in turn, leads to an increased risk of developing coronary artery disease.

Excess body weight (BMI) plays a certain role in the development of coronary artery disease. Most researchers note that the frequency of BMI among people engaged in mental work is higher than among people engaged in physical labor. According to an epidemiological study in Finland [6], BMI is more common among people with low physical activity than with normal physical activity. Moreover, the risk of death from CHD among people with BMI and low physical activity is much higher than the risk of death from CHD among people with normal body weight and sufficient physical activity. In patients with coronary artery disease and those suffering from BMI, increased anxiety, psychosocial maladaptation, a higher frequency of cardialgia, and lower tolerance to isometric load are significantly more likely to be observed. Among individuals with BMI suffering from coronary artery disease, the correlation coefficient between body fat mass and anxiety level is 0.53 ± 0.09 ($p < 0.001$). 60.6% of patients with angina have BMI [4]. In patients with coronary artery disease with BMI, low tolerance to

physical activity and lower efficiency of the cardiovascular system are observed [6]. It should be noted that disturbances of central and peripheral hemodynamics are considered one of the important risk factors for death from cardiovascular diseases [1]. The importance of tobacco smoking in the development of coronary artery disease is so great that many researchers attach great importance to passive smoking. Although the relationship between passive smoking and CHD is not yet fully understood, there are reports that passive smoking contributes to the development of CHD [8]. It should be noted that the significance of alcohol in the formation of coronary artery disease can be objectively assessed only on the basis of multifactor analysis. However, alcohol plays an important role in mortality from other, non-cardiovascular diseases. Studies conducted in various scientific centers indicate that the same risk factors, as well as their combinations, have different prognostic significance in relation to the development of coronary artery disease and the prognosis of this disease. Therefore, the need for further, in-depth research in the field of studying RF becomes obvious. The high significance of diabetes in the development of coronary artery disease and mortality from it is indicated by the results of many population studies [13, 15]. A 20-year prospective study conducted in the UK included 2779 people [2]. Overall, among all persons under observation, 31.1% developed IHD. Among patients with diabetes, the frequency of new cases of coronary artery disease was significantly higher and amounted to 57%. In Finland, the prevalence of coronary artery disease among patients with newly diagnosed type II diabetes was studied [2]. It turned out that among patients in whom diabetes was diagnosed for the first time, the incidence of coronary artery disease was 3 times higher than in the control group, i.e. among persons without diabetes. The Oxford study was conducted over 10 years and included 3055 men with type II diabetes, with an average age of 52 years [13]. During this period, 335 people developed IHD. The significance of such indicators as high- and low-density lipoprotein cholesterol, triglycerides, SBP, smoking and fasting glucose levels was analyzed. A pronounced connection between risk factors for coronary artery disease and diabetes has been established. The greatest relationship was established with SBP and low-density lipoprotein cholesterol, i.e. precisely with those risk factors that play an important role in the development of ischemic heart disease. At the same time, it should be noted that in the literature there are indications that there is no direct relationship between diabetes and coronary artery disease [15]. This view of this problem is explained by the fact that the etiopathogenetic aspects of diabetes and ischemic heart disease have much in common. The authors believe that in some cases, patients with coronary artery disease develop diabetes, and in other cases, patients with diabetes develop coronary artery disease. A 9-year prospective observation of patients with diabetes showed that diabetes is a very important risk factor for death from coronary artery disease [9]. This study found that the mortality rate from coronary artery disease per 1000 person-years of observation was 28.4 among patients with diabetes, and 10.2 among persons without diabetes. At the same time, the overall mortality from cardiovascular diseases in patients with diabetes was 39.6 per 1000 person-years of observation, and among people without diabetes – 15.5. It should be noted that mortality from other, non-cardiovascular diseases was 16.6 and 13.5, respectively. The course of MI in patients with diabetes is characterized by a large number of complications and high mortality. The severity of MI is to a certain extent related to the severity of diabetes, and the mortality rate for MI in patients with diabetes reaches 54% [9]. In patients with diabetes, the risk of recurrent myocardial infarction is significantly higher, and survival rate is significantly lower than in persons without diabetes [3]. The presence of diabetes increases the likelihood of left ventricular wall rupture during MI [2]. Along with a higher frequency of chronic painless forms of coronary artery disease in patients with diabetes, painless cases of myocardial infarction are also more often observed [13]. It should be noted that not all authors share the opinion of a higher frequency of painless forms of coronary artery disease among patients with diabetes. As a result of a study based on a retrospective analysis of the prognostic significance of the occurrence of non-painful myocardial ischemia during exercise on a treadmill, the authors came to the conclusion that the frequency of non-painful myocardial ischemia does not depend on the presence of diabetes [15]. Higher mortality from coronary artery disease in patients with diabetes is to a certain extent associated with such a factor as ethnicity [14]. A comparative analysis of mortality from acute MI in South Asia showed that out of 149 Asians and 313 whites admitted to the clinic with acute MI, significantly more whites than Asians survived [13]. It should be noted that among Asians admitted to the hospital, the incidence of diabetes was 38%, and among whites it was 11%. However, a study conducted among 150 Europeans and 77 Africans suffering from non-insulin-dependent diabetes mellitus showed that Africans have a lower risk of developing cardiovascular diseases than whites [7]. Among patients with diabetes, various

risk factors for coronary heart disease are found significantly more often than among people without diabetes [5]. In patients with coronary artery disease [6] suffering from diabetes, the concentration of blood triglycerides is higher, and high-density lipoprotein cholesterol is lower than among patients with coronary artery disease without diabetes (2.51 and 2.07 mmol/l, 0.93 and 1.19 mmol/l, respectively). Moreover, the atherogenicity coefficient in patients with coronary artery disease with diabetes was 1.4 times higher than among persons without diabetes (6.43 and 4.60, respectively). A prospective observation of 1342 men in Trinidad revealed 178 deaths, of which 38% were CVD, with 12% having cerebrovascular disease. With an increase in systolic blood pressure, the risk of overall mortality from CVD and cerebral stroke increased. When the SBP level is above 180 mmHg, mortality from CVD increased 4 times [16]. A study of mortality among men 50-59 years old in Moscow over a 7-year period revealed that hypertension is an important risk factor for death from coronary artery disease [10]. When comparing such risk factors as hypertension, overweight, smoking and impaired carbohydrate tolerance, it turned out that the most unfavorable factor is hypertension, since the mortality rate from coronary artery disease among people with high blood pressure is 7 times higher than with normal pressure, which is significantly higher than with other FRs.

In the presence of hypertension caused by SBP, the risk of death from CVD increases 5 times, and caused by DBP by 3 times. This study showed that with increasing blood pressure levels, the risk of myocardial infarction and cerebral stroke increases, and the risk of cerebral stroke increases more intensively [104]. It should be noted its growth not only among the urban, but also among the rural population. A study of the mortality structure in Tashkent showed that CVDs are the cause of death of men 20-59 years old in 33.1% of cases (CHD - 23.87%, hypertension - 7.16%, other CVDs - 2.06%) [11].

According to his data, mortality from CVD in the group of examined hypertension was 5 times higher, in the group of borderline hypertension - 1.8 times higher than in the group with normal blood pressure. Prospective observations of the male population of Bishkek showed that overall mortality from CVD and other causes increases significantly as SBP increases [11].

In Russia in 1995, for the first time since 1986, a decrease in population mortality was registered, and its decrease was noted in 70 regions of the country [9], which was the result of a significant reduction in mortality from diseases of the circulatory system and unnatural causes of death - accidents, poisonings and injuries at the same time, it was noted that the level of maternal mortality remains high and is not decreasing. The maternal mortality rate in Russia is 5-10 times higher than in developed Western European countries.

According to data, cardiovascular diseases are one of the main causes of mortality in the population of Moscow, accounting for 57% of total mortality, which exceeds similar indicators for Russia as a whole. A study of the mortality structure in Tashkent revealed that CVDs are the cause of death in 37.5% of cases [9,10]. According to [11], the female population has an increase in mortality from CVD in all age groups, starting from 30-39 years. Cardiovascular diseases also occupy first place in the structure of extragenital pathology, which is one of the main causes of death in pregnant women [10].

Based on the data presented in this section, we can conclude that hypertension is of great importance in the formation of coronary artery disease, cerebral stroke and mortality from them. Timely detection, treatment and prevention of hypertension significantly reduces the risk of death from CVD. Currently, a lot of work is being done in Uzbekistan to improve the health of women of fertile age, which is of decisive importance in the formation of a healthy generation.

From the information presented in the previous chapter it follows that, according to most studies, the significance of diabetes as a risk factor for coronary artery disease can be considered proven. At the same time, there is no consensus in the literature regarding the significance of IGT as a risk factor for the development of IHD and mortality from it.

According to a number of studies, IGT significantly increases the risk of developing arterial sclerosis [15, 16]. A long-term prospective observation that lasted 26 years in Framingham (USA) included 1672 men and 2264 women [16]. After 26 years, 210 men and 199 women developed CAD. Among people with IGT, along with damage to the coronary vessels, there was also damage to peripheral vessels (primarily the femoral artery). The authors concluded that in conditions of hyperglycemia, people with peripheral vascular disease have a high risk of developing coronary artery disease. Apparently, the combination of damage to the coronary and peripheral arteries causes hemodynamic disturbances and the formation of a hypokinetic type of blood circulation [11].

There are reports in the literature that IGT significantly affects the severity and clinical course of IHD [12]. Among people with IGT suffering from coronary artery disease, repeated, frequent hospitalizations, tachycardia, and ischemic changes on the ECG are much more common [15]. Over time, the glycemic level can change either in the direction of increasing or decreasing indicators of the glycemic curve, and in other cases the glycemic level stabilizes. In Tashkent, a study was conducted on the prevalence of IHD and levels of basal insulinemia among individuals with different dynamics of IGT [14]. It turned out that the development and severity of IHD are closely related not only to the presence of IGT, but also to the dynamics of hyperglycemic states. Thus, among individuals with initial IGT, when the glycemic level is normalized, the incidence of IHD is 25%, and when IG is stabilized, the incidence of IHD reaches 76.5%. At the same time, the level of basal insulinemia increases according to the progression of hyperglycemia. Among individuals whose hyperglycemia returned to normal, the level of basal insulinemia was 18.27-0.92 $\mu\text{U/ml}$; with the transition of IGT to overt diabetes, the insulin content was more than 2 times higher (39.08-2.1 $\mu\text{U/ml}$), and when IG stabilized, basal insulinemia turned out to be the highest - 44.56-3.32 $\mu\text{U/ml}$. During the entire observation period, 864 people developed coronary artery disease and 384 people died from this disease.

Along with works that show the important role of IGT in the formation of IHD and mortality from it, there is information in the literature that denies the role of IGT as a risk factor for IHD. Multivariate analysis, taking into account age, gender, education, hypertension, height-weight index and smoking, allowed the authors to conclude that, in contrast to diabetes, IGT is not a risk factor for ischemic heart disease. One of the largest works devoted to studying the significance of IGT in the formation of coronary artery disease and deaths from this disease is a cooperative study conducted by The International Collaborative Group in 14 scientific centers in 11 countries [15]. Studies were conducted in Australia, England, Denmark (2 populations: men 40 and 50 years old), Ireland, USA (2 populations: employees of the gas company and the Western Electric Company), Italy, Switzerland, Scotland, Finland (2 populations: policemen and the unorganized population), France, Japan [16]. Such indicators as the prevalence of ischemic heart disease, the presence of ischemic changes on the ECG, cases of myocardial infarction and mortality from ischemic heart disease among persons with IGT and different blood glucose levels were taken into account. The results obtained were very ambiguous. Data from studies among policemen in Finland, employees in Italy, and workers in Japan showed that ischemic heart disease among people with IGT is significantly more common than among people with normal glucose tolerance. A positive relationship was found between ischemic changes on the ECG and the presence of IGT in the populations of Australia, Italy, the unorganized population of Finland, and France. A higher mortality rate from coronary heart disease was found among persons with IGT in the population of the Gas Campaign of the USA, France and policemen of Finland. However, among those examined in England, Denmark, Switzerland and Scotland, no connection was found between the presence of IGT and the prevalence of IHD. As follows from these data, the results of studies of different centers differ significantly. These discrepancies can be explained by the fact that the studies used different methods for selecting populations, the age groups and periods of observation differed significantly, and not all studies of glucose tolerance covered the state of glycemia 1 and 2 hours after the glucose load. For example, in Denmark the population of policemen is represented by people aged 40 years, and in Italy a population aged 35-59 years was surveyed. A prospective study in Finland among an unorganized population lasted 4 years, in the same country a study of mortality among policemen was carried out for 10 years, and in the USA among employees of the Western Electric Company the observation period was 15 years. The significance of hyperglycemia on the formation of coronary artery disease was judged by the level of glucose: in Italy - on an empty stomach, in Australia - 1 hour after a glucose load, in the USA - 2 hours after a glucose load. Thus, discrepancies in the results of a cooperative study conducted by The International Collaborative Group in 14 research centers in 11 countries and in a number of other population-based studies examining the relationship between the prevalence of coronary artery disease and mortality from it with IGT are largely due to differences in methodological approaches to sample formation, as well as methods for identifying IGT, as well as different periods of observation. At the same time, the results of studies on the significance of IGT as a risk factor for ischemic heart disease can apparently also be influenced by other factors, as well as their combinations [14, 15, 16]. The results of a number of population-based studies indicate that when several risk factors are combined, the prevalence of IHD increases. At the same time, it has been shown that individual risk factors can contribute to the formation of other risk factors. In this regard, the question of the connection

between NTG and other risk factors for coronary artery disease is of particular interest. The prospective study, conducted in Italy and followed up for 11.5 years, included 1376 people aged 40–59 years. During the specified observation period, among persons with IGT, systolic blood pressure increased by 7.6 mmHg. more than among persons with normoglycemia, and diastolic blood pressure - by 3.3 mmHg. A study in Philadelphia conducted among black Americans also indicates a connection between the frequency of hypertension and the presence of IGT [15]. In a study of 437 people over 15 years of age in Central Australia, a direct correlative relationship was established between glucose levels, on the one hand, and the prevalence of hypercholesterolemia, hypertriglyceridemia, hypertension and BMI, on the other [16]. Another scientific study conducted in Western Australia among men and women aged 25-64 years examined the relationship between the presence of IGT and levels of risk factors for coronary artery disease. It has been shown that individual risk factors are differently associated with IGT. Thus, hyperglycemia was associated with BMI in both men and women. Systolic blood pressure was significantly higher with IGT than with normoglycemia in both men and women. Elevated triglyceride levels were observed in IGT only among women. However, there were no differences between the concentrations of total cholesterol and high-density lipoproteins among men and women depending on the presence of IGT. In general, it was found that in both men and women with hyperglycemia, the risk factors for coronary artery disease were more pronounced than in those with normoglycemia. Studies in the USA have shown that among obese individuals there is an increased release of insulin in response to a glucose load [12]. However, the authors do not specify what comes first in this regard: whether the presence of obesity leads to increased insulin release or whether hyperinsulinemia contributes to the development of obesity. According to the Framingham study, the role of diabetes and IGT as risk factors for coronary artery disease increases significantly when they are combined with other risk factors [14]. Observation of a population of 3595 people for 16 years allowed the authors to establish that diabetes and IGT lead to a significant increase in fibrinogen and triglycerides in the blood, as well as an increase in blood pressure and body weight. The combination of these factors increases the risk of developing coronary artery disease.

In Uzbekistan, back in 1985-1990. a study was conducted on the prevalence of diabetes in the regions of the republic [6]. At the same time, 5,000 people were examined in each region. The prevalence of diabetes was 1.9%, and IGT from 3.6% to 4.0%. This study shows that the true incidence of diabetes significantly exceeds official statistics. The results of another population-based study conducted in Tashkent [4] indicate a significant increase in the incidence of diabetes and IGT. During the period from 1980 to 1988, the prevalence of diabetes among men 40-59 years old increased from 3.9% to 6.92%, and IGT from 29.3% to 38.93%. According to the American Heart Association, more than 10 million Americans suffer from diagnosed diabetes [5]. The number of new cases of diabetes is 798,000 per year. The prevalence of diabetes among black men is higher than among white men.

Conclusion

Thus, summarizing the literature data, we can conclude that IHD is one of the most significant problems of modern medicine. This is determined by the widespread prevalence of coronary artery disease and the high mortality associated with this disease. In most countries of the world, including Uzbekistan, the number of patients with coronary artery disease continues to grow. The formation of IHD, its course and outcomes are influenced by various risk factors for this disease.

The role of a number of risk factors in the development of coronary artery disease (such as hypertension, obesity, age, etc.) is beyond doubt. One of the most significant risk factors for ischemic heart disease is diabetes. However, the literature on the role of IGT as a risk factor for coronary artery disease varies significantly. Meanwhile, in some cases, IGT may precede the development of diabetes and, in a certain sense, it can be considered as a “pre-illness” state in relation to diabetes. Hyperglycemia, including hidden ones, often occurs with hyperinsulinemia, which is considered one of the components of the “metabolic” syndrome, which plays an important role in the formation of cardiovascular diseases, including coronary artery disease. Differences in literature data, often contradictory, on the role of IGT in the formation of coronary artery disease, may be associated with rather significant differences in research methodology. Along with a fairly large number of single-stage and long-term prospective studies, there is a lack of work on studying the dynamics of the development of IHD among people with IGT in “cross-cutting” cohorts. Based on the above, further study of the role of IGT in the formation of coronary artery disease and outcomes in this disease is of particular interest.

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Entered 20.07.2024