MANIFESTATIONS AND MECHANISMS OF DEVELOPMENT OF SYNDROME X

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Abstract. *Metabolic syndrome, characterized by a constellation of metabolic abnormalities, including central obesity, insulin resistance, hypertension, and dyslipidemia, poses a significant risk for the development of atherosclerotic cardiovascular diseases and type II diabetes mellitus. The diagnosis of metabolic syndrome necessitates the presence of 3 or more of these metabolic abnormalities, signaling an urgent need for proactive identification and intervention strategies. The prevalence of MetS is rapidly increasing worldwide, largely as a consequence of the ongoing obesity epidemic. Environmental factors during periods early in development have been shown to influence the susceptibility to develop disease in later life. In particular, there is a wealth of evidence from both epidemiological and animal studies for greater incidence of features of MetS as a result of unbalanced maternal nutrition. The mechanisms by which nutritional insults during a period of developmental plasticity result in a MetS phenotype are now beginning to receive considerable scientific interest.*

Keywords: *insulin resistance, metabolic syndrome, type II diabetes mellitus, hypertension, atherogenic dyslipidemia*

ПРОЯВЛЕНИЯ И МЕХАНИЗМЫ РАЗВИТИЯ СИНДРОМА Х

Аннотация. *Метаболический синдром, характеризующийся совокупностью метаболических нарушений, включая центральное ожирение, резистентность к инсулину, гипертонию и дислипидемию, представляет значительный риск развития атеросклеротических сердечно-сосудистых заболеваний и сахарного диабета II типа. Диагноз метаболического синдрома требует наличия 3 или более из этих метаболических нарушений, что свидетельствует о срочной необходимости упреждающих стратегий выявления и вмешательства. Распространенность МС быстро растет во всем мире, в основном из-за продолжающейся эпидемии ожирения. Было показано, что факторы окружающей среды в периоды раннего развития влияют на восприимчивость к развитию заболевания в более позднем возрасте. В частности, имеется множество доказательств как эпидемиологических, так и животных исследований о большей частоте признаков МС в результате несбалансированного питания матери. Механизмы, посредством которых пищевые нарушения в период пластичности развития приводят к фенотипу МС, в настоящее время начинают привлекать значительный научный интерес.*

Ключевые слова: *резистентность к инсулину, метаболический синдром, сахарный диабет II типа, гипертония, атерогенная дислипидемия.*

Metabolic syndrome is an accumulation of several disorders that raise the risk of atherosclerotic cardiovascular disease, including myocardial infarction, cerebrovascular accidents, peripheral vascular diseases, insulin resistance, and type II diabetes mellitus. The cluster of metabolic disorders that define metabolic syndrome includes central obesity, insulin resistance, hypertension, and atherogenic dyslipidemia.

Evolution of the criteria or the metabolic syndrome since the original definition by the World Health Organization in 1998 reflects growing clinical evidence and analysis by a variety of consensus conferences and professional organizations. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low levels of high-density lipoprotein (HDL) cholesterol, hyperglycemia, and hypertension.

The most challenging feature of the metabolic syndrome to de ne is waist circumference. Intraabdominal circumference (visceral adipose tissue) is considered most strongly related to insulin resistance and risk of diabetes and CVD, and or any given waist circumference the distribution of adipose tissue between SC and visceral depots varies substantially. Thus, within and between populations, there is a lesser vs. greater risk at the same waist circumference. These differences in populations are reflected in the range of waist circumferences considered to confer risk in different geographic locations. The prevalence of the metabolic syndrome varies around the world, in part reflecting the age and ethnicity o the populations studied and the diagnostic criteria applied. In general, the prevalence of the metabolic syndrome increases with age. The global incidence of metabolic syndrome rises almost parallel to the incidence of obesity.

According to the National Health and Nutrition Examination Survey (NHNES), the prevalence of metabolic syndrome in adults increased from 25.3% to 34.2% in 2012.

RISK FACTORS:

Overweight/Obesity

Although the metabolic syndrome was first described in the early twentieth century, the worldwide overweight/ obesity epidemic has recently been the force driving its increasing recognition. Central adiposity is a key feature of the syndrome, and the syndrome’s prevalence reflects the strong relationship between waist circumference and increasing adiposity.

However, despite the importance of obesity, patients who are o normal weight may also be insulin resistant and may have the metabolic syndrome.

Sedentary lifestyle

Physical inactivity is a predictor of CVD events and the related risk of death. Many components of the metabolic syndrome are associated with a sedentary lifestyle, including increased adipose tissue (predominantly central), reduced HDL cholesterol, and increased triglycerides, blood pressure, and glucose in genetically susceptible persons. Compared with individuals who watch television or videos or use the computer 4 h daily have a two- old increased risk of the metabolic syndrome.

Aging

The metabolic syndrome affects nearly 50% of the U.S. population older than age 50, and at >60 years of age women are more often affected than men. The age dependency of the syndrome's prevalence is seen in most populations around the world.

Diabetes mellitus

Diabetes mellitus is included in both the NCEP and the harmonizing definitions of the metabolic syndrome. It is estimated that the great majority (~75%) of patients with type 2 diabetes or impaired glucose tolerance have the metabolic syndrome. T e presence of the metabolic syndrome in these populations relates to a higher prevalence of CVD than in patients who have type 2 diabetes or impaired glucose tolerance but do not have this syndrome.

Cardiovascular disease

Individuals with the metabolic syndrome are twice as likely to die of cardiovascular disease as those who do not, and their risk of an acute myocardial infarction or stroke is three old higher. The approximate prevalence of the metabolic syndrome among patients with coronary heart disease (CHD) is 50%, with a prevalence of ~35% among patients with premature coronary artery disease (be ore or at age 45) and a particularly high prevalence among women. With appropriate cardiac rehabilitation and changes in lifestyle (e.g., nutrition, physical activity, weight reduction, and—in some cases—pharmacologic therapy), the prevalence of the syndrome can be reduced.

Lipodystrophy

Lipodystrophic disorders in general are associated with the metabolic syndrome. Both genetic lipodystrophy (e.g., Berardinelli-Seip congenital lipodystrophy, Dunnigan amilial partial lipodystrophy) and acquired lipodystrophy (e.g., HIV-related lipodystrophy in patients receiving antiretroviral therapy) may give rise to severe insulin resistance and many of the components of the metabolic syndrome.

Pathophysiology:

Metabolic syndrome has been studied extensively over the past few decades. Insulin resistance, adipose tissue dysfunction, and chronic inflammation have been proposed as the basic components of the pathogenesis of metabolic syndrome.

Under normal circumstances, a sudden rise in serum glucose level triggers insulin secretion from the pancreatic β-cells, which promote cellular glucose uptake via glucose transporters. However, in those with insulin resistance, tissues are less sensitive to this acute rise in insulin, resulting in a higher serum glucose level and hyperinsulinemia. The impairment in insulin secretion and abnormal insulin signaling results in impaired glucose metabolism, fat deposition, cardiotoxicity, and chronic inflammation, the characteristic features of metabolic syndrome.

Visceral obesity is another essential component of metabolic syndrome. Free fatty acids released by the adipose tissues promote insulin resistance and inhibit insulin secretion from the pancreatic beta cells. The high-free fatty acids inhibit glucose uptake in skeletal muscles and increase hepatic gluconeogenesis and lipid synthesis by inducing protein kinases. Both insulin resistance and free fatty acids play a major role in the pathogenesis of hypertension, prothrombotic state, and chronic inflammation. Visceral adipose tissues also secrete multiple active metabolites and various pro-inflammatory cytokines, C-reactive protein, leptin, and resistin, which induce chronic inflammation, a possible mechanism of various complications of metabolic syndrome.

The inflammatory cytokines further increase insulin resistance in skeletal muscles, liver, and adipose tissues by inhibiting the insulin signaling pathway in these tissues. These cytokines, especially tumor necrosis factor-alpha, promote insulin resistance by inactivating insulin receptors in the skeletal muscles. Insulin resistance further activates inflammatory cytokines and promotes thrombogenesis by increasing the fibrinogen level.

Metabolic syndrome adversely influences several body systems. Insulin resistance causes microvascular damage, predisposing patients to endothelial dysfunction, vascular resistance, hypertension, and vessel wall inflammation. Endothelial damage can impact the body's homeostasis, causing atherosclerotic disease and the development of hypertension. Furthermore, hypertension adversely affects several body functions, including increased vascular resistance and stiffness, causing peripheral vascular disease, structural heart disease comprising of left ventricular hypertrophy and cardiomyopathy, and leading to renal impairment.

Accumulated effects of endothelial dysfunction and hypertension due to metabolic syndrome can further result in ischemic heart disease. Endothelial dysfunction due to increased levels of plasminogen activator inhibitor-1 and adipokine levels can cause thrombogenicity, while hypertension causes vascular resistance by which coronary artery disease can develop.

Dyslipidemia associated with metabolic syndrome can drive the atherosclerotic process, leading to symptomatic ischemic heart disease.

Conclusion: The metabolic syndrome (syndrome X, insulin resistance syndrome) consists of a constellation o metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus. The growing prevalence of metabolic disease challenges biological researchers to elucidate the mechanisms involved in the etiology and the pathogenesis of MetS and its associated features. Evidently, the disease itself and the mechanisms leading to its onset are multi-factorial. However, exposure to an inappropriate diet during the developmental period clearly plays a role in exacerbating the risk of disease onset.

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