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EFFECTS OF OBESITY ON THE HEMOSTASIS SYSTEM

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LIST OF ABBREVIATIONS:

AG	Arterial hypertension
AQB	Arterial blood pressure
YZLP	High density lipoproteins
QD	Diabetes
TVI	Body mass index
MS	Metabolic syndrome
JF	Physical activity
IDF	International Diabetes Federation
WHO	World Health Organization
PZLP	Low density lipoproteins
UX	Total cholesterol
TG	Triglycerides
EXACTLY	Erythrocyte sedimentation rate
Yuik	Ischemic heart disease
XF	Risk factor
EKG	Electrocardiography
NY	Shortness of breath
OSOK	Chronic obstructive lung disease
HbA1c	Glycosylated hemoglobin
PTI	Prothrombin index
PTV	Prothrombin time

ANNOTATION

Today, there is a wide spread of non-infectious diseases all over the world, and as a result of these diseases, the level of disability of the population is increasing. Among the population of developed and developing countries, it is found that the level of detection of components of the metabolic syndrome, such as excess body weight and obesity, high arterial blood pressure, dyslipidemia caused by inactivity and improper nutrition, as a result of which disorders in the hemostasis system have occurred, and this condition is one of the main diseases. aggravates the clinical course and increases complications. By developing measures to prevent this condition and implementing it among the population, it is possible to achieve high efficiency in the treatment of the main diseases and prevention of complications.

АННОТАЦИЯ

На сегодняшний день в мире наблюдается широкое распространение неинфекционных заболеваний, вследствие чего увеличивается уровень инвалидизации населения. Среди населения развитых и развивающихся стран установлено, что уровень выявления компонентов метаболического синдрома, таких как избыточная масса тела и ожирение, повышенное артериальное давление, дислипидемия, обусловленная гиподинамией и нерациональным питанием, в результате чего произошли нарушения в системе гемостаза, а это состояние является одним из основных заболеваний, утяжеляет клиническое течение и увеличивает осложнения. Разрабатывая меры профилактики этого состояния и внедряя их среди населения, можно добиться высокой эффективности в лечении основных заболеваний и профилактике осложнений.

INTRODUCTION

Metabolic syndrome is an urgent problem of the healthcare system not only in our country, but also in the whole world. From an epidemiological point of view, metabolic syndrome is a pandemic of today. According to a number of epidemiological studies, the prevalence of metabolic syndrome in different countries ranges from 12.4 to 28.5% in men and 10.7 to 40.5% in women. Metabolic syndrome is diagnosed in 30-40% of hypertensive patients (Khromylev AV, Makatsaria AD Pathogenetic mechanisms of thromboembolic complications of the metabolic syndrome in pregnancy. Obstetrics, Gynecology and Reproduction. 2014;8(1):68-73. (In Russ.))

In recent years, a lot of new information has been published about the development of metabolic syndrome as a result of metabolic disorders among the world's population. For example, according to Dallongeville J., excess body weight, high waist circumference, and high-density lipoprotein levels have a greater impact on the development of metabolic syndrome in women, while in men, systolic and diastolic blood pressure and apolipoprotein B level are more important. is considered These data lead to the conclusion that it is possible to create different diagnostic criteria for metabolic syndrome in men and women. In epidemiological studies of recent years, the manifestation of metabolic syndrome in various forms is studied with special importance in order to develop an effective prevention strategy. According to several researchers, the manifestation of symptoms of metabolic syndrome is characterized by a clear order. For example, patients under the age of 50 often have carbohydrate metabolism disorders and changes in the left ventricular myocardium, and patients over the age of 50 often have dyslipidemia, abdominal obesity, and arterial hypertension. However, type 2 diabetes rarely occurs as an early manifestation of metabolic syndrome, and other components of metabolic syndrome develop more rapidly after age 50. According to many studies, arterial hypertension is one of the main symptoms of metabolic syndrome, and today many researchers consider arterial hypertension to be a part

of metabolic syndrome (Alexandra V. Solovieva, International Heart and Vascular Disease Journal Volume 5, Number 15, September 2017)

Metabolic syndrome is known as a combination of diseases that increase the risk of atherosclerotic cardiovascular diseases and type 2 diabetes. There are also data on increased risk of disease outcomes and mortality in patients with metabolic syndrome with the COVID-19 disease pandemic. Examples of these risk factors are atherogenic dyslipidemia, high blood pressure, high level of glucose in plasma, thrombotic condition. Metabolic syndrome doubles the risk of cardiovascular disease and 5 times the risk of developing type 2 diabetes. The International Diabetes Federation estimates that approximately 25% of the world's population has metabolic syndrome (Hamidreza Pouragha, Mehdi Amiri, Journal of Diabetes & Metabolic Disorders (2021) 20:1169–1178).

The components of the metabolic syndrome have a significant impact on all systems in the body, as well as on the hemostasis system. The development of insulin resistance, which is the main pathogenetic factor of the metabolic syndrome, disrupts the synthesis of nitric oxide and prostacyclin in the endothelium of blood vessels. In addition to the vasodilating activity, impaired NO synthesis affects platelet adhesion and aggregation, reduces the permeability of the vascular wall, and the vascular smoothness. slows down the proliferation of muscle cells [8,20,24]

On the basis of the results of the studies carried out to date and the information presented in the literature, it is possible to understand how significant the impact of the metabolic syndrome on the life of society is. Many other complications can be prevented and the clinical course of the main disease can be alleviated by early detection and prevention of the changes that occur in the hemostasis system as a result of metabolic syndrome.

CHAPTER 1. LITERATURE REVIEW. METABOLIC SYNDROME AND ITS RELATIONSHIP WITH HEMOSTASIS

1.1 Epidemiology, definition and classification of metabolic syndrome

The first information about metabolic syndrome (MS) dates back to 1922, when GF Lang focused on the common combination of obesity, type 2 diabetes, and arterial hypertension with gout. In 1926, A.L. Myasnikov noted the natural connection between hypertension and hypercholesterolemia, hyperuricemia and obesity. YM Tareev in 1948 pointed out the connection between hypertension and obesity, the increase in the level of cholesterol and uric acid in the blood. In 1980, M. Henefeld and W. Leonardt called this type of metabolic disorder metabolic syndrome.

According to the World Health Organization (WHO), more than 1.9 billion adults are overweight. More than 600 million of them suffer from obesity. Over the past ten years, the number of obese patients has increased by 75%. By 2030, 73% of men and 63% of women in Europe are expected to suffer from obesity [1].

In the mid-20th century, scientists focused on the link between obesity and the risk of developing type 2 diabetes and cardiovascular disease. This combination was first described in 1988 by G. Reaven. In the following years, various terms were proposed to define such relationships: polymetabolic syndrome, dead quartet, syndrome X, etc. Currently, the name "metabolic syndrome" (MS) is more commonly used in the literature.

The prevalence of MS in the general population is 14 to 24%. The highest incidence was observed in the USA (23.7%) [2]. M.N. Mamedova (2007). according to him, MS is 2.4 times more common in women and the number of patients increases with age [3].

In recent years, a lot of new information has been published about the development of metabolic syndrome as a result of metabolic disorders among the world's population. For example, according to Dallongeville J., excess body weight, high waist circumference, and high-density lipoprotein levels have a

greater impact on the development of metabolic syndrome in women, while in men, systolic and diastolic blood pressure and apolipoprotein B level are more important. is considered These data lead to the conclusion that it is possible to create different diagnostic criteria for metabolic syndrome in men and women. In epidemiological studies of recent years, the manifestation of metabolic syndrome in various forms is studied with special importance in order to develop an effective prevention strategy. According to several researchers, the manifestation of symptoms of metabolic syndrome is characterized by a clear order. For example, patients under the age of 50 often have carbohydrate metabolism disorders and changes in the left ventricular myocardium, and patients over the age of 50 often have dyslipidemia, abdominal obesity, and arterial hypertension. However, type 2 diabetes rarely occurs as an early manifestation of metabolic syndrome, and other components of metabolic syndrome develop more rapidly after age 50. According to many studies, arterial hypertension is one of the main symptoms of metabolic syndrome, and today many researchers consider arterial hypertension to be a part of metabolic syndrome (Alexandra V. Solovieva, International Heart and Vascular Disease Journal Volume 5, Number 15, September 2017)

According to the information provided by various authors, the prevalence of metabolic syndrome among the population today is 5-20% [1]. The occurrence of 3 signs of metabolic syndrome together is 8.9% among urban residents, 8.4% in men, and 9.4% in women [2]. Metabolic syndrome increased according to age: 6.7% among 20-29-year-olds, 43.5% among 60-69-year-olds. Manifestations of metabolic syndrome include hyperinsulinemia, insulin resistance, arterial hypertension, impaired carbohydrate tolerance, non-insulin-dependent diabetes, and the "lipid triad" (increased levels of triglycerides and low-density lipoproteins, increased levels of high-density lipoproteins and decrease), the addition of abdominal obesity, hyperuricemia, hypercoagulation, hypobibrinolysis, microalbuminuria is significant. Metabolic syndrome occurs with or without obesity, as well as impaired carbohydrate tolerance [3].

MS is defined as a combination of various metabolic disorders and/or diseases that are risk factors for the early development of atherosclerosis. According to a number of authors, patients with MS have an increased risk of major cardiovascular events: stroke, myocardial infarction (MI), sudden cardiac death. A study by SMXoxlunova et al. (2013) showed that the severity of dyslipidemia and coronary atherosclerosis was greater in the presence of MS than in the absence [4]. Also, with the development of acute coronary syndrome in such patients, endovascular technologies (coronary artery bypass graft) are used more [5, 6]. According to AM. Abdellatif (2016), MS was an independent predictor of mortality in patients with acute ST-segment elevation MI during a 36-month follow-up period [7].

Currently, there are 3 groups of diagnostic criteria for MS: WHO criteria, criteria recommended by the Adult Treatment Panel III (ATP III), and criteria of the American Association of Clinical Endocrinologists. These MS criteria are combined with arterial hypertension (AG), hypertriglyceridemia, and reduced high-density lipoprotein (HDL) cholesterol. According to WHO criteria, the presence of obesity and insulin resistance must be confirmed by the laboratory to make a diagnosis of MS.

The main link in the pathogenesis of MS is primary insulin resistance and compensatory hyperinsulinemia. Insulin resistance - a decrease in the biological effect of endogenous or exogenous insulin - occurs in 58% of people with hypertension, 84% with hypertriglyceridemia, and 84% with type 2 diabetes. When type 2 diabetes (or impaired glucose tolerance) is combined with dyslipidemia, hyperuricemia, and hypertension—the main components of MS—the detection rate of insulin resistance is 95%. This suggests that the leading mechanism of MS development is indeed insulin resistance [8]. Initially, compensatory hyperinsulinemia allows normal carbohydrate metabolism, but at the same time contributes to the development of metabolic, hemodynamic and organ disorders leading to diabetes and cardiovascular diseases [9]. In obesity, the frequency and severity of insulin resistance increases with an increase in total body fat mass,

especially in the visceral region. The mechanisms of development of insulin resistance and abdominal obesity are related to the interaction of a number of factors: genetic, gender, age and hormonal. There are 3 types of insulin resistance: pre-receptor, receptor and post-receptor. Prereceptor insulin resistance may be due to the production of a genetically determined altered, inactive insulin molecule or incomplete conversion of proinsulin to insulin. Anti-insulin hormones, insulinase and non-hormonal insulin antagonists - free fatty acids - also play a role in the development of this variant of insulin resistance. Insulin resistance of receptors occurs as a result of impaired affinity of receptors to insulin in target organ cells and activation of tyrosine kinase, which leads to disruption of the "key-lock" mechanism of insulin action. Post-receptor insulin resistance develops due to a decrease in the number of glucose-transporting proteins and a decrease in the activity of pyruvate dehydrogenase and glycogen synthetase in muscle tissue [5].

Visceral fat tissue has high metabolic activity. The intense lipolysis that occurs in it leads to excessive release of free fatty acids, under their influence the binding of insulin to hepatocytes is disturbed. This leads to a violation of its metabolism in the liver, which contributes to the development of systemic hyperinsulinemia, which subsequently increases insulin resistance[89].

In recent years, the role of anti-inflammatory cytokines (interleukin-6 (IL-6), tumor necrosis factor α (TNF-α)) in increasing insulin resistance has also been discussed. The source of IL-6 is not only adipocytes, but also macrophages infiltrating adipose tissue. The cause of excessive production of IL-6 may be hypertrophy of adipocytes, which is characteristic for inflammation of adipose tissue. In fat cells, this cytokine has a lipolytic effect, and also stimulates the secretion and activity of lipoprotein lipase. In liver cells, IL-6 promotes glucose release, stimulates glycogen breakdown by activating glycogen phosphorylase and inhibiting glycogen synthesis [10, 11]. TNF-α, mainly synthesized by monocytes and macrophages, inhibits the expression of the intracellular glucose transporter GluT-4, resulting in reduced glucose utilization. SA Butrova et al. (2007) found a

positive correlation of TNF-α with markers of insulin resistance (insulin resistance index and hyperinsulinemia) in patients with abdominal obesity [12].

Also, an imbalance in the content of adipocytokines - substances produced by adipose tissue (leptin, adiponectin, resistin, etc.) can lead to the development of insulin resistance.

Adiponectin levels play an important role in the formation of insulin resistance, the development of type 2 diabetes and the development of atherosclerosis. Correlations between blood levels of this adipokine and various clinical and metabolic parameters have been described in the literature. Thus, data were obtained that plasma adiponectin levels are negatively correlated with body mass index (BMI), waist size, waist/hip ratio, systolic and diastolic blood pressure, fasting plasma glucose and insulin levels, and insulin resistance index [13, 14]. In the study of Verbovoy AF et al. (2011) found a decrease in blood adiponectin in patients with type 2 diabetes and impaired glucose tolerance [15]. A negative correlation between the levels of adiponectin and insulin and insulin resistance was found in those who tested glucose tolerance, which indicates the role of hypoadiponectinemia in impaired glucose tolerance and the development of insulin resistance. Such correlations were not established in patients with type 2 diabetes, which can be explained by the decrease in insulin resistance in these patients during treatment.

Hyperleptinemia can also be involved in the formation of insulin resistance. In the works of A.V. Pashentseva (2012) and E.I. Vorozhtsova (2013) found a positive correlation of leptin level with insulin resistance index [16,17].

The question of the role of insulin resistance and compensatory hyperinsulinemia as risk factors for cardiovascular diseases has been discussed by scientists for a long time. The results of several large prospective studies indicate that elevated insulin levels contribute to the development of ischemic heart disease and are independent predictors of the risk of myocardial infarction and death from ischemic heart disease. Insulin resistance has been found to be associated with the presence of myocardial infarction complications in the form of heart rhythm and

conduction disturbances, early post-infarction angina, high-grade acute heart failure, and the development of a poor prognosis [18].

In the work of Verbovoy A.F. et al. (2011) reports an increase in resistin in impaired glucose tolerance and a significant positive correlation between resistin and endothelin, which may indicate a possible role of adipokine in the development of endothelial dysfunction [15].

One of the most common conditions in patients with insulin resistance and obesity is heart attack and hypertension. One of the main links in its pathogenesis is endothelial dysfunction. The endothelium plays a major role in maintaining vascular tone by releasing mediators of vasoconstriction and vasodilation. Normally, insulin causes the walls of blood vessels to relax due to the release of nitric oxide. It should be noted that the ability of insulin to enhance endothelium-dependent vasodilatation is significantly reduced in obesity and insulin resistance [5]. An important effect of insulin on hypertension is its effect on the activity of the sympathoadrenal system in obesity. In obesity, hyperinsulinemia stimulates the activity of the sympathetic nervous system at the level of the heart, blood vessels, and kidneys and increases the production of catecholamines, which leads to an increase in cardiac output, peripheral vasospasm, and total peripheral vascular resistance. [19]. Reabsorption of sodium in the proximal tubules of the kidneys increases, which leads to an increase in circulating blood volume and peripheral vascular resistance. Cardiac output and minute blood volume increase. Additional narrowing of arterioles and an increase in peripheral vascular resistance occur due to the direct stimulating effect of insulin on the proliferation of vascular smooth muscle cells. In renal proximal tubular cells, the glucose-stimulating property of the angiotensin gene is suppressed, gene expression is inhibited, and angiotensinogen secretion is increased, which leads to the activation of the renin-angiotensin-aldosterone system [48].

There is evidence in the literature of a relationship between fasting immunoreactive insulin levels, insulin resistance, and arterial stiffness [20]. However, the ICARUS (LIFE) study showed that increased insulin levels and

insulin resistance in hypertension were independent predictors of arterial stiffness only in patients who did not receive hypotensive therapy [21].

In obese individuals, hypertension may also be associated with hyperleptinemia. The contractile effect of leptin is associated with the activation of the sympathetic nervous system [22]. I.A. Fomina (2009) found a significant association of leptin with systolic and diastolic blood pressure in obese young adult males [23].

Obesity is an independent factor associated with the development of left ventricular hypertrophy [24]. Left ventricular hypertrophy is also reported to occur more frequently in men and women with MS. A.S. Droganova (2016) also published data on the relationship between fasting insulin levels and the severity of left ventricular hypertrophy [25]. Insulin resistance is thought to be associated with the development of left ventricular hypertrophy via concentric myocardial hypertrophy [26].

The following morphometric parameters also change with obesity: left ventricular diastolic volume, left chamber volume, aortic root diameter, increased left ventricular myocardial mass, and functional parameters: increased cardiac output and stroke risk [27]. However, if the increase in left ventricular myocardial mass with excess weight corresponds to a greater hemodynamic load, the increase in left ventricular myocardial mass with obesity exceeds the compensatory needs. Thus, in obesity, the initial increase in left ventricular myocardial mass is a physiological response of the cardiovascular system, but later it turns into "disproportionate" left ventricular hypertrophy, which does not correspond to the existing hemodynamic load.

Hypoadiponectinemia may also affect the development of left ventricular hypertrophy in obese patients. According to Mitroshina E.V. (2011), it was found that the left ventricular myocardial mass and its indices were significantly increased in men with the onset of obesity in adulthood and adiponectin levels of less than 10 μg / ml compared to individuals with high adiponectin concentrations. [28]. An inverse relationship between left ventricular posterior wall thickness and

adiponectin was found in adolescent obese men. This is confirmed by experimental results showing that hypoadiponectinemia is accompanied by left ventricular hypertrophy during pressure loading. Administration of adiponectin prevented the formation of left ventricular hypertrophy [29].

Fatty infiltration of the myocardium and accumulation of epicardial fat occur in obesity. At the same time, fatty acids enter the myocardial cells in greater quantities and are then disposed of. Plasma lipid levels reflect a possible relationship between obesity and metabolic disorders in myocardial hypertrophy. Various researchers have studied the relationship between total cholesterol, high-density lipoproteins, triglycerides, and left ventricular myocardial mass [30]. According to the results of some studies, it was concluded that the level of triglycerides was one of the predictors of left ventricular hypertrophy [31]. In addition, there are data on the relationship between the mass of the left ventricular myocardium and the level of leptin in patients with type 2 diabetes mellitus against the background of abdominal obesity, which suggests the role of this adipokine in the development of left ventricular hypertrophy in these patients. allows to determine the role [15] . Information about the involvement of leptin in myocardial remodeling in people with type 2 diabetes is provided by AV Pashentseva (2012), in which the author found leptin levels and left ventricular diastolic size in women and leptin levels and death in men. found a positive correlation between ng ventricular diameter [16]. Resistin has also been reported to be important in myocardial remodeling in type 2 diabetes and adult-onset obesity [32]. Correlation analysis revealed an inverse relationship between resistin and diastolic volume. A.V. Pashentseva found a positive correlation between the diameter of the pulmonary artery and resistin in men with type 2 diabetes [16].

Obesity is associated not only with an increase in the mass of the left ventricular myocardium, but also with its systolic and diastolic dysfunction. Also, with obesity, the size of the cavity of the right ventricle and the thickness of the wall increase moderately [33]. There are data on enlargement of the left ventricle in patients with obesity compared to people with a normal body mass index [34].

The mechanisms of left ventricular enlargement in obesity are probably the same as those that cause left ventricular hypertrophy: increased BMI, hypertension, volume overload, and possibly impaired left ventricular diastolic filling.

Obesity is often combined with type 2 diabetes, arterial hypertension, dyslipidemia, and ischemic heart disease. It is also known that obesity is often accompanied by insulin resistance and hyperinsulinemia. The frequency and severity of obesity-related diseases and illnesses depend not only on the level of obesity (according to BMI), but also on the deposition characteristics of adipose tissue in the body. In 1947, J. Weig described two types of fat accumulation - android (or male) and gynoid (female), noting that android obesity is more common than gynoid obesity combined with diabetes, coronary artery disease, gout. and emphasized the importance of the topography of fat tissue in the body in the development of obesity-related diseases. In recent years, many observations and studies have confirmed the following: excessive accumulation of fat tissue in the abdomen, as a rule, is accompanied by metabolic diseases and significantly increases the risk of developing hypertension, type 2 diabetes and atherosclerotic diseases increases [1, 2, 3, 4]. Metabolic diseases and various combinations of diseases caused by obesity are described under different names - metabolic trisyndrome (Camus J., 1966) [5], polymetabolic syndrome (Avogaro P., Crepaldi G., 1965) [6], "abundance" syndrome (Mehnert H., 1968) [7]. All authors assumed the existence of a connection between the disorders they described and always pointed to their role in accelerating the development of coronary artery disease and other atherosclerotic diseases.

According to modern concepts, the basis of all manifestations of the metabolic syndrome is primary insulin resistance and concomitant systemic hyperinsulinemia. Hyperinsulinemia, on the one hand, is compensatory, that is, it is necessary to overcome insulin resistance and ensure normal glucose transport to cells; on the other hand, it contributes to the occurrence and development of pathological, metabolic, hemodynamic and organ disorders, resulting in the development of type 2 diabetes, coronary artery disease and other manifestations

of atherosclerosis. This is confirmed by many experimental and clinical studies [14].

Insulin resistance is a decrease in the response of insulin-sensitive tissues to insulin, if its concentration is sufficient. The study of genetic factors responsible for the development of insulin resistance showed its polygenetic nature. In the development of insulin sensitivity disorder, mutations in the insulin receptor substrate, glycogen synthetase, hormone-sensitive lipase, β3-adrenergic receptors, tumor necrosis factor-α, secretory protein genes, as well as molecular defects in insulin signaling proteins (Rad protein and UPC in muscle tissue -1 - increased expression of the insulin receptor tyrosine kinase inhibitor, decreased membrane concentration and activity of intracellular glucose transporters - there are data on the importance of GLUT-4) in muscle tissue [15].

Abdominal adipose tissue, neurohormonal disorders accompanying abdominal obesity, and increased activity of the sympathetic nervous system play an important role in the development and progression of insulin resistance and related metabolic diseases.

The use of computed tomography (CT) and magnetic resonance imaging (MRT) made it possible to study the topography of fat tissue in the abdomen and study its visceral (intra-abdominal) and subcutaneous distribution. It was also possible to confirm the relationship between visceral adipose tissue, insulin resistance and metabolic diseases. Studies have shown that a significant increase in the mass of visceral adipose tissue (according to CG, corresponds to an area of 130 cm2), as a rule, is accompanied by metabolic diseases [16]. However, the high cost of CT and MRI studies limits their use in clinical practice. A clear correlation was established between the degree of development of visceral fat tissue and the size of the waist circumference. In both men and women under 40, visceral adipose tissue with an area of 130 cm2 corresponds to a waist circumference of 100 cm, and in 40-60 years - 90 cm. Visceral adipose tissue, unlike adipose tissue of other localization, is richly innervated, has a wide network of capillaries and is in direct contact with the portal system. Visceral adipocytes have a high density of β-

adrenergic receptors (especially β3-type), corticosteroid and androgen receptors, and a relatively low density of α2-adrenergic receptors and insulin receptors. These characteristics determine the high sensitivity of visceral adipose tissue to the lipolytic effect of catecholamines and the low sensitivity to the antilipolytic effect of insulin (especially in the postprandial period), which is often associated with hormonal changes accompanying abdominal obesity. provides good sensitivity [147].

Leptin, which is secreted mainly by adipocytes, exerts its effects at the level of the hypothalamus, regulates the eating pattern and the activity of the sympathetic nervous system, as well as a number of neuroendocrine functions. The involvement of leptin in the regulation of glucose metabolism has been intensively studied. Many studies have shown that in the liver it can inhibit the effect of insulin on gluconeogenesis by affecting the activity of phosphoenolpyruvate carboxykinase, which is the rate-limiting enzyme of gluconeogenesis [23]. As a result of some studies, it was determined that leptin can have an inhibitory effect on the tyrosine phosphorylation of the insulin receptor substrate in muscle tissue. In adipose tissue, leptin can reduce insulin-stimulated glucose transport (autocrine effect) [24]. A positive correlation between leptin production, hyperinsulinemia, and insulin resistance, independent of TVI, was shown. However, there is evidence that leptin increases glucose uptake into fat cells.

Physical inactivity and excess fat consumption are the most important external factors that negatively affect the sensitivity of tissues to insulin. Physical inactivity is accompanied by a decrease in the translocation of glucose transporters (GLUT-4) in muscle cells. Reaven G. estimates that insulin resistance can be observed in 25% of inactive people [147].

Excessive consumption of animal fats containing saturated fatty acids leads to structural changes in the phospholipids of the cell membrane and disruption of the expression of genes that control the transfer of the insulin signal into the cell, that is, the development of insulin resistance. comes [25]. Postprandial hypertriglyceridemia, which is often observed in patients with abdominal obesity,

is accompanied by excessive deposition of lipids in muscles, which disrupts the activity of enzymes involved in glucose metabolism. In other words, it causes insulin resistance [26]. This is not an exhaustive list of the possible mechanisms of insulin resistance development in visceral obesity, which clearly highlights the need for further research in this area [147].

Almost all components of the metabolic syndrome are risk factors for the development of cardiovascular diseases, and their combination significantly accelerates their development. In addition, the combination of individual components of the syndrome can be considered within the framework of the metabolic syndrome only when insulin resistance is present [147].

Disorders included in the metabolic syndrome are asymptomatic for a long time and often begin to form in adolescence and young adulthood, long before the clinical appearance of type 2 diabetes, hypertension, and atherosclerotic plaques of blood vessels. The earliest manifestations of metabolic syndrome are dyslipidemia and arterial hypertension. Of course, not all components of metabolic syndrome occur at the same time. Which phenotype of metabolic syndrome manifests depends on the interaction of genetic and environmental factors [146].

In conditions of insulin resistance in abdominal-visceral obesity, the breakdown of triglyceride-rich lipoproteins slows down due to changes in the activity of lipoprotein lipase and liver triglyceride lipase, hypertriglyceridemia develops, which leads to enrichment with high and low-density triglycerides. There is an increase in the concentration of small dense low-density lipoprotein particles and a decrease in the level of high-density lipoprotein and cholesterol in the plasma. Excessive uptake of plasma fatty acids into the liver increases triglyceride synthesis and apoprotein B secretion [147].

In conditions of insulin resistance, the activity of lipoprotein lipase and liver triglyceride lipase changes, as a result of which the amount of triglycerides, low-density lipoprotein increases, and cholesterol concentration decreases. Impaired lipid metabolism, in turn, increases the state of insulin resistance[72].

The incidence of metabolic syndrome in patients with gout is 67.8% [4,5]. The level of hyperuricemia increases with the development of other components of the metabolic syndrome, for example, excess body weight. In gout, the level of hyperuricemia is lower in cases without metabolic syndrome than in cases accompanied by metabolic syndrome. According to the information presented in many literatures, it is possible to achieve high efficiency in the treatment of gout due to the effect of siofor (metformin) on tissue insulin resistance. The use of siofor (metformin) for 6 months in gout caused a significant decrease in plasma uric acid levels and joint syndrome [6]. Metformin belongs to biguanides and is a traditional drug in the treatment of diabetes. At the same time, siofor is known to have a positive effect in the treatment of obesity, arterial hypertension, dyslipidemia, that is, the main manifestations of the metabolic syndrome.

As a result of the conducted research, the frequency of hyperuricemia in hospitalized patients with gout and metabolic syndrome was 72.9%. According to the literature, the degree of hyperuricemia, as well as the severity of insulin resistance, dyslipidemia, and arterial hypertension increases due to an increase in body mass index [5, 8]. In this study, pre-treatment serum uric acid concentrations were found to be significantly associated with biochemical indicators of metabolic syndrome such as triglycerides, cholesterol, glucose, creatinine, and urea concentrations. Only 75% of patients with gout and metabolic syndrome have insulin resistance, and 30% of patients with insulin resistance have no symptoms of metabolic syndrome [5]. In this regard, clinical (somatometric examination, measurement of blood pressure) biochemical diagnosis of metabolic syndrome significantly increases the probability of correctly prescribing siofor therapy for gout and metabolic syndrome.

The mechanism leading to increased uric acid concentration in the blood of patients with metabolic syndrome and gout is impaired renal excretion [9], which explains the positive significant correlation between uric acid, creatinine and urea concentrations. Hyperinsulinemia leads to increased reabsorption of sodium in the tubules, which is accompanied by a decrease in the excretion of uric acid by the

kidneys. Increased blood uric acid levels in insulin resistance and hyperinsulinemia may also be related to renal vascular resistance and may be inversely related to renal blood flow [10].

Concentrations of uric acid, triglycerides, cholesterol, and blood glucose were significantly positively correlated in patients with metabolic syndrome and gout. Significant correlation coefficients were found between uric acid and triglycerides, insulin and blood glucose levels in a population with metabolic syndrome [11]. A similar trend was found in patients with coronary heart disease [12]. At the same time, there is no convincing evidence in the literature that influencing insulin resistance in the absence of diabetes reduces the risk of cardiovascular disease [13]. In the study conducted, treatment of insulin resistance with siofor was performed taking into account the positive experience of six months of treatment of gout with metformin reported in the literature to reduce hyperuricemia and other manifestations of metabolic syndrome [6]. It can be assumed that this approach is effective for the treatment of the majority of patients with gout and further development of this treatment method is required. The stationary stage of treatment is necessary to determine the clinical and biochemical indicators of siofor therapy, to choose the optimal dose of the drug, to evaluate its effectiveness and possible adjustments. At the same time, the study helped to determine the dependence of the level of arterial hypertension on a number of somatometric parameters describing the composition and distribution of fat. In addition, the same trend was found in patients with metabolic syndrome and hypertension, and in patients with metabolic syndrome. It can be concluded that this shows the importance of fat in the occurrence of arterial hypertension and its role in the spread of metabolic syndrome.

30.5% of cases of metabolic syndrome occur together with arterial hypertension, and in many cases high arterial pressure occurs together with the components of metabolic syndrome [3]. According to the conducted experiments, the presence of metabolic syndrome with excess body weight, dyslipidemia and arterial hypertension components together with hypertension is 24.4%, and 25.6%

of this condition was found in men and 23.1% in women. Considering the average, it was found that the arterial hypertension was raised according to the II degree according to the classification. Increased systolic arterial pressure was more observed in women than in men. Overweight and obesity were found in 88.9% of patients. The somatometric study of physical development showed that, according to the average body weight index, men are overweight, and women have obesity of the 3rd degree.

Cardiovascular pathology, that is, ischemic diseases of the heart and brain, occlusive diseases of peripheral arteries are the most common cause of morbidity, death and disability among the population of developed countries. According to statistics of the World Health Organization, cardiovascular diseases account for 57% of the total death rate in Russia. Most of these cases are related to diseases caused by atherosclerosis [1]. The development of atherosclerotic damage of the vascular wall is a complex multistage process. Studies have shown that even before endothelial damage, blood components begin to interact with the surface of the endothelium. In particular, low-density lipoprotein, cholesterol and their active component apolipoproteins enter the subendothelial space, undergo oxidation and affect endothelial cells. In this context, the initial stage of atherosclerosis is described as a response to the retention of atherogenic particles [2]. The main risk factors that play an important role in endothelial damage are smoking, arterial hypertension and hypercholesterolemia. With an increase in the amount of cholesterol more than 8.5 mmol/l, the risk of death from cardiovascular diseases is shown to increase 4 times, when combined with arterial hypertension - 9 times, with smoking, with hypercholesterolemia and arterial hypertension - 16 times. [3] .

Dyslipidemia and associated metabolic diseases are not only atherosclerosis and its multifocal ischemic manifestations, but also alimentary-constitutional conditions accompanied by metabolic diseases in the organs of the hepatobiliary system (cholelithiasis, cholestasis in the bile ducts, an increase in cholesterol cells) including obesity. A large amount of cholesterol synthesis in the body is accompanied by a violation of the rate of transit of exogenous and

endogenous cholesterol through the gastrointestinal tract. The speed and level of absorption of cholesterol and its derivatives from the intestine changes, it becomes difficult to convert it into bile acids and steroid hormones. The processes of converting cholesterol and its derivatives into non-absorbable forms of neutral sterols and breaking down sterols to final products are impaired [6, 8, 12, 15]. Microorganisms of the gastrointestinal tract affect cholesterol metabolism and directly affect enzyme systems of body cells that synthesize endogenous cholesterol. Cholesterol synthesis by microorganisms increases, and the process of connecting cholesterol with cell membranes of organisms and microorganisms is disrupted. Any intervention that affects the composition of anaerobic bacteria changes the amount of acetate, propionate and other volatile fatty acids in the body, and also affects the amount of cholesterol synthesized by cells. Increased bacterial growth in the small intestine disrupts the natural mechanism of cholesterol homeostasis - the enterohepatic circulation of bile acids, which contributes to the further development of pathological changes in the liver. When microbial contamination of the small intestine occurs, it is damaged, the concentration of cholesterol, triglyceride and other fats increases, which leads to the development of hepatic steatosis[44].

Metabolic syndrome (MS) is a complex of metabolic, hormonal and clinical disorders that are strong risk factors for the development of cardiovascular diseases based on insulin resistance (IR) and compensatory hyperinsulinemia. In other words, MS can be interpreted as a syndrome of "abundance". WHO experts assessed the situation regarding the spread of MS as follows: "We are facing a new pandemic of the 21st century, which covers industrialized countries. The prevalence of MS is 2 times higher than the prevalence of diabetes mellitus (DM) and its rate of increase is expected to increase by 50% in the next 25 years" [1].

For years, it was believed that metabolic syndrome develops in adulthood and in the elderly, most often in men, and that young people are almost not prone to metabolic syndrome. It is also assumed that under normal conditions, the body of a healthy young person does not tend to accumulate fat and is able to regulate its

own metabolism at the neurohumoral level, and metabolic syndrome is an exception for young people and children [13]. However, it later became known that the lifestyle of modern society is such that the metabolic syndrome is rapidly aging, and also "invades" the weaker sex [10]. Thus, metabolic syndrome is more common among men, and its prevalence increases during menopause in women. The high variability of prevalence of metabolic syndrome in different studies is primarily due to the lack of clear and consistent definition of diagnostic criteria. According to a 2001 analysis of a public database in the United States, the prevalence of metabolic syndrome among adults was 23.7% (24% among men and 23.4% among women) [2]. According to Russian data in 2004, the incidence of metabolic syndrome in men aged 40-55 is 44.4%, and in women of the same age - 20.8% [14].

Today, infectious diseases are decreasing, and non-infectious diseases are increasing not only in developed but also in developing countries, and this remains the main cause of death [12; 41-45-b; 16]. Among them, metabolic syndrome is one of the main factors that threaten human health throughout the world. This syndrome is also referred to in the literature as syndrome X, insulin resistance syndrome, and a number of other terms. At this point, it should be remembered that the metabolic syndrome is not a single disease, but a complex that includes the risk factors of cardiovascular diseases, and it is interpreted differently by different medical institutions [2;39 p.].

The following 3 classifications are used in the diagnosis of metabolic syndrome [1]:

I. Classification recommended by the World Health Organization (1999):

a) in addition to two or more of the following symptoms, insulin resistance or glucose level in the blood at dinner >6.1 mmol/l (110 mg/dl), after 2 hours glucose is >7.8 mmol/l (140 mg/dl) cases;

b) YZLP <0.9 mmol/l (35 mg/dl) in men, <1.0 mmol/l (40 mg/dl) in women;

d) triglycerides >1.7 mmol/l (150 mg/dl);

e) waist circumference index >0.9 in men, >0.85 in women or TVI > 30 kg/m2;

f) arterial blood pressure > 140/90 mmHg;

II.NCEP (National Cholesterol Curriculum) ATP3 (2005):

The presence of three or more of the following signs:

a) having a blood glucose level of 5.6 mmol/l (100 mg/dl) or taking procedures that increase its indicators in the blood;

b) HDLP <1.0 mmol/l (40 mg/dl) in men, <1.3 mmol/l (50 mg/dl) in women or taking anti-drugs when the HDLP indicator is low in the blood;

c) triglyceride level >1.7 mmol/l (150 mg/dl) or taking drugs against it;

d) waist circumference >102 cm for men, >88 cm for women;

e) arterial blood pressure >130/85 mm.sim.ust. and taking drugs against it;

III. IDF (International Diabetes Federation) (2006):

a) Waist circumference >94 cm (men) or >80 cm (women) Presence of three or more of the following signs:

b) The diagnosis of diabetes was established with a blood glucose level of 5.6 mmol/l (100 mg/dl);

v) HDLP <1.0 mmol/l (40 mg/dl) in men, <1.3 mmol/l (50 mg/dl) in women, or receiving treatment with drugs when the HDLP indicator is low;

g) Blood triglyceride level >1.7 mmol/l (150 mg/dL) or taking drugs against it;

d) Arterial blood pressure >130/85 mm sim. above or taking drugs against it.

In the case of type 2 diabetes or impaired glucose tolerance, two of the above criteria are sufficient to diagnose MS. If there is no violation of carbohydrate metabolism, it is recommended to determine the fact of insulin resistance. It is known that the "gold standard" for measuring tissue insulin sensitivity is the euglycemic hyperinsulinemic clamp test proposed by RA De Fronzo. Due to its invasiveness, high cost and complexity of implementation, this

research method is used only in specialized scientific institutions and is not used in widespread clinical practice. Suggested modifications of the test with intravenous glucose administration and subsequent administration of tolbutamide to suppress endogenous glucose production by the liver are also laborious and expensive, and therefore not widely used in clinical practice [144].

Metabolic syndrome is often accompanied by obesity and type 2 diabetes (type 2 diabetes) (one of the components of metabolic syndrome). According to NHNES, US 1988-2010. body mass index (BMI) increased by 0.37% in men and women, waist circumference (WB) by 0.37% in men and 0.27% in women. [23; p. 82-93.].

According to CDC data released in 2017, about 30.2 million people age 18 and older, or 12.2% of the US adult population, have type 2 KD. A quarter of them (23.8%) did not know that they had the disease. Type 2 diabetes is known to become more common with age, with 25.2% of the US population aged 65 and older suffering from it. Prediabetes, or MS, is about three times more common, accounting for one-third of the country's older population. [29; pp. 994-1004].

Also, there is no general understanding of the etiopathogenetic mechanisms of MS development. The most common point of view is the importance of the role of insulin resistance as the main pathogenetic mechanism that triggers the whole cascade of metabolic diseases [6, 12]. A number of researchers believe that obesity, which is an independent disease and is associated with hyperinsulinemia and insulin resistance, is the main mechanism in the pathogenesis of MS [6, 13]. The causative role of arterial hypertension and lipid metabolism disorders in the pathogenesis of MS cannot be denied [7, 8]. There are different mechanisms for the development of this syndromic complex, in which each of the currently hypothesized causes may be primary in the pathogenesis of MS [9].

Impaired carbohydrate metabolism is one of the most typical and dangerous components of MS. Their prevalence among people with MS is natural, since insulin resistance plays a leading role in the pathogenesis of MS and type 2 diabetes [2,10]. Insulin resistance is manifested as a decrease in the response of

insulin-sensitive tissues to the physiological concentration of insulin. Hyperinsulinemia increases with the development of insulin resistance. This process continues while the pancreas maintains its ability to increase insulin secretion. Compensated hyperinsulinemia, while maintaining normoglycemia, is considered pathological at the same time, because it increases appetite, activates the sympathetic-adrenal system, causes an increase and spasm of smooth muscle cells in the arterial wall, and thus accelerates the development of hypertension, obesity, and dyslipidemia.

The status of carbohydrate metabolism can be evaluated according to the criteria of the American Diabetes Association. According to him, if the glucose concentration in the fasting venous blood plasma is less than 6.7 mmol / l, and if the glucose level is less than 7.8 mmol / l 2 hours after giving a 75 g glucose load, carbohydrate metabolism is considered normal. If the fasting glucose level is less than 6.7 mmol / l and 2 hours after exercise is more than 7.8 mmol / l, it is considered a violation of glucose tolerance. Diabetes mellitus is diagnosed if the plasma glucose level is greater than 6.7 mmol/l on an empty stomach and/or 11.1 mmol/l after 2 hours [144].

According to the data presented in the literature, compared to the general population, the development of ischemic heart disease is 3-4 times higher with metabolic syndrome, and death is 3 times higher, ischemic stroke is 2 times higher, and all causes of death are 2 times higher [3].

Despite the fact that the theory of the development of the metabolic syndrome has undergone certain changes in the last 10-15 years, the role of insulin resistance as a triggering factor for the pathogenesis of metabolic diseases and diabetes cannot be denied.

According to the WHO classification (1999), the main criteria of the metabolic syndrome include insulin resistance and type 2 diabetes, but according to the classification of the Association of Clinical Endocrinologists [ACE, 2003], these conditions are not separated by separate conditions and defined in fasting glucose level is more important. In recent years, it has been shown that the level of

glycemia 2 hours after a meal is not important, because a patient with type 2 diabetes is in a state of hyperglycemia after eating for more than 13 hours a day. In the presence of carbohydrate metabolism disorders, the prevalence of metabolic syndrome increases significantly. Thus, metabolic syndrome is present in 50% of patients with impaired glucose tolerance, and in 80% or more of patients with type 2 diabetes.

In recent years, the spread of type 2 diabetes has become a "non-infectious epidemic". According to the WHO, the number of people with diabetes in the world now exceeds 200 million and by 2025, their number will exceed 360 million, and the prevalence of early disorders of carbohydrate metabolism: impaired glucose tolerance and impaired fasting glycemia will be 2-3 times higher. . Also, the second fastest growing "epidemic" is obesity.

85-90% of the total number of diabetes patients are type 2 diabetes patients, which usually develops with a genetic predisposition in people over 40-60 years of age, who are overweight and lead a sedentary lifestyle.

According to the WHO definition, diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia and caused by impaired insulin secretion, its action, or both.

The pathogenesis of type 2 diabetes mellitus is based on a decrease in the sensitivity of peripheral tissues to insulin (insulin resistance), a gradual progressive impairment of insulin secretion, and a high production of glucose by the liver.

The number of patients with type 2 diabetes increases with age and obesity. Thus, the risk of carbohydrate metabolism disorders and type 2 diabetes in patients with 1st degree obesity increases 2-5 times, with 2nd degree obesity - 10 times, with 3rd degree obesity the risk of developing diabetes increases 30-40 times .

Economic development, urbanization of people's lives (computers, cars, microwave ovens, fast high-calorie foods) contribute to the development of a sedentary lifestyle, a decrease in physical activity and the development of obesity, which leads to insulin resistance [148].

Insulin resistance is a decrease in insulin sensitivity of peripheral tissues, primarily muscles, which make up the main part of the human body. Working muscles actively absorb glucose and reduce its level in the blood plasma. Loose muscles and a sedentary lifestyle hardly absorb glucose, and blood glucose levels rise. In type 2 diabetes, glucose absorption by peripheral tissues is reduced by about half.

In patients with diabetes or obesity, insulin resistance of skeletal muscles is associated with dysfunction and a decrease in the number of glucose transporters - GLUT-4, which has been proven by studying muscle biopsies in vitro.

The function of glucose transporters increases under the influence of insulin and the active work of muscles, therefore, increasing physical activity in type 2 diabetes helps to reduce the level of glucose in the blood by increasing the absorption of glucose by muscles.

Normalizing blood glucose with a sedentary lifestyle requires increased insulin secretion. Hyperinsulinemia increases appetite and contributes to the development of obesity, and with a high-calorie diet that includes a large amount of carbohydrates (including sweets), fats, and often alcohol, obesity develops at a very high rate. As a result, the following will develop: less movement, more obesity; The more obese, the more difficult it is to move. With the tendency to develop type 2 diabetes and insulin resistance, fat accumulates mainly in the abdominal cavity, especially around the peritoneum and internal organs. Abdominal or visceral obesity develops, the size of the waist grows especially strongly. If waist circumference is >94 cm in men and >80 cm in women, they have visceral obesity and insulin resistance. Waist size and the development of obesity are signs of increased insulin resistance.

Adipose tissue is an active endocrine organ that secretes more than 90 biologically active substances, including adipokines, cytokines, angiotensin, a number of hormones: leptin, adiponectin, and others. Leptin is important in regulating energy metabolism, controlling blood formation, immune system function, and angiogenesis. The level of leptin in the blood plasma is proportional

to the amount of adipose tissue [4]. Adiponectin, considered one of the symptoms of metabolic syndrome, plays an important role in the development of insulin resistance [5]. It is inversely associated with severity of obesity, TVI, severity of metabolic syndrome, type 2 diabetes, insulin resistance, dyslipidemia, fasting hyperinsulinemia, and cardiovascular disease and may play a protective role in these conditions. Reducing body weight, especially from abdominal obesity, leads to an increase in adiponectin levels and a decrease in the risk of cardiovascular pathology [148].

Against the background of insulin resistance, excess production of free fatty acids by visceral adipose tissue leads to a decrease in the sensitivity of the liver to the blocking effect of insulin on the processes of gluconeogenesis and glucose production by the liver, resulting in starvation. Hyper- and dyslipidemia leads to "lipotoxicity" and atherogenesis.

Currently, more than 90% of people with type 2 diabetes are overweight or obese and have insulin resistance. Insulin resistance is directly proportional to obesity: the more severe the obesity, the greater the insulin resistance and it precedes the development of diabetes. For example, first-degree relatives of patients with type 2 diabetes develop insulin resistance 7-12 years before their diabetes is diagnosed.

Insulin resistance has been proven to be an independent risk factor for the development of atherosclerosis and cardiovascular diseases: hypertension, coronary heart disease, myocardial infarction, ischemic brain disease, stroke. Hyperinsulinemia, lipid metabolism disorders, and hyperglycemia are also risk factors for the development of atherosclerosis and cardiovascular diseases, which develop several times more often in patients with type 2 diabetes than in nondiabetic patients.

The incidence of type 2 also varies somewhat among certain ethnic groups. It is more common among American Indians (15%) and less common among Chinese (4.3%). MS and abdominal obesity are reported to be more common among South Asian Americans. [24; p. 30:63-65]. The prevalence of overweight

and obesity in China increased from 14.6% to 21.8% between 1992 and 2002, as measured by WHO criteria. The prevalence of MS is 20% and 29% when obesity is assessed by Chinese standards. The prevalence of MS among urban dwellers ranged from 8% to 10.6%, while among rural dwellers it ranged from 4.9% to 5.3%. If the incidence increases at this rate, the prevalence of MS in China is predicted to reach 15.5% by 2017. [25; pp. 3-9].

The meeting of DM in patients with tuberculosis is of particular importance. Published in February 2018 and based on 2,291,571 patients diagnosed with active TB. A meta-analysis showed that the prevalence of DM among them reached 15.3%, and in some cases it reached 20%. [87; pp. 14-15].

I. Cimino et al. (2017) co-authored a low-calorie, low-protein, and low-carbohydrate but ketogenic diet for 4 days in the morningA high-fat diet enhances pancreatic beta cell generation and reverses T1D and T2D phenotypes in mice. [34; pp. 1119-1120]. In rats, a 4-day fasting diet (IGD) induces Sox17 and Pdx-1 stepwise expression of Ngn3 and changes in insulin-producing cells similar to those observed during pancreatic development. [34; pp. 1119-1120].

Liu et al. (2015) found that follicle-stimulating hormone (FSG) thermogenically breaks down adipose tissue and reduces fat storage in the body. The authors also reported that the nonspecific eicosanoid lipoxin A4 attenuated obesity-induced adipose inflammation and associated liver and kidney disease. [86; p. 999-1011]. Profession also has a certain importance in the formation of DM. For example, the prevalence of DM and MS among South American taxi drivers is twice that of the general population. In addition, the prevalence of prediabetes and diabetes was 17% and 16%, respectively. [4c].

Metformin is a traditionally used and effective drug for the prevention of MS. Although it is considered an antidiabetic medicine, its mechanism of action has not been fully studied. [90; pp. 349-357]. But it has not been proven to have the same effect as physical exercise. Many contain plant-based functional nutrients that slow down the progression of MS. The main biologically active ingredient in rosemary tincture is carnosic acid, a fatty acid preservative that reduces diet-

induced obesity and MS in mice. [123; p. 118]. Indian researchers in 2014 showed that adding 3 grams of cinnamon to the diet for 16 weeks led to positive changes in all components of MS in a region of northern India. Another important herb in the fight against MS is Ashwagandha and Celastrol. [70; p. 1-21].

Kefir and milk-based drinks are widely available in supermarkets in Western countries. One of their positive effects is the increase in the development of metabolic syndrome. [99; pp. 1215-1219].

Physical inactivity and excess fat consumption lead to obesity. Abdominal fat accumulation is a leading symptom of MS. Physical inactivity is accompanied by a decrease in the translocation of glucose transporters (GLUT-4) in muscle cells, and excessive consumption of animal fats leads to structural changes in the phospholipids of cell membranes and disruption of the expression of permeability-controlling genes. [3, 5, 6].

Intensive lipolysis in visceral adipocytes mainly leads to portal circulation and accumulation of free fatty acids in the liver. In the liver, free fatty acids prevent the binding of insulin by hepatocytes, which leads to the development of insulin resistance at the level of the liver, a decrease in the extraction of insulin by the liver, and the development of systemic hyperinsulinemia [5, 9, 10]. In turn, hyperinsulinemia increases peripheral insulin resistance by disrupting insulin receptor autoregulation. Free fatty acids also block the depressive effect of insulin on gluconeogenesis, which helps to increase the production of glucose in the liver. Free fatty acids, which compete with the substrate in the glucose-fatty acid cycle in muscle tissue, prevent the use of glucose by myocytes, which also contributes to the development of hyperglycemia and hyperinsulinemia [7, 8, 9].

Insulin resistance is a violation of insulin sensitivity of peripheral tissues (liver, muscles, adipose tissue, etc.). Insulin resistance is a genetic condition. Genetic susceptibility to insulin resistance is associated with mutations in genes: insulin receptor substrate I (insulin receptor tyrosine kinase), glycogen synthetase, glucose transporters II or IV, hexokinase II, free fatty acid binding protein (FABP-II). [26].

Genetic predisposition to insulin resistance and obesity, combined with low physical activity and overeating, determines the development of obesity and tissue insulin resistance and, as a result, compensatory hyperinsulinemia [1-5,8].

Metabolic diseases with insulin resistance syndrome can affect the functional activity of platelets. In the literature, there are experimental data on the effect of insulin on the ability of platelets to aggregate [7]. Hyperglycemia has been shown to induce increased platelet aggregation due to ADP and thrombin [8]. At the same time, a number of studies have been conducted on the relationship between metabolic disorders and changes in platelet aggregation activity associated with cardiovascular diseases.

Visceral adipose tissue is one of the leading factors that cause the development and progression of insulin resistance and the main manifestations of the metabolic syndrome [7].

Currently, in various fields of medicine, great importance is attached to the treatment of lipid metabolism disorders. This is due, on the one hand, to the prevalence of diseases associated with dyslipoproteinemia, and on the other hand, to the increase in metabolic diseases. Researches based on the most modern achievements of theoretical and clinical medicine have advanced a fundamentally new approach to the diagnosis and treatment of a number of pathological conditions caused by lipid metabolism disorders. At the same time, the introduced methods do not depend on nosology and refer to the pathological processes characteristic of these diseases, the basis of which is dyslipidemia.

The term "lipid distress syndrome" is increasingly used in the medical literature [6, 8, 11]. So, what is lipid distress syndrome: a newly identified disease or a new name for a well-known nosology? In 1998, academician V.S.Saveliev's diseases caused by lipid homeostasis disorders were combined into the lipid distress syndrome, which was later named after him. The concept of dyslipidemia and associated metabolic diseases (lipid distress syndrome according to VS Saveliev) is that the nosological forms included in them are, in fact, the only pathological basis of the disturbance of lipid metabolism due to changes in the

natural mechanism of cholesterol homeostasis are clinically different manifestations of the process.

According to the World Health Organization, 8.8% of the world's population suffers from DM. In addition, its prevalence varies somewhat among different regions, populations, and depending on a number of factors. [92; pp. 428-435]. A population-based study conducted abroad (2006) confirmed a significant prevalence of type 2 diabetes and pre-diabetes in Pakistan, contrary to previous opinion. [89; pp. 35-41]. Among the 18,856 examined population, the prevalence of prediabetes was 10.91% (95% CI from 10.46 to 11.36, n=2057), DM 2 - 16.98% (95% CI from 16.44 to 17.51, n=3201) proved. Glycosylated hemoglobin was equal to 5.62% among all examined, and 8.56% among newly examined. In this case, the disease was most often detected among the 51-60-year-olds. (26.03%, r<0.001), among them uneducated (17.66%, r<0.001), those with III degree obesity (35.09%, r<0.001), those with a family predisposition to the disease (31.29 %, r<0.001) and women (17.80%, r=0.009) were more common. At the same time, the multivariate analysis showed a direct positive correlation with age, BMI, central obesity, family history, hypertension, and inverse correlation with the mental capacity of the patient. Overall statistics on 1027 people showed that the sensitivity of HbA1c in diagnosing DM was 84.7%. As a result, the authors emphasized the need to develop complex, including screening, diagnostic criteria for the prevention and treatment of QD 2. [89; pp. 35-41].

In 2015, in 195 countries, 712 million people worldwide were obese. 604 million of them were adults, 108 million were children. [86; 999-1011-b].

Since 1980, according to observations made in most countries of the world, (73) obesity has increased by 2 times, while in other cases it has decreased on the contrary. [21; pp. 531-543]. However, it should be noted that earlier obesity was considered a disease of only "wealthy" people, but it was found that this observation is also common in the poor population. In addition, it has been confirmed that it is common among children. Obesity rates are increasing among

young adults aged 25-29 years, and more so among low-income people. [20; pp. 231-235].

Between 1980 and 2015, a wave-like spread of obesity was observed. In the 1990s, it decreased slightly, and then increased significantly. Overall, obesity increased 3.5 times between the recorded years. It should also be noted that during this period, obesity-related deaths increased by 1/3 times. [30; pp. 74-78].

Between 1990 and 2015, BMI-related deaths increased by 28.3%. Obesity also caused the death of 120 million people. Most of the cases are related to BMI. At the same time, BMI-related deaths, standardized for age and death status, decreased by 37.2% and 43.7% respectively in Turkey [29; pp. 994-1004].

Human body mass index (BMI) or Kettle index is a value derived from the mass (weight) and height of a given person. The obtained value allows you to classify a person's weight into insufficient, normal, overweight and determine the level of obesity. Ketle's body mass index is very important in assessing a person's health, and allows to assess the importance and necessity of treatment. This index is calculated according to the following formula:

$$\text{BMI}=\frac{m}{p^2}$$

here, m- body weight, kg; p- height, m; unit of measure: kg/m2;

Body mass index	Result
<16	Severe body weight deficiency
16-18.5	Lack of body weight
18.5-25	Normal body weight
25-30	Excess body weight
30-35	I degree of obesity
35-40	II degree of obesity
>40	Severe obesity

It should be noted that obesity is not synonymous with MS. Because there is also a healthy metabolic expression, this group includes people with high insulin sensitivity, but without hypertension, hyperlipidemia and other symptoms of MS.

A number of epidemiologic observations suggest that healthy metabolic obesity makes up a significant portion of the population where obesity is identified. [6]. Co Laus (2010), conducted by Co Laus (2010), randomly selected one center, 6188 Caucasian residents and extensively phenotyped 35-70-year-old residents of Lausanne, Switzerland, prevalence of overweight, obesity, respectively, hypertension, hyperlipidemia, diabetes and microalbuminuria 36.6% ; 15.7%; 36.7%; 34.2%; It was 6.6% and 6.3%. In this case, the prevalence of all mentioned parameters was more common in men than in women and increased with age. This situation has been confirmed in other population studies. [31; p. 961-975.].

According to the IDF [32;pp.181-187], Diabetes Atlas, the prevalence of metabolically healthy obesity was 8.8% (415 million) in 2015, and these figures are expected to increase to 10.4% by 2040. (642 million) is enough.

It should be noted that the highest prevalence of DM is recorded in the countries of North America and the Caribbean basin (11.5%). More than half of the patients with diabetes lived in Southeast Asia and the Western Pacific, and the prevalence was relatively lower in African regions. However, according to the predictions of scientific observers, it is estimated that in the next 25 years, the highest prevalence of DM will be observed in Africa, sub-Saharan Africa, the Middle East and North Africa (141% and 104%, respectively). [55; pp. 1262-1268].

It is more difficult to record the prevalence of MS among the population, because it is 3 times more common than diabetes and, according to scientists' estimates, it makes up a quarter of the world's population [64].

Despite the fact that the epidemic growth of metabolic syndrome in the short term has turned its hereditary predisposition into a secondary component, today genes associated with obesity and metabolic syndrome have been identified. Metabochip (2012) identified 97 associated loci in 339,224 BMI individuals and

56 of them were new. 97 loci accounted for 2.7% BMI variation, >20% of the total variation belonged to it [143]. However, epigenetics is thought to play an important role in MS. Because there is information that parenteral obesity can be observed in the offspring of those with epigenetic changes in spermatozoa or oocytes, or more often around the uterus. When a child is born to parents who are obese, but have undergone bariatric surgery before pregnancy, they are less prone to MS compared to those born to parents who did not undergo surgery [145; 113 p.].

The spread of MS can be explained by the following mechanism. Physical activity and exercise are crucial components of energy expenditure and its balance. But their effect is not immediately apparent [33; pp. 96-106]. As a result of regular chronic physical load or increased physical activity, structural changes are observed in the muscles. In particular, the number of mitochondria, metabolically useful hormone irisin increases in them and tissues, and as a result, the inversion of muscle resistance to insulin and liver postprandial lipogenesis decrease [34; pp. 1119-1120]. However, according to NHANES data, the number of adults with excess BMI in the USA in 1988-2010 showed a lack of physical activity in their free time from 19.1-51.7% in women and 11.4-43.5% in men. ``payed." According to this study, the average calorie intake during this period did not change, and the increase in TVI and waist circumference was related to the lack of physical activity in free time [35; 1265-1275 p.].

According to the CDC's Centers for Disease Control and Prevention, 40.8% of Americans are physically inactive and need at least 10 minutes of physical activity per day. Although such a situation is relatively rare among the population of developing countries, today the increased use of cars, staying at home for a long time watching TV or various games brings them closer to a sedentary lifestyle. A sedentary lifestyle is the main reason for the development of MS [48; pp. 319-328].

A number of previous studies have confirmed that the traditional Mediterranean diet is beneficial in preventing DM and MS. [73; pp. 1274-1279]. Observations by Predimed (2013) showed that adding one ounce of olive oil to the

daily diet reduced the occurrence of metastases and had a positive effect on the course of hypertension. [80; pp. 294-307.]. Certain dietary factors have also been shown to prevent the development of MS. Among them, zarchiva, luteolin, red hot pepper extract, cinnamon, olive oil, rosemary and others are indicated separately. In addition, systematic analyzes conducted in recent years have shown that a relatively large amount of nutritional polymephenols has a positive effect on MS characteristics, including bean flower, citrus products hesperidin, quercetin has a positive effect on lipid metabolism, a small amount of cocoa has a positive effect on blood pressure and blood glucose levels. and green tea has been shown to reduce BMI, waist circumference, and improve metabolism. [82; pp. 1023-1036].

Epidemiological studies have shown that consumption of capsaicin-containing foods is associated with a reduction in MS. It is abundant in hot peppers and has been shown to reduce metabolic dysregulation, obesity and DM in mice by upregulating the expression of adinopectin and its receptors. [85; pp. 792-800].

In clinical practice, isolated arterial hypertension (AG) is very rare. In most cases, hypertension is associated with other metabolic risk factors, such as abdominal obesity, dyslipidemia, and impaired carbohydrate metabolism, which are components of the metabolic syndrome (MS). Studies have shown that in young patients with MS, in addition to the balance of cytokines and adipokines, changes in hemostasis are detected with the activation of blood coagulation, the slowing down of the activity of the fibrinolytic system, and the reduction of the thrombogenic properties of blood coagulation [1, 2]. Before the development of cardiovascular complications in young patients with various components of MS, it is effective to evaluate the correlation of the above changes with damage to target organs in the subclinical state, which will expand the understanding of the features of pathogenesis, as well as timely diagnosis approaches. develops and allows to correct these violations [3-7].

Currently, much attention is paid to the study of the molecular genetic basis of the development of MS. The search for genes that predispose to metabolic diseases continues. There is evidence that MS is associated with polymorphic

variants of some genes whose expression products play an important role in adipogenesis and regulation of carbohydrate and lipid metabolism. These include: adiponectin, leptin, resistin, aliprotein A1, paraoxonase 1 and other genes [7].

Insulin resistance and hyperinsulinemia are one of the main factors leading to the development of type 2 diabetes, especially in people with a genetic predisposition [35]. It is known that one of the most frequent complications of insulin resistance is hyperinsulinemia and hyperglycemia. In conditions of insulin resistance, the use of glucose by peripheral tissues decreases and the production of glucose by the liver increases, which contributes to the development of hyperglycemia. With compensatory hyperinsulinemia, the state of normoglycemia is maintained with the ability of β-cells to adequately respond to an increase in blood glucose. At the same time, constant stimulation of β-cells, possible genetic diseases that affect their functionality, and the effect of an increase in the concentration of fatty acids in the plasma on β-cells (the phenomenon of lipotoxicity) contribute to the development of secretory dysfunction of β-cells, insulin secretion progressive disorder, insulin resistance and type 2 diabetes develop over time.

With the development of type 2 diabetes, the resulting hyperglycemia leads to further development of impaired insulin secretion by β-cells (the phenomenon of glucose toxicity) and increased peripheral insulin resistance.

With insulin resistance syndrome, vascular endothelial dysfunction develops and, in particular, the synthesis of nitric oxide in the vascular wall is disturbed (nitric oxide is a powerful vasodilator). It has an inhibitory effect on the proliferation of smooth muscle cells, reduces the adhesion of monocytes to the endothelium of the vascular wall, and reduces lipid peroxidation, that is, protects the walls of blood vessels from damage. Therefore, developing endothelial dysfunction contributes to the acceleration of atherosclerotic vascular damage, as confirmed by many studies [36]. According to the data presented in the literature, mortality from ischemic heart disease among patients with metabolic syndrome is 2-3 times higher than in the general population.

From the analysis described above, it can be concluded that MS is a complex pathophysiological condition. An important role is played in its development by the imbalance between the calories consumed and the energy lost. Also, the genetic and epigenetic composition of the population, the quality and composition of the food consumed are important.

MS is not sudden, it cannot be quickly eliminated or controlled, but it can be done if there is a will of society. It is also important to regularly inform the population about the dangers of MS.

1.2 Changes in the hemostasis system and their role in the development of diseases

Hemostasis is a system of various components that constantly maintains the structural integrity of the vessel, ensures the liquid state of the blood and the ability of the blood to clot when the blood vessels are damaged.

Usually, the state of the hemostatic system depends on the balance and interaction of its 5 main components:

1. Vascular wall (primarily endothelium and collagen), as well as a number of substances synthesized in the intima.
2. Blood cells are mainly platelets and their factors, as well as leukocytes and erythrocytes.
3. Proteins or factors of the coagulation system.
4. Activators of the fibrinolytic system.
5. Inhibitors of the fibrinolytic system.

In general, the hemostatic system is a complex neurohumoral regulation with a forward and feedback mechanism, as a result of which cellular homeostasis is constantly maintained.

Depending on the components and mechanisms involved in stopping bleeding, the hemostasis system is divided into 2 parts:

1. Primary, or vascular-platelet hemostasis.

2. Secondary hemostasis involving plasma coagulation factors and platelet factor 3. It lasts 5-10 minutes and ends with the formation of fibrin, which holds the platelet clot.

Primary (vascular-platelet, microcirculatory) hemostasis.

It initiates all hemostasis reactions in capillaries, venous and arterial vessels up to 100 microns in diameter. In the case of injuries and damage, blood vessels and platelets are the first to participate in the reaction to stop bleeding.

Endothelial function. Under normal conditions, the endothelium of blood vessels is very resistant to thrombosis and plays an important role in maintaining the liquid state of blood and preventing thrombosis. This feature of the endothelium is provided by:

• the contact inertness of the inner surface of these cells facing the vascular surface, as a result of which it does not activate the hemostasis system;

• strong inhibitor of platelet aggregation - synthesis of prostaglandin \2 or prostacyclin;

• the presence of a special glycoprotein of endothelial cells - thrombomodulin in the cytoplasmic membrane, which binds thrombin, as a result of which the latter loses its ability to clot, but has an activating effect on two important anticoagulant systems - S and S proteins.;

• abundance of mucopolysaccharides on the inner surface of blood vessels and fixation of the heparin-antithrombin III complex in the endothelium;

• synthesis and secretion of tissue plasminogen activator (TPA), as well as the ability to stimulate fibrinolysis through the "protein C+S" system;

• removal of activated blood coagulation factors and their metabolites from the blood.

At the same time, the endothelium has a unique ability to change its antithrombotic potential to thrombogenicity. This change occurs due to blood stasis, hypoxia, physical and chemical factors on vascular walls, exo- and endotoxins, including bacterial endotoxins, immune complexes, antiendothelial and antiphospholipid antibodies, inflammation mediators play a leading role.

interleukins, tumor necrosis factor, etc.), as well as cell and plasma proteases (elastase, trypsin, thrombin, etc.). The same transformation is observed with metabolic changes in the vascular wall (atherosclerosis, diabetic angiopathy).

Properties of subendothelium. When the endothelial cells die, the subendothelium, which contains a large amount of collagen, is exposed, in contact with which the activation, adhesion and spreading of platelets, as well as the activation of the blood coagulation system, take place. This process is carried out with the participation of large molecular glycoproteins, primarily von Willebrand factor, fibronectin and fibrinogen. The important role of this mechanism is confirmed by genetically determined defects of the subendothelium - thinning and reduction of collagen (Rendu-Osler disease, mesenchymal dysplasia), abundant and long-lasting bleeding from damaged microvessels, as in von Willebrand factor deficiency. observed.

Structure and function of platelets.

Thrombocytes are disc-shaped cells with a smooth cytoplasmic membrane provided with a ring of microtubules in the uninjured state. When activated, the cell membrane invaginates and connects to a network of multiple channels called the open tubular system, which are tightly interconnected within platelets. It was found that the central channels of this system connect to the extracellular space and express the same glycoproteins as the cell membrane. 4 types of granules are found in the cytoplasm of unactivated platelets: α-granules, dense granules, lysosomes and peroxisomes. Most α-granules contain platelet-specific and platelet-specific peptides, which participate in the mechanisms of coagulation, inflammation, immunity, and restore and modulate these processes.

The outer cell membrane is covered with glycoproteins that play an important role in platelet adhesion and aggregation. These molecules consist of extracellular adhesion glycoproteins (fibrinogen, collagen, von Willenbrand's factor) and external domains that act as receptors that bind glycoproteins and transmembrane peptides that mediate the processes of platelet activation and their shape change. Most platelet glycoproteins, except glycoprotein complex Ib-IX, are

encoded by genes of the integrin family. Platelet membranes contain receptors for the physiological mediators of platelet activation (ADP, adrenaline, serotonin and thromboxane A2) and the Fc fragment of immunoglobulins. In addition, HLA class I antigens are expressed on the platelet membrane.

Functions of platelets.

Platelets perform various functions in vivo:

1) due to the adhesion and aggregation of platelets, the hemostasis system is immediately triggered, which leads to the formation of a thrombus from platelets;

2) local release of vasoconstrictors to reduce blood flow in the affected area;

3) catalyzing the reactions of the humoral coagulation system with the formation of a fibrin thrombus as a result;

4) start tissue regeneration;

5) regulation of local inflammatory response and immunity;

6) angiotrophic function.

Unstimulated platelets circulate as smooth discoid cells with metabolic activity. Such platelets do not enter into physiologically significant interactions with other formed elements of peripheral blood or with the monolayer of endothelial cells lining the endovascular space.

There are a number of pathological conditions that lead to disruption of these processes in normal physiological conditions, and as a result of their influence, the occurrence of pathological conditions in the hemostasis system aggravates the clinical course of the main disease and increases the risk of complications. Metabolic syndrome is a systemic pathological condition that affects the entire body and has a significant effect on the hemostasis system.

MS encompasses a number of clinically and pathogenetically interrelated conditions (insulin resistance, arterial hypertension, and hyperinsulinemia) and increases the risk of atherosclerotic damage to blood vessels. In patients with MS and type II QD, due to increased activity of fibrinogen and blood clotting factors,

thrombocyte hyperaggregation and hypercoagulation occur, and thrombogenic risk increases.[28; pp. 33-89]. The formation of microthrombi in the myocardial microcirculation due to the increase in the activity of platelets plays an important role in the worsening of heart failure [27; pp. 260-267].

Modern studies have shown that metabolic syndrome is accompanied by changes in the blood coagulation system. Pathological processes occur in all parts of the hemostasis system - platelets, plasma, as well as affect the system of anticoagulants and fibrinolytics. According to the literature, disruption of plasma hemostasis in MS is accompanied by an increase in the level of various coagulation factors - II, VII, VIII, IX, X, XIII, and fibrinogen [3]. Many studies have proven that changes in the plasma part of the hemostatic system develop in response to hyperinsulinemia. More and more information is emerging about the association between factor VII, insulin resistance and the metabolic syndrome. Genetic studies have also revealed a correlation between increased synthesis of factor VII and low sensitivity of tissues to insulin [4-6].

In metabolic syndrome, the balance of prothrombotic and fibrinolytic activity of blood is also disturbed [16], which causes a high frequency of vascular pathologies of various localization and often leads to death. Increased thrombogenic risk in patients with metabolic syndrome is associated with hypercoagulation of platelets due to hyperaggregation of platelets, increased levels of fibrinogen and activity of blood clotting factors, as well as thrombocytes and hypofibrinolysis as a result of the effects of a complex of metabolic disorders and hemodynamic factors. [1, 18, 19].

The components of the metabolic syndrome have a significant impact on all systems in the body, as well as on the hemostasis system. The development of insulin resistance, which is the main pathogenetic factor of the metabolic syndrome, disrupts the synthesis of nitric oxide and prostacyclin in the endothelium of blood vessels. In addition to the vasodilating activity, impaired NO synthesis affects platelet adhesion and aggregation, reduces the permeability of the

vascular wall, and the vascular smoothness. slows down the proliferation of muscle cells [8,20,24]

Features of hemostasis system disorders in patients with metabolic syndrome are currently not sufficiently studied. The question of which components cause changes in blood rheology is still open. In this regard, the aim of this study was to study parameters of plasma-platelet hemostasis and their relationship with components of metabolic syndrome [15].

MS and type 2 DM are major risk factors for cardiovascular disease. MS encompasses a number of clinically metabolic and pathogenetically interrelated conditions (insulin resistance, arterial hypertension, and dyslipidemia) and increases the risk of atherosclerotic vascular damage. In patients with MS and type 2 DM, the activity of fibrinogen and blood clotting factors, as well as hyperaggregation and hypercoagulation of platelets due to increased fibrinogen, increase the thrombogenic risk. [28; pp. 33-89]. Metabolic disorders associated with insulin resistance significantly affect the functional activity of platelets. [36]. The formation of microthrombi in the myocardial microcirculation due to the increase in the activity of platelets plays an important role in the worsening of heart failure. [27; pp. 260-267].

According to the information in the literature, the increase in the activity of type 2 DM platelets is associated with the following metabolic changes: the I phase of platelet aggregation is associated with changes in the storage of proteins in the blood plasma, the second phase is associated with granulocytes with polymorphous nuclei. [105; pp. 132-135]. Also, some observations show an increase in the average size of platelets in type 2 DM. According to other data, platelet size and volume do not differ between type 2 DM and healthy individuals. [101; pp. 15-18].

A number of published scientific works have proven the existence of a connection between MS and platelets in the blood. K. Kotani and co-authors in 2007 showed that when there are three or more components of MS, they have a significant increase in the amount of platelets in the blood compared to those who have two or one or none. [78; pp. 376-379]. After the documented correction of

various biosocial factors (age, smoking, alcohol consumption and physical activity), a strong biogenic correlation was found between the components of MS and the number of platelets in the blood. Thus, thrombocytosis partially explains the risk of cardiovascular diseases in patients with MS [78; 376-379-b; 79; pp. 758-765].

Based on the platelet size, there are data confirming that its spontaneous occurrence in the formed aggregation is significantly higher in MS patients compared to healthy ones. According to the characteristic of light transmittance of the curve between the size of the aggregate line, the induced collagen aggregation of individual MS platelets was significantly higher compared to healthy ones [81; pp. 195-199].

A number of scientists, based on their observations, noted that the sensitivity of platelets in type II diabetes occurs under the influence of its aggregation inducers, in particular, ADF, thrombin and collagen [51; 1168-1174-b; 72; 13-15-b.] . A direct correlation between glycosylated hemoglobin and platelet aggregation induced by ADF and collagen was found [43; pp. 3045-3060]. Not the interaction based on cholesterol and phospholipids, but the increase of glycosylated proteins in the platelet membrane sharply reduces its sensitivity [44; pp. 707-709]. The increase of glycosylated protein of platelets in diabetes models its cellular activity. In particular, the glycosylation of calmodulin has a modulating effect on the activation of nitric oxide (NO3) and leads to a decrease in nitric oxide synthesis [47; pp. 1-17].

C-peptide has been shown to model thrombus formation in vitro [42; pp. 711-715]. Observations confirmed that the basal level of C-peptide is positively related to the rate of platelet aggregation induced by collagen ADF [50; pp. 654-662]. The identified positive correlation is the basis for saying that there is an interaction between platelet aggregation and type II DM with protein C exceeding the norm. Type II DM, insulin resistance, hyperglycemia, and non-enzymatic glycosylated protein are factors that increase sensitivity to inducers of platelet aggregation [53; pp. 792-807].

According to some data, hyperglycemia increases platelet aggregation, on the contrary, its return to normal slows down this process.[54; pp. 415-445]. According to P. Gresele and co-authors (2010), a short-term increase in blood glucose in patients with type II DM quickly activates platelets. This process is confirmed by the interaction of platelets with collagen, the increase in platelet antigen expression associated with the increase in urinary excretion of 1-dehydro-TXB2, which is a marker of platelet activation..[55; pp. 1262-1268]. A high concentration of glucose hypogenetically activates osmotic mechanisms, in particular, C 9 isozyme protein kinases and intracellular calcium [75; p. 1982-1988].

The NO molecule is a universal regulator of the cardiovascular, immune and nervous systems in the body. It is synthesized in endothelial, nervous, mucous, muscle cells and platelets. Therefore, NO is a universal regulator of autoregulation of platelet activity. It is synthesized in endothelial, nerve, smooth muscle cells and platelets. Consequently, NO improves the autoregulation of platelet activity. It is also an unwelded neutral, electronic. Compared to others, this molecule (O 2 i CO 2) v has the highest diffusion coefficient in the body and passes freely through cell membranes. [83; pp. 208-219]. NO is synthesized via NO3 and exists as three different isoenzymes NOS, neuronal (nNOS, NOS-1), inducible (iNOS, NOS-2) and endothelial (eNOS, NOS-3). [88]. Enzymes catalyze the five-electron oxidation of L-arginine to L-citrulline and NO. Constitutive as well as inducible NOS is expressed in most cells. In addition, constitutive NOS isoforms are components of two signaling pathways in the cell. [90; 349-357-b; 94; pp. 1126-1167].

There is a large body of data revealing the involvement of iNOS in the physiological synthesis of NO and its effects on the co-synthesis of eNOS and nNOS in infectious, allergic, and autoimmune diseases. [96; pp. 893-900; 100; pp. 2494-2498]. iNOS activation is a component of numerous protective-adaptive reactions [108; 101-104-b; 109; pp. 397-404]. Basal iNOS-catalyzes and its regulation of NO vascular tone is still a matter of debate. [120; pp. 1176-1189].

Because eNOS is very weakly expressed in the plasma membrane of endotheliocytes and co-localizes with caveolin. [121; pp. 383-399]. In most cases, free synthetic fatty acids, which are elevated in obesity, inhibit eNOS in vitro. [124; 264-274-b; 125; pp. 4-7]. According to the results of some investigations, the activity of eNOS in platelets is much lower in patients with diabetes than in healthy people. [111; pp. 56-65]. The literature we reviewed states that platelet eNOS is activated by β2-adrenoceptors. Therefore, the activation of eNOS in platelets is caused by the increase of sAMF and the activation of protein kinase A (RKA), sAMF and sGMF are manifested through a strong system connection between them [91; p. 58-62.].

Activation of iNOS leads to the synthesis of high concentrations of NO, which stimulates T-cell immunity and exerts cytotoxic effects. iNOS is present in macrophages, neutrophils, keratinocytes, fibroblasts, chondrocytes, osteoclasts, neurons, astrocytes, epithelial cells (respiratory, retinal, pigment, kidney, tubular and adenocarcinomas), hepatocytes, b-cells of the pancreas, endothelium and endothelial cells, vascular smooth muscle cells is identified. The enzyme is activated under the influence of cytokines affecting the synthesis of sAMF (adrenaline, glucagon), bacterial antigens in inflammation, as well as ultraviolet, ozone, nicotinic acid and hormones. This isoform of NOS, unlike other forms, creates several times more NO and does not require Ca 2+ for the process. [128; pp. 155-164]. In the investigations of a number of foreign scientists, basal NO production by monocytes was isolated from patients with MS, and this was probably due to the activation of iNOS. [133; pp. 978-992].

NO stimulates endothelial growth factor synthesis, but inhibits smooth muscle cell proliferation and migration, resulting in neointima and vascular hypertrophy. Its low concentration inhibits apoptosis, while its high concentration stimulates apoptosis, reduces extracellular matrix synthesis, and ultimately , the normal structure of the vessel wall is preserved. [138; pp. 27-35]. NO has anti-inflammatory and antithrombotic properties. [139; pp. 327-358]; [145; p. 113]). In

healthy individuals, NOS inhibition significantly increases blood clotting time and adversely affects other parameters of the coagulogram. [26; pp. 816-823].

Many physiological and toxic effects are observed in the direct interaction of NO with iron. Cyclic guanosine monophosphate regulates vascular tone, immune responses, neuronal mediation, platelet aggregation, platelet-endothelial action, and effects on various types of muscle cells and other processes. [37; p. 475-480;], [46; p. 99].

NO production is reduced in insulin-stimulated endothelial cells and smooth muscle cells with insulin resistance. [63; pp. 1451-1458]. In diabetes, platelet adhesion and self-aggregation increase. Increased NOS activity in platelets in patients with MS plays a decisive role in the occurrence of hyperactivity of platelets and the development of macro and microangiopathy. Examination of NO production in platelets showed that NO basal production was reduced in all groups of patients with MS compared to healthy donors. In addition, the lowest levels of NO were observed in patients with DM in the decompensation stage [69]. Also, there is an inverse correlation with the synthesis of sGMF in platelets with the participation of NO, and the blood glucose index with glycosylated hemoglobin. [64]. Decreased basal production of NO cells in MS depends on a number of factors. In the process of glucose autooxidation, the presence of hyperglycemia creates conditions for the formation of superoxide anion. [71; pp. 146-154].

Insulin resistance syndrome with endothelial dysfunction also reduces the production of NO and (PGI2) in endotheliocytes. [Dandona and Aljada, 2004]. Adenylate and guanylate cyclase are synthesized by NO and PGI2 acting on platelets, through which sAMF and sGMF are synthesized. Adenylate and guanylate cyclases are regulated by prostacyclin and NO, respectively [68]; [65; s. 1939-1945]. Degradation of sAMF and sGMF occurs in the presence of phosphodiesterases. [66]. Platelet hyperactivity can lead to an abnormal pathway. EM Idrisova, co-authors (2007y) in patients with diabetic retinopathy, reduction of platelet adenyl cyclase and reduction of sGMF was found. [62; pp. 106-112].

According to literature, platelets of diabetic patients are less sensitive to NO and PGI2. The number of PGI2 receptors is not reduced and this is a defect

Some investigators have shown increased activity of sGMF-dependent phosphodiesterases, ultimately leading to reduced NO sensitivity. [142; pp. 78-85]. Modern approaches against eNOS use antibodies to predict the presence of a 135 kDa protein in human platelets. However, currently the data do not clearly confirm that it is an eNOS protein. [140; pp. 1517-1530]. NOS inhibitors have no effect on human platelet activity and wild-type mice with baseline induced platelet aggregation. No difference was detected between mRNA iNOS and eNOS. It should be noted separately that human platelets are determined using standard methods. [144; p. 76-82] However, the use of modern technologies does not fully confirm this. Some ideas based on this fact suggest that some platelet agonists have a direct effect on soluble adenyl cyclases. [137; pp. 1387-1395]. Although regulation of NOS in platelets is currently debated, insulin-induced cGMP synthesis is reduced and type 2 DM agonist-induced platelet aggregation is insensitive to NOS inhibitors. [130; pp. 2380-2384].

The effects of leptin are known to science and the concept of "leptin resistance" exists[1-4]. Leptin, a polypeptide hormone produced by adipocytes in proportion to the content of triglycerides, connects changes in body energy (fat) reserves with adaptive reactions in the body and controls energy balance centrally. According to studies, by binding and activating the long form of its receptor (LEPR-B) in the brain, leptin reduces food intake and increases energy expenditure[5-7]. Evolutionary considerations, together with numerous experimental data, suggest that the main physiological role of leptin is to respond to and protect against depletion of body fat, which can impair reproductive performance. In addition to markedly increased body fat mass, the phenotypes of humans and rodents lacking leptin or LEPR-B reflect a physiological response to starvation (e.g., starvation, decreased metabolic rate, infertility, immune dysfunction, insulin resistance). Thus, leptin is essential for sensing energy reserves in the central nervous system.

Obesity threatens the lives of millions of people around the world, because it is one of the most important risk factors for the development of cardiovascular diseases, cerebral strokes, diabetes, joint pathologies and depression. It is estimated that more than 110,000 deaths in the United States in 2000 were attributable to obesity [9], and therefore the economic cost of diagnosing and treating obesity-related problems in the United States is estimated at $117 billion [10].

Currently available conservative treatment of obesity, including several groups of drugs, is palliative and effective only during its implementation. After stopping treatment, weight gain is inevitable. For antiobesity drugs to be effective, they must affect energy intake, absorption, expenditure, or storage of nutrients. An important drawback of currently available drugs for the treatment of obesity is the high frequency of negative side effects. When using them, patients may experience insomnia, asthenia, fecal incontinence, arterial hypertension, tachycardia, and heart valve disease. All obesity medications, except orlistat, are unsafe and may increase mortality in patients with organic heart disease, particularly those with myocardial infarction and heart failure. As a result, some drugs have been banned by the Food and Drug Administration. For example, deoxyephedrine and d-Fenfluramine and ephedrine alkaloids, which were the first drugs approved for weight loss, are no longer used [11, 12]. In this regard, the search for new approaches to body weight control is the most important task and requires a systematic approach.

Hyperinsulinemia promotes the accumulation of abdominal fat and is thought to be a trigger for metabolic syndrome. Scientists assumed that obesity in the abdomen is a consequence of a decrease in the activity of lipolytic processes. Hormone-sensitive lipase is the key enzyme that controls the rate of lipolysis in adipose tissue. Its activation occurs through cyclic adenosine monophosphate (sAMF)-dependent phosphorylation under the influence of catecholamines, while insulin increases the hydrolysis of sAMF, inhibits lipolysis, and increases lipogenesis. At present, the mechanism of insulin resistance is still not well understood. However, there is now convincing evidence that obesity is not caused by insulin resistance [13].

Studies of acute weight changes have shown that experimental weight gain leads to increased serum insulin concentrations and reduced weight loss. Furthermore, a reduction in insulin resistance in response to weight loss has been directly demonstrated using the euglycemic hyperinsulinemic clamp technique. The method is based on intravenous injection of constant doses of insulin. Glycemic levels are regulated by exogenous administration of 20% glucose with blood glucose monitoring every 5-7 minutes. Within 1-2 hours, a balance between the intake and consumption of exogenous glucose is achieved. In this case, it is believed that the production of glucose in the liver is completely suppressed, but to obtain reliable data for the test, it is necessary to use labeled glucose. This method allows you to calculate the amount and rate of glucose utilization by muscles using the following formula: M=Ginf. + HGO - Ugl, where Ginf - the amount of glucose taken, HGO - the amount of glucose released from the liver, Ugl - the amount of glucose released with urine. It has been hypothesized that insulin resistance develops as a defense against persistent, uncontrolled weight gain. At the same time, when the ideal body weight exceeds 35-40%, tissue sensitivity to insulin decreases by more than 40% [146].

Visceral adipose tissue plays an important role in the development of insulin resistance [14]. The data of many studies are consistent with the hypothesis that the main disorder in the examined patients is an increase in body weight, which leads to an increase in the concentration of insulin in the blood. The latter is evidence of insulin resistance [15].

Thus, the activation of platelets poses a great risk in the occurrence of complications in the cardiovascular system of MS [134; pp. 3176-3180]. QD is related to changes in the intracellular signaling system that controls platelet activity. Due to the expression and activity of NOS, it changes platelet and prothrombin potentials. [129; pp. 167-176]. The antiaggregatory effect of insulin-dependent NOS and NO acting through cyclic GMF is abnormal. Aggregation-inducing agonist effects are controlled by inflammatory factors. MS and type II QD are associated with mechanisms of increased platelet aggregation activity,

including insulin resistance, hyperglycemia, and dyslipidemia. Platelet aggregation and antiaggregation are associated with metabolic disorders. It is necessary to continue to study the secondary messenger systems involved in these processes, and it should be aimed at early detection of metabolic disorders. The results of this examination serve as a foundation for the treatment and prevention of complications in the cardiovascular system in patients with MS and type II DM.

1.3 Correlation between metabolic syndrome and hemostasis system disorders

Metabolic syndrome is an urgent problem of the healthcare system not only in our country, but also in the whole world. From an epidemiological point of view, metabolic syndrome is a pandemic of today. According to a number of epidemiological studies, the prevalence of metabolic syndrome in different countries ranges from 12.4 to 28.5% in men and 10.7 to 40.5% in women. Metabolic syndrome is diagnosed in 30-40% of hypertensive patients (Khromylev AV, Makatsaria AD Pathogenetic mechanisms of thromboembolic complications of the metabolic syndrome in pregnancy. Obstetrics, Gynecology and Reproduction. 2014;8(1):68-73.)

In cases accompanied by metabolic syndrome, insulin resistance, arterial hypertension, dyslipidemia lead to a high risk of atherosclerotic vascular damage and are accompanied by changes in coagulation and platelet hemostasis [1, 2, 3]. Mechanisms of participation of platelets in atherogenesis have not been fully studied, but the results of experimental studies show that these cells are involved in the active intake of blood lipids and subsequent rapid formation of platelet aggregates [4]. Activated platelets release biologically active substances (histamine, serotonin, adrenaline, thromboxane), which increase the permeability of the endothelium, contribute to the deposition of lipids in the vascular wall [4]. Aggregates of platelets form the basis of the primary parietal thrombus, their formation can lead to the development of unstable angina, and its increase and reinforcement by fibrin threads can lead to the complete closure of the vessel and the development of myocardial infarction [5,6] .

In recent years, many researchers have attached great importance to hypertriglyceridemia, especially in the postprandial period, as a factor that accelerates the development of cardiovascular diseases. There are reports of an independent correlation between hypertriglyceridemia and carotid atherosclerosis [30]. Many studies show that hypertriglyceridemia, especially in the postprandial period, leads to a decrease in the level of high-density lipoproteins, the formation of small dense low-density lipoprotein particles and a violation of the homeostatic system: an increase in factors VII and PAI-1, as well as blood rheology Among them are the violations of the characteristics [31].

Blood coagulation disorders in metabolic syndrome are characterized by an increase in the level of fibrinogen and the level of fibrinolysis inhibitors - factor VII and plasminogen activator inhibitor 1 (PAI-1). High levels of PAI-1 are mainly produced by visceral adipose tissue and are one of the most important indicators of metabolic syndrome. Studies show that high levels of PAI-1 are independent predictors of heart attack in men with coronary artery disease [32]. Hyperinsulinemia, hypertriglyceridemia, and elevated levels of TNF-α are also thought to be important in increasing PAI-1 levels in patients with metabolic syndrome [33]. It has also been shown that a decrease in visceral fat mass is accompanied by a decrease in PAI-1 levels.

Cardiovascular system diseases, DM and MS, which is the cause of many deaths, consists of a number of interrelated physiological, biochemical, clinical and metabolic factors [75; p. 982-1988]. The basis of its clinical diagnosis is a general assessment of insulin resistance, a concomitant increase in plasma insulin, visceral obesity, atherogenic dyslipidemia, triglycerides and cholesterol, LDLP excess, HDLP endothelial dysfunction, high blood pressure, and hypercoagulability. It is now generally accepted that the inflammatory state is a component of MS [40; pp. 199-203].

Metabolic syndrome is one of the most urgent problems in medicine. Its importance is, firstly, its prevalence among the population (25-35%) [1]; secondly, patients with metabolic syndrome have a 2-3 times higher risk of cardiovascular

disease and a 5-9 times higher risk of type 2 diabetes than people without metabolic syndrome. Atherogenic potential in metabolic syndrome is 5-6 times higher than individual risk factors [2, 3, 4, 5, 6].

Metabolic syndrome is a complex set of symptoms, a combination of arterial hypertension, abdominal-visceral obesity, dyslipidemia, impaired glucose tolerance, insulin resistance, hyperinsulinemia, hyperuricemia, microalbuminuria, and hemostasis pathologies. In Russia, hypertension is 39.2% among men and 41.1% among women. Hypertension shortens the life of men by 8-10 years and women by 5-6 years. Hypertension was found to be combined with one, two and three risk factors such as hyperlipidemia, obesity, hemostatic system pathology and carbohydrate metabolism in 92% of cases. All these factors increase coronary risk [9, 10].

In addition, recent studies have shown that inflammation observed in type II DM can cause vascular damage along with metabolic disturbances. One of its effects is the simultaneous observation of endothelial dysfunction and procoagulant state [76; pp. 989-994].

According to the results of the study conducted to study the aggregation of platelets in cases induced by ADF, the level and speed of platelet aggregation along the light transmission curve increased with the increase of ADF concentration, but no statistically significant differences were observed. Patients also showed different platelet aggregation activity according to mean aggregate size curves with different ADF concentrations. Thus, at low ADF values, an increase in the degree of aggregation was observed along the mean aggregate size curve. Also, a tendency to increase the rate of aggregation along the curve of the average size of aggregates was observed in the patient group with a decrease in ADF concentration.

It is known that ADF is one of the strong inducers of platelet aggregation and is released from the secretory granules of platelets during the initial activation stage under the influence of collagen and thrombin [10, 11, 12]. When ADF binds to platelet receptors, the concentration of calcium ions in the cytoplasm of cells

increases and their shape changes, which is accompanied by inhibition of adenylate cyclase [11,12]. The metabolic effect of platelet ADF receptor activation is carried out by binding to the membrane G-protein. The final pathophysiological effect of platelet stimulation by ADF molecules is the activation of platelet glycoprotein complex II b/III a with fibrinogen receptors, which creates conditions for binding of fibrinogen and platelets [11, 12, 13]. Activated platelets release more ADF, which allows platelet thrombus to grow.

Coagulation is the process of blood clotting. The basis of the blood clot consists of components such as fibrin and protein network [77].

Thrombocytes are one of the central components of a blood clot. It is activated under the influence of various coagulation signals. After activation, they take on a star-like appearance and stick to the activated endothelium. From fibrinogen, fibrin and coagulant cytokines and enzymes participating in the formation of various blood clots are released [78; pp. 376-379].

It is known that the role of endothelial cells in inflammatory reactions, hemostatic processes, including platelet stimulation of the immune process, has recently been studied [80; 294-307-b; 81; pp. 195-199]. Platelets participate in the development of inflammatory processes with the participation of a number of low molecular and protein cytokines [56;28-30-b; 58; pp. 1577-1589].

Type I and II DM and MS are associated with increased blood glucose, lipid metabolism disorders, cardiovascular diseases, and these processes are associated with inflammation [60; pp. 1321-1326].

Complications observed in blood vessels in type I and II DM are common and are caused by a number of factors. On the one hand, passive diffusion of glucose into endothelial cells causes an increase in its concentration inside cells, which increases oxidative stress. This leads to the oxidative degradation of glucose metabolites. Also, as a result of intracellular hyperglycemia, end products of glycosylation participate in vascular damage [66]. In addition, hyperglycemia can cause glycation of proteins. This, in turn, leads to micro and macro damage of vessels. Hyperglycemia has also been reported to induce hypercoagulability [74].

In 2003, JMMiles and co-authors [93; pp. 675-681] showed that in cases where DM was not clearly detected for 2 years, adhesion and aggregation processes in platelets are activated due to short-term hyperglycemia, which is the basis for saying that glucose directly controls platelet activation. . 2003 Keating and co-authors [72; p. 13-15] increases the effect of ADF by causing platelet aggregation even in healthy people. Acute, not long-term, increase of glucose indicators changes the functional capabilities of platelets. The mentioned results revealed that platelets can be activated in the postprandial phase in patients with insulin resistance or diabetes [89; 35-41 p.; 90; pp. 349-357].

The postprandial activation of platelets was analyzed in patients with type I and II DM conducted abroad. According to him, the noted effect is observed only in type II DM [91; pp. 58-62]. In another study that investigated the characteristics of platelets in type I and II DM, it was shown that the number of platelets decreased in both cases [92; pp. 428-435]. Such a situation in type I and II diabetes mellitus can be related to the correlation between the high level of glucose in the plasma and the decrease in insulin in the plasma, as well as the high activity of platelets and the tendency to the formation of thrombus. Taking into account the crucial parameter of the metabolic syndrome - disturbances in the cardiovascular system and its coexistence with insulin resistance, it is necessary to pay attention to the high level of insulin in the plasma of patients with this syndrome and study its role in healthy endothelium. In addition to its role in glucose absorption in muscle and adipose tissue with the participation of GLUT-4 (glucose transporter-4 type of insulin-sensitive protein) translocation, which is well known from the literature, insulin is also important in vascular function, in particular, in vasodilatation. plays a role [95; pp. 1126-1167]. Insulin receptors are expressed in endothelial cells, and their endothelial-specific knockout leads to disturbances in the control of blood pressure and vascular tone [97; pp. 10-19].

Insulin exerts its vasodilating activity due to the modulation of NO derivatives. The oxidation process plays an important role in this. NO free radicals

are important vasodilators and are released from endothelial cells [107; pp. 971-981].

Considering the vasodilator properties of NO, it has a strong inhibitory effect on the activation of platelets [112; pp. 528-530]. In addition, it is involved in the activity of immune cells as a toxic radical and a neurotransmitter [114; pp. 1105-1110]. It depends on AKT and insulin in humans induces phosphorylation of endothelial NO synthases and causes its release [115; pp. 3390-3394]. The vasodilator property of insulin is related to the functional reduction of glucose in the blood [113; pp. 700-711].

From a systemic point of view, the effect of endothelial insulin plays an important role in its delivery to muscles. Insulin produced in the pancreas must pass through the endothelium to reach the target cells [117, 118, 119]. The transfer of insulin to the trans-endothelium has been studied mainly in the direction of muscle and brain [116; pp. 6-12].

Although the long-term effects of obesity and low levels of inflammation cause insulin resistance in all tissues, the question of what is the main driving force of endothelial insulin resistance remains open [122; pp. 189-199].

Platelet reactivity and coagulation increase when the patient has insulin resistance and when they eat a high-calorie diet. Postprandial vascular disorders are usually detected in the brachial artery. Changes in movement under the influence of pressure lead to a sharp release of NO from the vessels. This situation, in turn, leads to the expansion of veins. This is determined by dopplerography of the wrist artery [126; pp. 8-15].

Numerous studies have shown that patients with obesity and diabetes have a stronger decrease in platelet reactivity and coagulation after consuming a vasodilating food compared to healthy people. But in this case, it remains unknown what factors can cause the postprandial effect. Taking into account the high levels of both glucose and lipids in the postprandial state, both of them were recommended as mediators. In addition, hormones released in response to food intake may also influence vasodilation. When glucose and lipids are injected into

the vein, it has been found in some observations that it directly affects the endothelium and causes vasodilation [127; pp. 155-164].

From a physiological point of view, there is a high probability that lipids are important vasodilator mediators. Because a number of studies have shown that foods containing a large amount of fat cause more changes in the dilation of blood vessels than those containing less [131]. It can be assumed that there is a certain relationship between the fats in the consumed food and the reactivity of the vessels. Long-chain saturated fatty acids, which are considered the main inflammatory mediators, have a clear effect on vascular reactivity [135; pp. 9597-9602].

Also, there is evidence that in obesity and type II diabetes, eating foods with a lot of fat has not only a cumulative effect on the activity of vessels, but also a long-term preservation of this effect [136; pp. 103-123]. On the contrary, physical exercises have a positive effect on vascular activity, including their adaptation to metabolic stress [122;. pp. 189-199].

There are a variety of mediators and cytokines that contribute to increased vascular disease as a result of obesity. In pre-diabetes [145], fatty acids increase strongly and decrease less after eating compared to healthy people [146; pp. 902-909]. As mentioned above, high plasma glucose has the property of activating platelets, which leads to the formation of chronic AGEs in the case of endothelial dysfunction.

But it should be taken into account that in MS there is an increase in the amount of glucose in the blood, therefore, compared to AGE, it has a higher hemostatic and vascular effect.

There is a broad consensus that the consumption of foods rich in lipids, which lead to an increase in plasma fatty acids, can lead to vascular diseases and type II diabetes [146; pp. 902-909]; [144; pp. 76-82]. In addition, in a number of clinical observations, careful control of blood glucose levels in patients with diabetes showed that not only the risk of cardiovascular diseases, but also the death

rate in these patients was somewhat reduced. But glucose alone is insufficient to explain these effects [140; pp. 1517-1530].

The relationship between obesity, glucose and fatty acids in the development of type II diabetes and cardiovascular diseases and reactive oxygen synthesis may be of some importance [138; pp. 27-35]. Similarly, the complications observed in type I diabetes are also related to oxidative stress [128; pp. 155-164].

When discussing the relationship between metabolic syndrome and type 2 diabetes, they point out that both are related to inflammation. In addition to the increase in arterial blood pressure, which is a decisive risk factor in cardiovascular diseases, it also includes an increase in plasma lipids, atherosclerosis, and thickening of the blood vessel wall due to leukocyte invasion [95; pp. 1126-1167]. At first, atherosclerosis was considered a disease caused by the accumulation of lipids in the vessels, but later one of the causes of atherosclerosis is wrongly considered to be inflammation [97].

It has also been mentioned that insulin resistance in type II diabetes is mainly manifested by metabolic changes.

In a number of scientific works, information is given that stopping or reducing inflammation in adipose tissue stops insulin resistance [61; p. 40-52]. Despite inflammation, the main cause of inflammation of adipose tissue has not been fully studied until now. Although one of the first proposed ideas was that apoptosis of macrophages in adipose tissue occurs as a result of metabolic stress, at the same time endoplasmic reticulum stress and hypoxia are deeply studied [46].

In addition to the above-mentioned information, in other scientific observations, systemic resistance to endothelial resistance before insulin was noted [43; pp. 3045-3060]. It is shown that inflammation and invasion of adipose tissue immune cells are observed before endothelium activation. In one of the investigations conducted in 2015, in rats with obesity and HFD, a higher interaction between platelets and leukocytes is observed and ICAM 1 moderates the inflammatory marker [47; pp. 1-17].

A large number of observations show that insulin resistance plays an important role in the occurrence of disorders in the hemostasis system. But taking into account the importance of other factors in hemostasis disorders, it is necessary to study the pathogenetic mechanisms of this process in depth [73; pp. 1274-1279].

Standards for the diagnosis of many diseases have been developed in Uzbekistan. In particular, a number of standards have been developed in the field of hematology. However, standards for diagnosing hemostasis in metabolic syndrome have not yet been created. Therefore, there is a need to develop diagnostic standards of hemostasis changes in patients with metabolic syndrome [19].

CHAPTER 2.
SPECIFIC CHANGES IN THE HEMOSTASIS SYSTEM OF PATIENTS WITH METABOLIC SYNDROME

2.1. The dependence of changes in the hemostasis system of patients with metabolic syndrome on living conditions.

Today, the increase in the use of cars, staying at home for a long time watching TV or various games brings them closer to a sedentary lifestyle. A sedentary lifestyle is the main reason for the development of MS [48; pp. 319-328]. It is known that physical activity among people living in rural areas is much higher than physical activity among people living in cities. Taking this into account, the body weight index of patients selected from 30 urban and 30 rural residents with metabolic syndrome was calculated in this study. When comparing the obtained results, it was found that the average body weight index is higher among urban residents compared to rural residents (Fig. 1).

Figure 1.

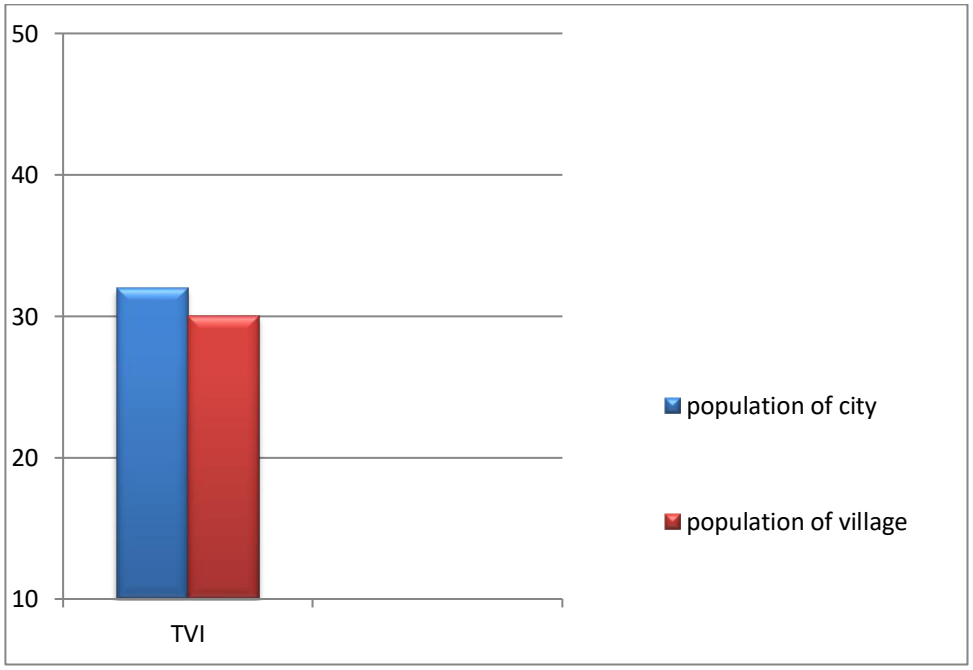

Figure 1. Comparison of the average TVI of patients in the control group, taking into account the region of residence.

In addition, when comparing the levels of obesity between rural and urban residents according to the defined body mass index, TVI: 31-35, i.e. obesity level I is more common and this indicator is rural It was found that it is observed more in patients selected from the population of the city than among the population (Fig. 2).

Figure 2.

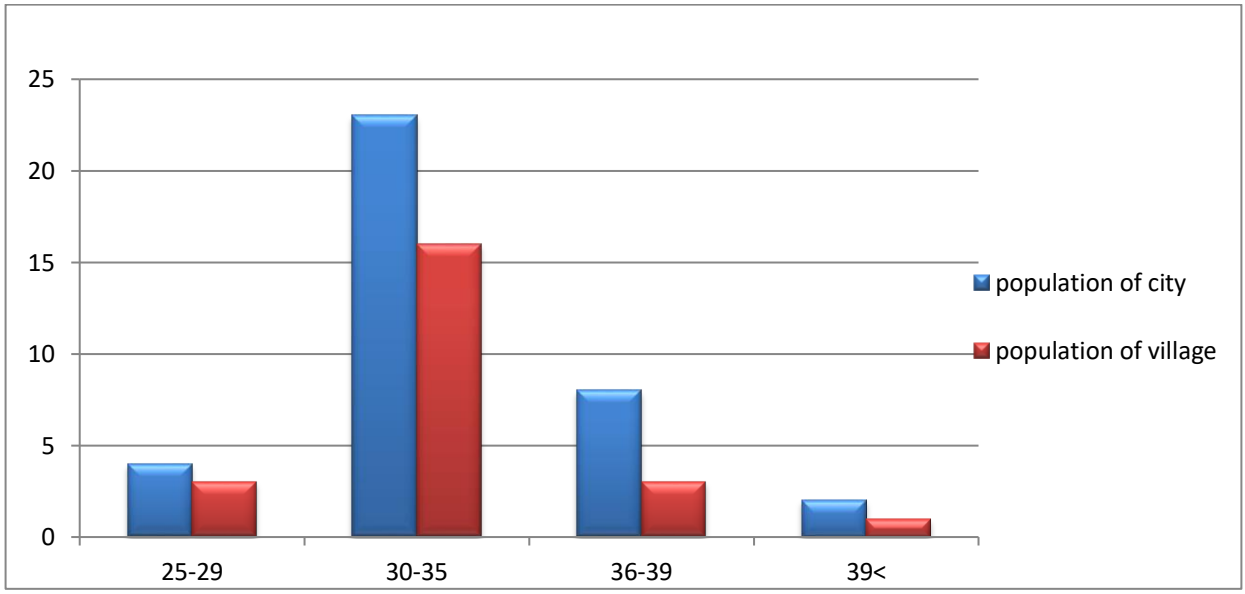

Figure 2. Comparison of overweight and obesity in rural and urban residents according to the body mass index determined in patients in the control group.

When the main clinical diagnosis of 60 patients selected for the study was studied in order to study the frequency of cardiovascular system diseases in patients with metabolic syndrome, it was found that arterial hypertension or ischemic heart disease was detected in 92% of patients. . Other systemic diseases were observed in the remaining 8% of cases (Fig. 3).

Figure 3.

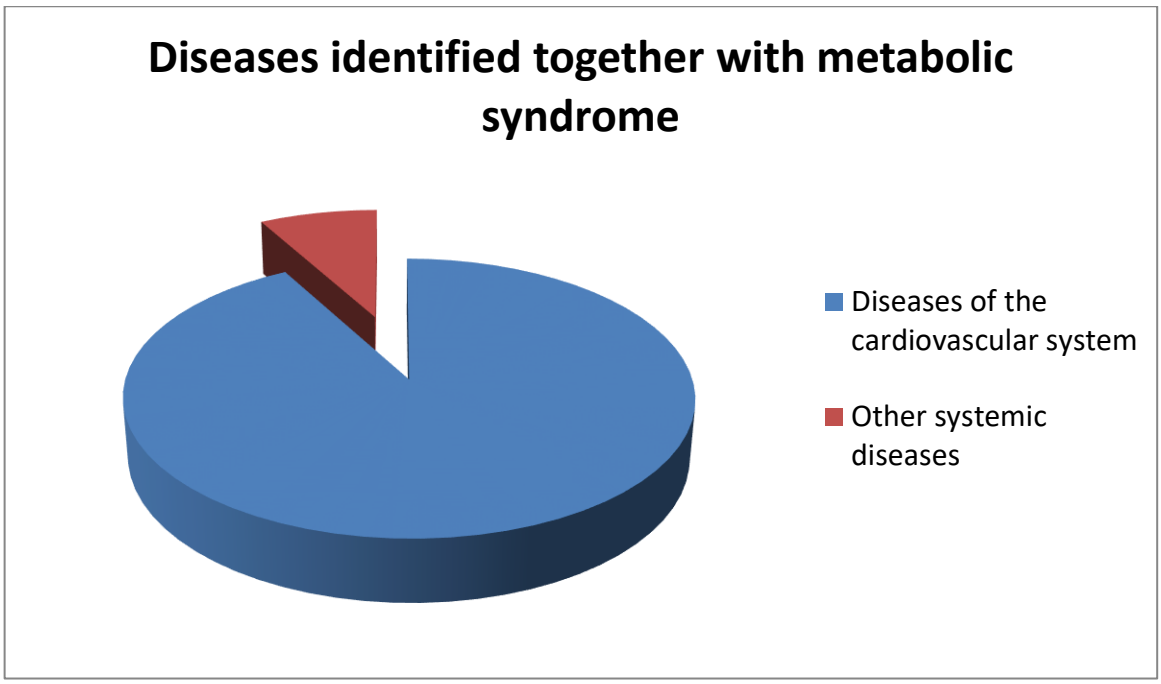

Figure 3. Comparison of cardiovascular and other system diseases together with metabolic syndrome.

It is known that during metabolic syndrome, the balance between prothrombin and fibrinolytic activity is disturbed [47; p. 1-17]. This, in turn, causes severe, sometimes fatal, changes in various parts of the body. Increased thrombogenic risk in metabolic syndrome is caused by metabolic disorders, hemodynamic factors, high fibrinogen content and activity of blood clotting factors, hyperaggregation of platelets caused by hypofibrinolysis [62; 106-112-b; 89; pp. 35-41].

It is important to objectively assess the importance of the hemostasis system in the formation of the risk of cardiovascular diseases, and in most cases to what extent they are related to related diseases and risk factors. From this point of view, the connection of vascular-platelet and coagulation hemostasis indicators with the main components of metabolic syndrome is of certain importance. Considering this, the results of our research showed that the amount of platelets in the blood is normal (244.0±8.14x109/l).

Table 3.1

Indicators of hemostasis system in patients with metabolic syndrome and control group.

(M±m)

Indicators	Patients with MS (n=116)	Control group (n=60)
Platelets, x109/l	244.0±8.14	238.6±7.86
Blood clotting time, seconds	96.0±3.4***	311.8±2.18
Partially activated thromboplastin time, seconds	20.0±1.4	27.18±2.8
Prothrombin index, %	124.1±4.2*	95.2±3.7
Prothrombin time, seconds	8.4±0.13	11.3±0.16
International relative unit	0.89±0.01	1.01±0.01
Fibrinogen, g/l	5.01±0.06*	3.1±0.09

Note: * ($p<0.05$), ** ($r<0.01$), *** ($r<0.001$)- statistically reliable compared to the control group and ($r>0.05$)– statistically unreliable differences.

In addition, in the diagnostic analysis of the hemostasis system of patients diagnosed with metabolic syndrome, it was found that 87% (52) of patients had fibrinogen levels above the norm (>4 g/l). The fact that 53% of these (52) patients are urban patients shows that the metabolic syndrome and the resulting hypercoagulation are intrinsically dependent on the physical activity of the population.

The analysis of the mechanisms of the activation of the process of vascular-platelet hemostasis is the main motivation of blood vessels and subendothelial tissue structures, in particular, collagen. Under the influence of Willebrand's factor present in collagen and subendothelium, thrombocytes are rapidly activated, they change their shape, swell, form thorn-like branches, and adhere to the damaged surface. In this case, adhesion of platelets to the subendothelial surface of damaged vessels is related to the interaction of a number of its components, in particular, the main components of the platelet membrane, the Willibrand factor and a number of other proteins (thrombospondin, fibronectin). At the same time, ADF,

catecholamines and serotonin are released from damaged cells, and collagen enhances adhesion of platelets. Here platelets are α-granule platelets (ADF, serotonin, adrenaline, some proteins, factor IV involved in blood aggregation and clotting, β-thromboglobulin, plastic growth factor, some clotting factors, glycoproteins II b and IIIa), fibrinogen, thrombospondin and interacts specifically with other proteins. The occurrence of such a process causes irreversible aggregation in blood platelets and disrupts the formation of thromboxane A 2 and protocyclin from arachidonic acid in platelets.[106; pp. 898-918].

Under the influence of ADF, serotonin, and adrenaline, the platelet aggregation process increases sharply, and a sharp spasm of the affected blood vessels is observed.

The process of blood coagulation begins with the interaction of factors released from plasma and blood platelets and tissue thromboplastin. At the same time, a small amount of thrombin is formed in the primary hemostasis system, which, on the one hand, ends the irreversible changes of platelets, and on the other hand, creates an opportunity for fibrin formation. It adheres to the platelet alloy and hardens it [69; pp. 343-351].

In addition, in order to determine the level of risk of heart and blood vessel diseases, we also studied the relationship between them as well as the identified risk factors. For this purpose, we studied the correlation between the main components of the metabolic syndrome and the state of the indicators of the hemostasis system and found out the existence of certain relationships (table 3.2).

Table 3.2

Indicators of correlations between blood pressure and hemostasiogram parameters

Blood pressure (mm.wire.top.)	Trom botsites	INU	PATT	Fibri nogen	PTI	PTT
Systolic arterial pressure	0.31*	- 0.26*	- 0.10	0.27*	0.19	0.25*
Diastolic arterial pressure	0.37*	- 0.31*	- 0.20*	0.35*	0.32*	0.32*

As shown in the table, almost all indicators of hemostasis have a reliable correlation with blood pressure levels. A negative correlation was noted between international relative unit and partially activated thromboplastin time and blood pressure. On the other hand, there was no reliable correlation between mean arterial pressure, partially activated thromboplastin time and prothrombin index.

Correlations between body weight index and hemostasiogram indicators of lipid indicators were also determined and they are presented in table 3.3.

Table 3.3

Kettle's index, lipids and hemostasiogram parameters

Blood pressure (mm.wire.top.)	Trom botsites	INU	PATT	Fibri nogen	PTI	PTT
Kettle index	0.45*	- 0.28*	- 0.26*	0.39*	0.31*	0.35*
Cholesterol	0.18	- 0.11	- 0.14	0.24	0.20*	0.21
Triglyceride	0.22*	- 0.34*	-0.45*	0.39	0.25*	0.36*

A reliable relationship was found between cholesterol and platelets, fibrinogen, prothrombin index and prothrombin time. A negative correlation was found with international relative unit and partially activated thromboplastin time.

Given the prevalence of metabolic syndrome among the population and its high social and medical importance, it is important to investigate metabolic syndrome. With its help, it is possible to determine the main and additional components of the metabolic syndrome. The components of the metabolic syndrome, such as impaired glucose tolerance, diabetes, excess body weight, arterial hypertension, dyslipoproteinemia, are recognized as the main cause of cardiovascular diseases and death. However, it is necessary to further study some mechanisms of the formation of cardiovascular diseases in insulin resistance. In particular, from a scientific point of view, the relationship between the state of the blood coagulation system and glycemia indicators is important.

Different methods are used to determine the nature of this or that risk factor. Although the one-factor analysis method is generally recognized, it is difficult to draw a conclusion about the interrelationship of risk factors and their combined effect on the pathological process. Therefore, multifactorial analysis is used in the study of risk factors.

In this scientific study, we investigated the relationship between PTI and carbohydrate metabolism in order to study its relationship with glycosylated hemoglobin (Figure 3).

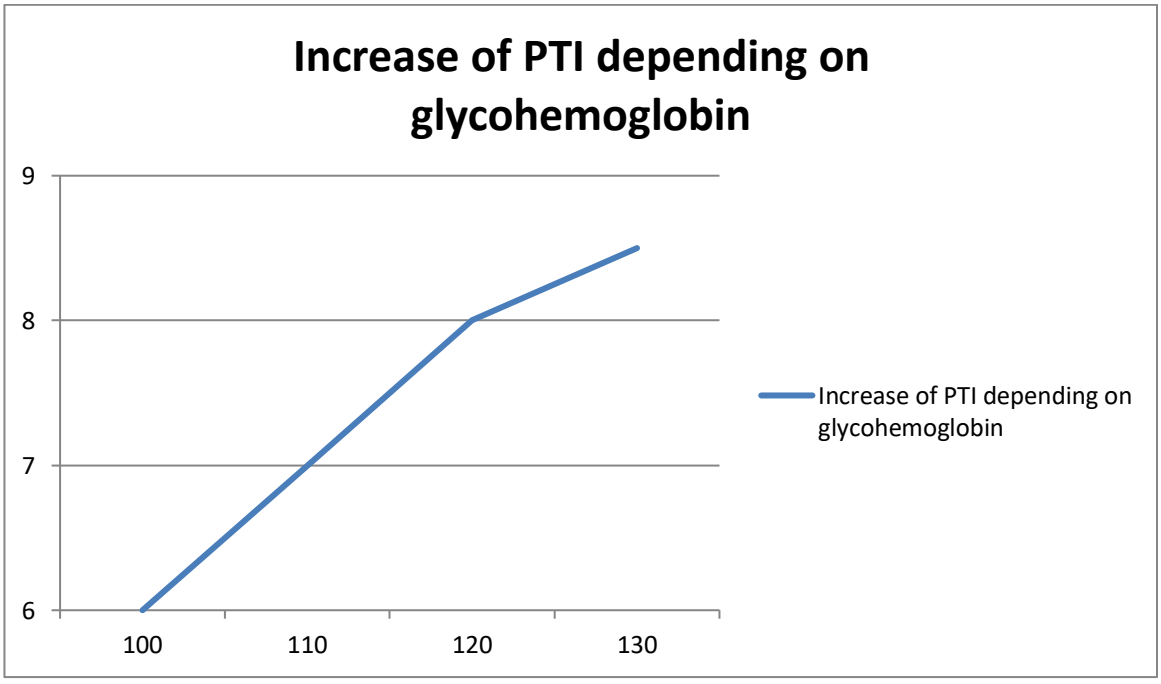

Figure 4. Indicators of correlation between glycosylated hemoglobin and prothrombin index.

The purpose of our selection of glycosylated hemoglobin is that it is known that this indicator of carbohydrate metabolism shows a stable ratio of blood glucose level. It does not indicate the amount of glucose in the immediate or first hours, but its indicator over a period of 3 months (Table 3.4).

Table 3.4

Degree of correlation between glycated hemoglobin indicators and prothrombin index.

Number of selected patients	60
Correlation coefficient	0.5941
The difference	P<0.0001
Confidence interval 95% p	0.4441 to 0.7117

According to the obtained data, a strong correlation between prothrombin index and glycosylated hemoglobin was found. This relationship was statistically reliable.

CHAPTER 3.
DYNAMICS OF PREVALENCE AND RISK FACTORS OF MAIN COMPONENTS OF THE METABOLIC SYNDROME.

3.1. Prevalence of metabolic syndrome components and risk factors

Adequate assessment of the risk of ischemic heart disease depends on the epidemiological situation with regard to risk factors, their levels and distribution, as well as the dynamics of these indicators. This part of the scientific work provides an objective assessment of the importance of hemostasis indicators in the occurrence of cardiovascular risk and an analysis of their relationship with co-occurring diseases and risk factors. Because the connection of hemostasiogram indicators with the main components of metabolic syndrome is of great interest from a scientific point of view. At the same time, the dynamics of changes in arterial hypertension, diabetes and glucose intolerance, dyslipidemia, obesity, body mass index, lipids and glycemic indicators were studied before that. According to the results of this study, the number of patients with arterial hypertension has increased by 1.5 times. It should be noted that in most population studies, increasing age of the population leads to an increase in the number of patients with arterial hypertension. At the same time, such dynamics of arterial hypertension indicates a serious deterioration of the medical and social situation. Because the increase in the prevalence of arterial hypertension is closely related to the population, disability and death rate. The prevalence of diabetes increased by 2.6 times. According to the World Health Organization, based on the results of a number of promising studies, the prevalence of diabetes mellitus in the world will double every 10 years. The obtained data showed that the growth rate of the prevalence of diabetes mellitus in the studied population is much higher than that of the world population. As a result of the observations, it was found that the number of glucose tolerance disorders decreased by 1.4 times. However, the dynamics of the spread of the disorder at different stages of the glycemic curve has

become uncertain. Thus, with a decrease in the number of violations of glucose tolerance associated with the violation of the glycemic curve of the sympathoadrenal phase, it was found that there is a significant change in the number of the glycemic curve of the vagoinsular phase. The negative dynamics of the distribution of disorders of the glycemic curve of the sympathoadrenal and vagoinsular phases have remained unclear. The number of disorders of glucose tolerance is considered to be related to this appearance of distribution dynamics and changes in various stages of the glycemic curve, physiological and pathogenetic characteristics that occur in the human body as the patient ages. With age, the activity of the sympathoadrenal system decreases, which is related to the activity of the 1st phase of the glycemic curve and to some extent to hyperglycemia within 1 hour after glucose loading, which is explained as a consequence of the decrease in the number of glucose tolerance disorders. At the same time,The increase in the number of violations of the 2nd stage of the glycemic curve may be related to the decrease in insulin activity due to the increase in age of various counterinsular factors. During the period of the study, a significant decrease in the body weight index was observed. A number of countries, including the Commonwealth of Independent States, especially in Russia, are dealing with this problem due to changes in lifestyle and diet. Also, unclear changes have been identified in relation to the dynamics of distribution of types of hyperlipidemia. In addition to a significant increase in the prevalence of impaired glucose tolerance and β-hyperlipidemia, a decrease in the number of hypercholesterolemia (statistically reliable) was observed. The obtained results indicate the need to conduct special studies for more in-depth study of the comprehensive dynamics of the spread of various hyperlipidemias. In addition, during the study, the dynamics of average changes in risk factors of metabolic syndrome were studied. According to the results of his analysis, it was observed that changes in the dynamics take place in different ways. An increase in arterial blood pressure, as well as a decrease in glycemia 2 hours after breakfast and glucose loading, and a decrease in body weight index 1 hour later. It should be

noted that the average indicators of systolic blood pressure and diastolic blood pressure have reliably increased. It was found that there was no reliable difference in the degree of blood pressure increase between them. A slight increase in glycemia and a decrease in body mass index were also observed in Naxor, but they were not statistically reliable. During the study, glycemia increased by 14.42 mg% 2 hours after glucose loading and decreased by 17.52 mg% 1 hour after loading. It was noted above that the body weight index reliably decreased during the conducted research. However, it should be mentioned that a reliable reduction of the Ketle index has not been determined. In order to find out the reason for this, the dynamics were studied in people with normal and high body mass index. Kettle's index increased from 0.245±0.028 to 0.253±0.40 in those with normal body weight, and in the second group, this index decreased from 0.322+0.034 to 0.252+0.042 ($R<0.05$). The average level of lipids in the subjects was consistent with the dynamics of hyperlipidemia. Along with an increase in the average indicators of triglycerides and β-lipoproteins, a decrease in the average indicators of cholesterol was observed. The obtained results showed that the prevalence of arterial hypertension and high blood pressure increased as the age of the population increased. An increase in systolic and diastolic pressure was observed. It has also been studied that cases of hyperglycemia increase with age.Along with the number of diabetes mellitus and the vagoinsular phase of the glycemic curve, the incidence of the sympathoadrenal phase of the glycemic curve is reduced. The decrease in the prevalence of body mass index with increasing age did not fully reflect the characteristics of height and weight in the population. From this point of view, it is appropriate to study the body mass index in the norm of the body mass index and in the dynamics of those who are overweight. The number of risk factors increases in parallel with age, so it is necessary to take necessary measures to identify and eliminate them in time. It is known from the literature that when several risk factors come together, their negative impact increases. Considering this situation, we studied the number of occurrences of risk factors depending on age. The obtained data confirm that as the age increases, the co-occurrence of various risk

factors also increases. At the same time, their coming together was observed mostly in the 30-39 and 40-49 age group. Although such a situation is observed later, but its occurrence has decreased somewhat. It should be noted that not a single patient with MS was identified in the age group of 20-29 years. However, as the age increases, the number of those without risk factors also decreases, as well as the observation [149].

3.2. Early diagnosis and prevention of changes in the hemostasis system in metabolic syndrome

An increase in the adhesiveness and aggregation activity of platelets in the main group of patients with metabolic syndrome was observed in combination with an increase in its thickening due to an increase in blood glucose and total cholesterol. Such a change has been proven in a number of other observations. [91; 58-62-p.]. The analysis of mechanisms of activation of vascular-thrombocytic hemostasis processes in its occurrence, blood vessels and subendothelial tissue structures, in particular, collagen is the leading impetus. Under the influence of Villibrand factor present in collagen and subendothelium, thrombocytes are rapidly activated, they change their shape and swell, and adhesion to the damaged surface is observed, forming spiny branches. In this case, adhesion of platelets to the subendothelial surface of damaged vessels is related to the interaction of a number of its components, in particular, components of the platelet membrane, Willibrand's factor and a number of other proteins (thrombospondin, fibronectin). At the same time, ADF, catecholamines and serotonin release from damaged cells and collagen enhances platelet aggregation. In this case, platelets are α-granule platelets (ADF, serotonin, adrenaline, some proteins, factor IV involved in blood aggregation and clotting, β-thromboglobulin, plastic growth factor, some clotting factors, glycoprotein IIb and IIIa), fibrinogen, thrombospondin and other proteins. specific reaction. The occurrence of such a process causes irreversible aggregation

of blood platelets and disrupts the formation of thromboxane A2 and prostacyclin from arachidonic acid in platelets. [106; pp. 898-918].

Under the influence of ADF, serotonin and adrenaline, platelet aggregation processes increase sharply and spasm of damaged microvessels is observed. The process of blood coagulation begins with the interaction of factors released from plasma and blood platelets and tissue thromboplastin. In this case, a small amount of thrombin is first formed in the area of primary hemostasis, which, on the one hand, completes the irreversible transformation of platelets, and on the other hand, creates an opportunity for fibrin formation. It adheres to the platelet alloy and hardens it. [69; pp. 343-351].

Taking into account these evidences, it is useful to study thromboxane A2 levels in patients with metabolic syndrome using its important metabolite. In particular, thromboxane A2 was found to be 2.69 times higher in the patient group compared to the control group (28.2±0.17 pg/ml) and (10.5±0.12 pg/ml) [149].

In addition, a reliable correlation was established between cholesterol and platelets international relative unit, partially activated thromboplastin time, fibrinogen and prothrombin time. It was found that there is a negative correlation between the international relative unit and activated thromboplastin time. Also, the relationship between glycemia level indicators and hemostasis indicators was studied. It is considered that there is a highly reliable correlation between the level of glycemia and thromboxane A2 and the number of platelets. Prevention is the most reliable way to maintain and strengthen the health of the population. At present, special attention is being paid to this direction of medicine all over the world, including Uzbekistan. One of the first steps to effective prevention is screening. Since its implementation requires a large amount of work and economic costs, it is of particular importance to introduce cost-effective non-invasive methods. Given the prevalence of metabolic syndrome among the population and its high socio-medical importance, it is important to carry out metabolic syndrome screening. With its help, it is possible to determine the main and additional components of the metabolic syndrome. Components of the metabolic syndrome,

such as impaired glucose tolerance, diabetes mellitus, excess body weight, arterial hypertension, dyslipoproteinemia, are recognized worldwide as the main risk factors for cardiovascular diseases and death. However, it is necessary to further study some mechanisms of the development of cardiovascular diseases in insulin resistance. In particular, from a scientific point of view, the relationship between the state of the blood coagulation system and glycemia indicators is important. Different methods are used to determine the nature of this or that risk factor. Although the one-factor analysis method is recognized all over the world, it is difficult to draw conclusions about the interrelationship of risk factors and their combined effect on the pathological process. Therefore, multivariate analysis is used in the study of risk factors. Taking this into account, during the research, the correlation between the prothrombin index and the glycemic index at different points of the glycemic curve (after one and two hours after the glucose load) was studied. According to the obtained data, it was found that there is a positive correlation between the prothrombin index and glycemia at lunch. In addition, it was found that even after loading, a reliable relationship between them remained, and this relationship was negative [149]. This inexplicable result means that further research is needed.

Conclusion

Metabolic syndrome is a classic clinical manifestation of comorbidity and is one of the main risk factors of cardiovascular diseases. Components of the metabolic syndrome, such as insulin resistance, arterial hypertension, dyslipidemia, hyperglycemia, lead to the development of atherosclerosis in blood vessels, and this process is accompanied by hemostasis disorders.[89; pp. 35-41]. Hyperactivity of thrombocytes takes the leading place among those involved in atherothrombosis processes. Hyperglycemia, dyslipidemia, and arterial hypertension are pathogenetically linked in the process of atherogenesis and thrombus formation, therefore it is pathogenetically reasonable to carry out antithrombogenic treatments based on long-term hypotensive treatments [91; pp. 58-62].

Prescribing antiaggregant drugs includes all coagulation processes, including the prevention of cardiovascular diseases. On the other hand, atherothrombotic complications are the main cause of death in arterial hypertension. In several studies, the use of small doses of acetylsalicylic acid as a hypotensive treatment in patients with arterial hypertension reduces the risk of myocardial infarction without increasing the risk of hemorrhagic stroke.[106; pp. 898-918]. However, insulin resistance is observed in 25-64% of cases. Among the factors affecting the effectiveness of antithrombogenic treatments, lipid metabolism is of particular importance. It is known that in dyslipidemia sensitivity of platelets to aggregation inducers increases and their secretory activity increases. In insulin resistance characteristic of metabolic syndrome, release of free fatty acids from the liver increases as a result of lipolysis.

These changes lead to a specific lipid profile with an increase in the amount of cholesterol, triglycerides, and low-density lipoproteins. Due to their tendency to oxidation, low-density lipoproteins play an important role in atherogenesis. On the other hand, according to recent studies, low-density lipoproteins lose their protective activity due to changes in the structure of the protein included in the pro-oxidant and pro-inflammatory state [113; pp. 700-711].

All researchers note that in the metabolic syndrome, disorders of the platelet link of hemostasis play an important role, and platelet hyperactivity and endothelial dysfunction play an important role in this. In this case, the specificity of platelet aggregation is of particular importance, distinguishing aggregation from itself, including high endogenous inducers of ADF. The high resistance of thrombocyte aggregation leads to its active formation and multiplication. At the same time, it is influenced by complex risk factors such as insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, and hemodynamics, and increases thrombogenic risk in metabolic syndrome. However, the opinions about the relationship between the individual components of the metabolic syndrome and the violation of the functional activity of platelets differ among scientists. [128; pp. 155-164].

Taking into account these evidences that require additional scientific foundations, we set the following goal: to study the state of the hemostasis system based on the development of metabolic syndrome risk factors, early diagnosis, and to study the dependence of these changes on the living conditions and region of the population.

For this purpose, 116 patients were observed. The control group consisted of 60 people with metabolic syndrome. 30 of them were selected from urban and 30 from rural areas.

During the research, the following examination methods were used: general clinical (questioning the patient and objective examination), instrumental (measurement of blood pressure, Kettle index, body weight index), laboratory (biochemical: cholesterol, triglycerides (TG), hemostasiological: determination of platelet count in capillary blood, partial activated thromboplastin time (PATT), prothrombin index (PTI), prothrombin time (PTT), fibrinogen indicators and statistical methods.

Today, the role of risk factors in the occurrence of diseases is not disputed. They not only create conditions for the occurrence of the disease, but also play an important role in its aggravation, severe course and deterioration of the prognosis. Therefore, the principles of early detection and elimination of risk factors lie in the prevention of non-communicable diseases. Currently, special attention is paid to the prevention of non-communicable diseases in our republic. Unfortunately, in recent years, the main components of the metabolic syndrome, which are considered a risk factor for many diseases, are increasing rapidly. Overt type 2 diabetes or its hidden form in the form of impaired glucose tolerance, arterial hypertension, body mass index, and dyslipidemia are the main risk factors for cardiovascular diseases. For example, hyperuricemia increases the risk of ischemic heart disease. The issue of risk factors is also important for endpoints. The components of the metabolic syndrome, especially when several of them come together, significantly increase the death from cardiovascular diseases.

In our rapidly developing age, not only traditional risk factors, but also mental states affect the formation of diseases. High-quality and high-tech medical methods of doctors do not always give the desired effect. For him, the patient should be able to take a critical approach to his health, actively participate in the treatment process and follow the recommendations on time. The patient's susceptibility to treatment is inextricably linked to treatment and diagnosis. It is difficult to conclude that the patient actively participates in the process, depending on whether the patient only addresses the doctor or only follows the doctor's recommendations.

An objective assessment of the role of hemostasis indicators in the formation of the risk of cardiovascular diseases is in most cases related to existing concomitant diseases and risk factors. From this point of view, the relationship between hemostasiogram indicators and the main components of metabolic syndrome is of particular interest. In addition, before studying this relationship, we studied arterial hypertension, diabetes, impaired glucose tolerance, body mass index, average blood pressure, glycemia, and some indicators.

The monad evaluation of risk factors of metabolic syndrome is in many cases closely related to the epidemiological situation of risk factors, their prevalence and dynamics. Therefore, the distribution dynamics of the studied risk factors were also carried out during the primary screening and re-examination process. It was noted that the number of detections of arterial hypertension increased by 1.5 times. Here, most population-based observations show that the number of detections of arterial hypertension increases with age. Considering that the presence of high blood pressure is associated with morbidity, disability and death of the population, such a situation indicates a serious worsening of the medical and social situation.

Diabetes increased by 2.6 times. According to the predictions of the WHO based on a series of prospective studies, diabetes mellitus will double in the world every 10 years. According to our data, the rate of diabetes in our study population is slightly higher than the global rate.

When the prevalence of hyperlipidemia was studied, their diversity was noted. Along with an increase in triglycerides, a statistically reliable decrease in cholesterol was noted. Finding a clear answer to such a change within the framework of this research is somewhat difficult. In our opinion, for this, it is necessary to study different types of lipids separately.

The obtained results show that patients with arterial hypertension and hyperglycemic condition increase with age.

Body mass index decreases with age and does not fully reflect the characteristics of height, length and weight. Therefore, it is appropriate to study the height-weight index separately in the dynamics of normal and overweight people. The number of risk factors and their increase depending on age indicate the need to actively identify them and take appropriate measures in time.

A study of the distribution of various risk factors in age groups revealed that they differ from each other. In particular, systolic isolated arterial hypertension is more often observed after the age of 50. In most cases, arterial hypertension, high body mass index and hyperglycemia were present, and the incidence of co-occurrence increased with increasing age. It should be noted that hyperglycemia, body mass index, and hypercholesterolemia were not observed in the youngest (20-29 years) under observation. There was no relationship between age and hypercholesterolemia, arterial hypertension, hyperglycemia, and body weight index. The co-occurrence of all four risk factors for metabolic syndrome increased with age, and a statistically reliable increase was observed after age 40 and continued until age 60.

Thus, it can be seen from the presented data that there is a certain relationship between age and the presence of risk factors and their number and co-occurrence.

However, the obtained data cannot be the basis for concluding that this relationship has a certain systematic nature. However, risk factors increase intensively after the age of 40. Taking this into account, it is advisable to take active preventive measures against risk factors no later than 40 years of age.

After that, we evaluated indicators of hemostasis in patients diagnosed with metabolic syndrome. The analysis showed that the number of platelets in the patients' blood was normal. In addition, partial activated thromboplastin time (20.0±1.4 seconds) was significantly higher than the control group (27.18±2.8 seconds) and international relative unit (0.89±0.01 and 1.01±0, respectively) 01), was almost not different. However, it was found that the prothrombin index decreased by 1.34 times in patients diagnosed with metabolic syndrome, and fibrinogen increased by 1.3 and 1.6 times, respectively.

In order to assess the relationship between the hemostasiogram and the components of the metabolic syndrome, a reliable correlation was found between the main indicators and the level of blood pressure. In part, activated thromboplastin time and international relative unit were found to be inversely related to blood pressure indicators. It should be noted that a reliable correlation with systolic blood pressure, on the one hand, with partially activated thromboplastin time and international relative unit, on the other hand, was not determined.

A high correlation was also found between platelet count and systolic blood pressure, and more so diastolic blood pressure. Correlation between body mass index and lipids and hemostasiograms was also confirmed.

No correlation was found between cholesterol level and platelet count, partially activated thromboplastin time and international relative unit, fibrinogen and thrombin time indicators. In part, a negative correlation between activated thromboplastin time and international relative unit was noted. At the next stage, the correlation between glycemia and hemostasis indicators was studied. It was noted that glycemia has a high and reliable correlation with the number of platelets.

In the study, an attempt was made to compare the average level of glycemia with glycosylated hemoglobin. According to the obtained data, glycemic indicators correspond to the level of risk of glycosylated hemoglobin.

To study the role in hemostasis disorders, indicators were analyzed in patients with hemostasis disorders. In cases of hemostasis disorders, all studied indicators were confirmed to be higher than in intact cases.

Based on the results of the examination of patients with metabolic syndrome, depending on the changes in hemostasis, we created an algorithm that determines the level of its risk. The use of this algorithm provides an opportunity for early diagnosis and prevention of hemostasis disorders in metabolic syndrome.

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