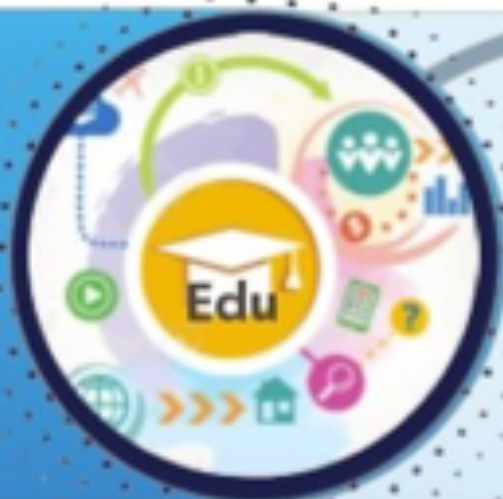


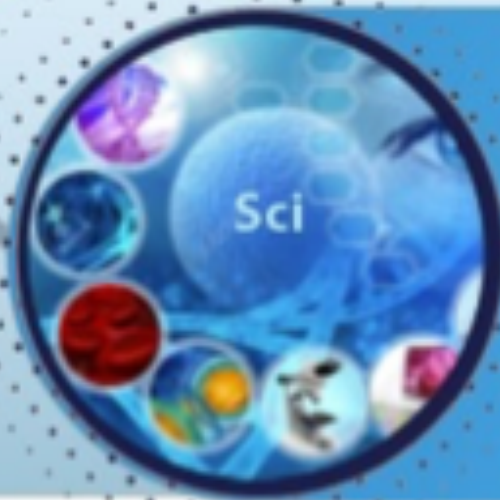


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# Current Information on the Prevalence, Diagnostic Criteria and Clinical Presentation of Metabolic Syndrome

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## ABSTRACT

*Epidemiological data from the World Health Organization indicate that obesity and metabolic syndrome are an important risk factor for the development of gastroesophageal reflux disease. Studies in this direction over the past half century confirm the fact of a close relationship between obesity and possible complications of gastroesophageal reflux disease in the form of erosive esophagitis, Barrett's esophagus, esophageal adenocarcinoma, etc  $\geq 30$  kg/m<sup>2</sup>, the prevalence of the number of patients with this indicator is growing not only in the Western world, but also in the Asian continent. It is widespread in the Western world and is growing in other parts of the world, especially in Asia. To date, a close relationship has been proven between the incidence of gastroesophageal reflux disease depending on the growth of the body mass index disease and a high risk of spreading adenocarcinoma of the esophagus. Along with the above, there is evidence that central abdominal obesity, as opposed to an elevated body mass index, is the most important factor associated with Barrett's disease. This review article is devoted to the presentation of current information regarding the prevalence, diagnostic criteria and clinical manifestation of metabolic syndrome.*

**Key words:** metabolic syndrome, etiopathogenesis, diagnosis and treatment.

The first reports and subsequently more detailed descriptions of metabolic syndrome were presented in the publications of the American Journal of Clinical Nutrition as early as 1956 based on the results of research by J. Vague [29]. Based on the results of numerous studies, he suggested that there is a close relationship between the development of obesity and type 2 diabetes mellitus and their possible impact on the formation of hypertension and coronary heart disease. This assumption is beyond doubt, since today metabolic syndrome is known

primarily as a disease that occurs in a set of interrelated several (cluster) metabolic signs, which are based on diseases of the cardiovascular system and type 2 diabetes mellitus.

Subsequently, in 1965, M.J. Albrink and J.W. Meigs [2] presented evidence of the important role of increased triglycerides in the blood in the pathogenesis of metabolic syndrome. This report, and subsequently the results of studies by A. Avogaro [5] as early as 2006, made it

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possible to supplement the range of signs of metabolic syndrome at the expense of hypertriglyceridemia and hyperinsulinemia, respectively. However, these studies were observational in nature, and large prospective randomized trials were required to create an indisputable evidence base for the proposed theory.

S.M. Haffner et al. [8] suggested that although diabetes mellitus often has a close chronological relationship with the subsequent development of vascular complications, nevertheless, the duration of the underlying disease, which occurs against the background of an increased level of insulin in the blood, directly leads to the development of microangiopathy rather than macroangiopathy. Because individuals with prediabetes have hyperinsulinemia, and because hyperinsulinemia may be a risk factor for cardiovascular disease, the authors hypothesized that people with prediabetes may have atherogenic risk factors even before the onset of clinical diabetes, thereby explaining the relative absence of association of macrovascular complications with glycemia severity or duration of disease. In order to identify the evidence base for their assumptions, the authors documented the status of cardiovascular risk factors in 614 Mexican-Americans who did not initially have diabetes mellitus, who later took part in an 8-year follow-up of the San Antonio Heart Study, a population-based study of diabetes mellitus and cardiovascular disease. Individuals who did not have diabetes mellitus at the time of baseline examination but who subsequently developed diabetes mellitus (i.e., patients with confirmed prediabetes,  $n=43$ ) had higher levels of total cholesterol and low-density lipoprotein cholesterol, triglycerides, fasting glucose and insulin, 2-hour glucose, body mass index and blood pressure, and lower levels of high-density lipoprotein cholesterol, than subjects who remained non-diabetic ( $n=571$ ). Most of these differences persisted after adjusting for obesity and/or glycemia levels, but were resolved after adjusting for fasting insulin concentrations. When patients with impaired glucose tolerance at baseline ( $n=106$ ) were excluded, a more atherogenic pattern of cardiovascular risk factors was still evident (and statistically significant) among patients with initially normoglycemic prediabetes. These results indicate that patients with prediabetes have atherogenic risk factors (possibly caused by obesity, hyperglycemia, and especially hyperinsulinemia) that may be present for many years and may contribute to the risk of macrovascular disease as much as the duration of clinical diabetes itself.

In another study conducted by M. Pyorala et al. [15] In 1998, the first prospective epidemiological study was conducted to demonstrate a strong relationship between hyperinsulinemia and the risk of coronary heart disease. The aim of this study was to investigate the prognostic value of hyperinsulinemia with respect to the risk of coronary heart disease during a 22-year follow-up of a specific population in Helsinki. The cohort consisted of 970 men aged 34 to 64 years who did not suffer from coronary heart disease, other cardiovascular diseases and type 2 diabetes mellitus. Measurements of risk factors at baseline included an oral glucose tolerance test measuring blood glucose and plasma insulin at 0, 1, and 2 hours. The area under the plasma insulin response curve (insulin AUC) during the oral glucose tolerance test was used as a composite variable reflecting plasma insulin levels. During the 22-year follow-up period, 164 men had a serious event: coronary artery disease. The authors concluded that hyperinsulinemia predicted the risk of coronary heart disease over 22 years of follow-up and was largely independent of other risk factors for coronary heart disease.

In general, metabolic syndrome should be considered a heterogeneous type of disease. The spectrum of signs of metabolic syndrome can vary in wide ranges. This is what does not allow us to fully reveal the etiological essence of metabolic syndrome, which includes hyperinsulinemia, glucose intolerance, dyslipidemia, arterial hypertension and obesity.

P. Poulsen and colleagues [13] studied the relative influence of genetic and environmental factors on the development of metabolic syndrome components among male and female twins. They conducted a study in 303 pairs of elderly twins and reported on the concordance and heritability of the components using classical twin analysis to estimate the proportion of variation attributed to genetic factors. The findings showed that all components were significantly correlated. Concordant rates of glucose intolerance, total obesity, and low high-density lipoprotein cholesterol were significantly higher among monozygotic than dizygotic twins, indicating a genetic influence on the development of these phenotypes. Estimates of heritability of glucose concentration, body mass index, and high-density lipoprotein cholesterol among monozygotic twins confirmed these findings. However, estimates of the heritability of waist-to-hip ratio, fasting insulin, and triglycerides were low, indicating a major environmental influence. The authors found a higher genetic effect on glucose intolerance and systolic blood

pressure and a lower genetic effect on low cholesterol, high-density lipoprotein, and diastolic blood pressure among male twins compared to female twins. Overall, based on the correlations between the components of the syndrome, the team proposed a major complex that included hyperinsulinemia, obesity, hypertriglyceridemia, and low-cholesterol high-density lipoproteins with weak associations with glucose concentrations and blood pressure levels. The study confirms the idea of a multifactorial etiology of components, including genetic and non-genetic factors. Differences in etiology between male and female twins indicate the influence of sex on several components of metabolic syndrome. From a practical point of view, the data obtained made it possible to create prerequisites for the large-scale development of criteria that would contribute to the unification of the diagnosis of metabolic syndrome.

For example, in 2001 and further in 2002, within the framework of the National Cholesterol Education Program (NCEP), a group of researchers on the Treatment of High Blood Cholesterol in Adults (ATP III) developed a unified system based on the diagnostic criteria for metabolic syndrome [12, 20].

The NCEP and ATP III guidelines identified five factors that determine the criteria for the development of metabolic syndrome. At the same time, the minimum value of the development of metabolic syndrome is possible only if at least three of the following names are present in each examined patient:

- the presence of abdominal obesity, which is determined by waist circumference ( $\geq 102$  cm for men and  $\geq 88$  cm for women);
- Increased blood triglyceride levels
- lowering the level of high-density lipoprotein cholesterol;
- increased blood pressure;
- fasting hyperglycemia.

All of the above ATP III criteria were modified by the American Association of Clinical Endocrinologists (AACE) in 2003. However, the recommendations did not indicate the need to take into account the minimum number of combinations of signs to make a qualified diagnosis of metabolic syndrome. Also, in addition to the characteristics specified in ATP III, other factors were added to aid in diagnosis, which included polycystic

ovary syndrome, hyperuricemia, and a family history of cardiovascular disease or type 2 diabetes mellitus [4].

The pathophysiology underlying metabolic syndrome is a matter of debate, with both insulin resistance and obesity being considered important factors. Based on multivariate analyses and observations, the International Diabetes Federation (IDF) has amended the definitions proposed by ATP III. At the same time, the predominance of this sign in addition to the development of insulin resistance turned out to be important [25].

Thus, I. Lemieux et al. [16] Studies have been conducted to test the hypothesis that simple variables such as waist circumference and fasting plasma triglycerides (TG) can be used as screening tools to identify men characterized by the metabolic triad of non-traditional risk factors. The results of a metabolic study conducted on 185 healthy men indicated that the majority ( $>80\%$ ) of men with waist circumference values of  $\geq 90$  cm and elevated triglyceride levels ( $\geq 2.0$  mmol/L) were characterized by an atherogenic metabolic triad. Model validation in an angiographic study on a sample of 287 men with and without coronary artery disease showed that only men with elevated waistlines and triglyceride levels had an increased risk of coronary heart disease compared to men with low waistlines and triglyceride levels. It is suggested that the simultaneous measurement and interpretation of waist circumference and fasting triglycerides can be used as low-cost screening tools to identify men characterized by an atherogenic metabolic triad and at high risk of coronary heart disease.

In 2004, a group of clinicians led by D.B. Carr [18] published the results of assessing the differential effects of insulin resistance and fat distribution in the central part of the body in determining metabolic syndrome. Specifically, they investigated which criteria of the National Cholesterol Education Program were associated with insulin resistance and central obesity. The subjects were quantified the insulin sensitivity index and the area of intra-abdominal fat and subcutaneous fat.

Metabolic syndrome was present in 34 (15.6%) patients with a lower sensitivity index and a higher area of intra-abdominal adipose tissue and subcutaneous fat compared to subjects without the syndrome ( $P < 0.001$ ). Multivariate models, including estimates of sensitivity index, visceral fat area, and subcutaneous fat thickness, demonstrated that each parameter is associated with the syndrome. However, the area of intra-abdominal adipose tissue was independently associated with all five criteria

for metabolic syndrome. In multifactorial models containing criteria in the form of covariates, waist circumference and triglyceride levels were independently associated with the sensitivity index and visceral adipose area and subcutaneous fat thickness ( $P < 0.001$ ). Although insulin resistance and central body fat are associated with metabolic syndrome, the visceral fat index is independently associated with all criteria, suggesting that it may play a pathophysiological role.

From the criteria of the National Cholesterol Education Program, waist circumference and triglycerides can best determine insulin resistance and visceral obesity in individuals with fasting plasma glucose levels  $< 6.4$  mmol/L.

In general, the so-called hypertriglyceridemic waist as a marker of visceral obesity and associated metabolic abnormalities is a useful and practical clinical phenotype for screening individuals at risk of coronary heart disease and type 2 diabetes mellitus [17]. The International Federation for Diabetes Mellitus has determined lower thresholds for abdominal obesity in Asians ( $\geq 90$  cm in men and  $\geq 80$  cm in women) [9]. It should be noted that body weight tends to increase with age, peaking at the age of 50–59 years [14]. Currently, the ATP III criteria are the generally accepted definition for diagnosis, but the threshold for fasting glucose abnormality has been lowered from 110 to 100 mg/dL.

To date, it is already generally recognized that excess body weight increases mortality from cardiovascular diseases in adults [7, 26]. About 2 billion adults in the world are currently obese.

Overweight and obesity are associated with adverse health outcomes, including cardiovascular disease, type 2 diabetes, and malignant disease. Strikingly, there is a linear relationship between body mass index and mortality from coronary heart disease, stroke, and type 2 diabetes mellitus [6, 24], which starts with the "normal" range of body mass index [27].

Pathological studies of patients who died from acute myocardial infarction under the age of 35 years established a close relationship between the level of body mass index and the thickness of subcutaneous adipose tissue, as well as the presence of atherosclerotic lesions of the coronary arteries [21], and epidemiological studies have shown that obesity accounts for approximately 20 percent of the population risk of first myocardial infarction [10, 23].

It should be noted that the use of body mass index to define obesity has been controversial, as many insulin-resistant people, such as those of South Asian descent, have central obesity but a normal body mass index [22].

The existence of a close relationship between the incidence of obesity and the presence of risk factors for cardiovascular diseases, in particular coronary heart disease, has long been proven. Among these factors, many researchers also include arterial hypertension, elevated blood cholesterol levels, and insulin resistance [1, 3, 19, 22].

It has also been convincingly proven that weight loss after bariatric surgery reduces the incidence of type 2 diabetes mellitus, arterial hypertension, and hyperlipidemia [11].

However, there are few fundamental studies that have an evidence base for the presence of molecular mechanisms of the pathogenesis of the development of obesity and cardiovascular diseases. Meanwhile, understanding the pathogenetic mechanisms of the ability to control and regulate body weight, as well as the consequences of transforming such changes, can be crucial in developing strategies to prevent an obesity pandemic. This may allow for the development of effective pharmaceutical development of drugs for the treatment of metabolic syndrome.

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Metabolik sindromning tarqalishi, diagnostika mezonlari va klinikasi to'g'risida dolzarb ma'lumotlar

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Jahon sog'liqni saqlash tashkilotining epidemiologik ma'lumotlari shuni ko'rsatadiki, semirib ketish va metabolik sindrom gastroözofageal refluks kasalligining rivojlanishi uchun muhim xavf omili hisoblanadi. So'ngi yarim asr davomida ushbu yo'nalishda olib borilgan tadqiqotlar semirib ketish va gastroözofageal refluks kasalligining eroziv qizilo'ngach, Barrett qizilo'ngach, qizilo'ngach adenokarsinomi va boshqalar ko'rinishidagi mumkin bo'lgan asoratlari o'rtasida yaqin bog'liqlik mavjudligini tasdiqlaydi  $\geq 30 \text{ kg / m}^2$ , bu ko'rsatkichga ega bemorlar soni faqat G'arb dunyosida emas, balki Osiyo qit'asida ham o'sib bormoqda. G'arb dunyosida keng tarqalgan va dunyoning boshqa qismlarida, ayniqsa Osiyoda o'sib bormoqda. Bugungi kunga qadar tana massasi indeksining o'sishiga bog'liq gastroözofageal refluks kasalligi bilan kasallanish o'rtasida yaqin bog'liqlik isbotlangan kasallik va qizilo'ngachning adenokarsinomi tarqalishining yuqori xavfi. Yuqorida aytib o'tilganlar bilan bir qatorda, yuqori tana massasi indeksidan farqli o'laroq, markaziy qorin bo'shlig'ining semirib ketishi Barrett kasalligi bilan bog'liq eng muhim omil ekanligi haqida dalillar mavjud.

Ushbu sharh maqola metabolik sindromning tarqalishi, diagnostika mezonlari va klinik ko'rinishi bilan bog'liq hozirgi ma'lumotlarni taqdim etishga bag'ishlangan.

Kalit so'zlar: metabolik sindrom, etiopatogenez, tashxis va davolash.

Современные сведения относительно распространенности, критериев диагностики и клинического проявления метаболического синдрома

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Эпидемиологические данные Всемирной организации здравоохранения свидетельствуют, что ожирение и метаболический синдром является важным фактором риска развития гастроэзофагеальной рефлюксной болезни. Исследования в данном направлении за последние пол века подтверждают факт о тесной взаимосвязи ожирения и возможных осложнений гастроэзофагеальной рефлюксной болезни в виде эрозивного эзофагита, пищевода Барретта, аденокарциномы пищевода и др. Так как ожирение определяется при индексе массы тела  $\geq 30 \text{ кг/м}^2$ , распространенность количества больных с данным показателем растет не только в странах западного мира, но и в Азиатском континенте. распространено в западном мире и растет в других частях мира, особенно в Азии. На сегодняшний день доказана тесная взаимосвязь частоты развития гастроэзофагеальной рефлюксной болезни в зависимости от роста показателя индекса массы тела. Соответственно следует ожидать и рост частоты регистрации больных с гастроэзофагеальной рефлюксной болезнью и высокого риска распространения аденокарциномы пищевода. Наравне с вышеуказанным, существуют доказательства того, что центральное абдоминальное ожирение, в отличие от повышенного индекса массы тела, является наиболее важным фактором, связанным с болезнью Барретта.

Данная обзорная статья посвящена представлению современных сведений относительно распространенности, критериев диагностики и клинического проявления метаболического синдрома.

Ключевые слова: метаболический синдром, этиопатогенез, диагностика и лечение.