

COMORBID CONDITIONS IN METABOLIC SYNDROME AND DIABETES MELLITUS: PATHOPHYSIOLOGICAL LINKS AND CLINICAL IMPLICATIONS.

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Abstract

Metabolic syndrome and diabetes mellitus represent two of the most prevalent chronic metabolic disorders worldwide and are frequently accompanied by multiple comorbid conditions. These interconnected disorders significantly increase the risk of cardiovascular disease, chronic kidney disease, non-alcoholic fatty liver disease, and other systemic complications. The coexistence of metabolic syndrome and diabetes creates a complex clinical situation that accelerates disease progression and worsens patient outcomes. The present review aims to analyze the major comorbid conditions associated with metabolic syndrome and diabetes mellitus, focusing on their pathophysiological mechanisms, epidemiological relevance, and clinical consequences. Data from recent epidemiological and clinical studies demonstrate that more than 70% of individuals with type 2 diabetes also meet the diagnostic criteria for metabolic syndrome. Moreover, cardiovascular complications account for nearly two-thirds of mortality in this population. Understanding the interaction between these disorders is essential for early detection, prevention strategies, and personalized therapeutic approaches.

Keywords

Metabolic syndrome, diabetes mellitus, comorbidity, insulin resistance, cardiovascular risk, obesity.

Introduction. The global prevalence of metabolic diseases has increased dramatically over the past several decades. Among them, metabolic syndrome and diabetes mellitus constitute major public health challenges due to their high incidence, chronic course, and association with severe complications. Metabolic syndrome is defined as a cluster of interrelated metabolic abnormalities that include central obesity, insulin resistance, dyslipidemia, and arterial hypertension. When these metabolic disturbances coexist, they significantly elevate the risk of

developing type 2 diabetes and cardiovascular diseases. Diabetes mellitus, particularly type 2 diabetes, is characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. According to international epidemiological reports, the number of individuals living with diabetes has exceeded 530 million globally, and projections suggest a continuous rise in the coming decades. The coexistence of metabolic syndrome and diabetes leads to a higher probability of developing additional comorbid conditions. These include cardiovascular diseases, chronic kidney disease, non-alcoholic fatty liver disease, and certain inflammatory disorders. Because of these associations, the management of metabolic syndrome and diabetes requires an integrated approach that addresses multiple physiological systems simultaneously.

Relevance and Scientific Significance. The study of comorbid conditions associated with metabolic syndrome and diabetes has gained increasing attention in modern clinical medicine. The relevance of this topic is primarily related to the high prevalence and substantial morbidity associated with these disorders. Large-scale epidemiological studies indicate that approximately 25–30% of the adult population worldwide meets the diagnostic criteria for metabolic syndrome. Among patients with type 2 diabetes, the prevalence of metabolic syndrome is even higher, reaching 70–80% in many populations. Clinical research has demonstrated that individuals with both conditions have a significantly increased risk of cardiovascular mortality compared with those who have either disorder alone. For instance, longitudinal cohort studies report that patients with combined metabolic syndrome and diabetes have a two- to three-fold higher risk of cardiovascular events, including myocardial infarction and stroke. Furthermore, metabolic syndrome contributes to the progression of insulin resistance, which represents the central pathophysiological mechanism linking these disorders. The identification and management of comorbid conditions therefore play a crucial role in improving long-term outcomes and reducing healthcare burden.

Pathophysiological Mechanisms Linking Metabolic Syndrome and Diabetes. The relationship between metabolic syndrome and diabetes is primarily mediated through insulin resistance and chronic low-grade inflammation. Insulin resistance refers to the reduced responsiveness of peripheral tissues—especially skeletal muscle, liver, and adipose tissue—to the action of insulin. Excess adipose tissue, particularly visceral fat, produces various bioactive molecules known as adipokines. These include tumor necrosis factor-alpha, interleukin-6, and resistin, which promote inflammatory responses and interfere with insulin signaling pathways. As a result, glucose uptake by tissues decreases, leading to persistent hyperglycemia. In addition to inflammation, oxidative stress also contributes to

metabolic dysfunction. Elevated levels of free fatty acids in individuals with central obesity stimulate hepatic gluconeogenesis and impair pancreatic beta-cell function. Over time, this process results in progressive deterioration of insulin secretion and the development of type 2 diabetes. Another important mechanism involves endothelial dysfunction. Hyperglycemia and dyslipidemia damage vascular endothelial cells, reducing nitric oxide availability and promoting atherosclerosis. This explains the strong association between metabolic syndrome, diabetes, and cardiovascular disease.

Cardiovascular Disease. Cardiovascular disease is the most common and clinically significant comorbidity associated with metabolic syndrome and diabetes. Studies indicate that approximately 65–70% of deaths in diabetic patients are related to cardiovascular complications. Hypertension, dyslipidemia, and chronic inflammation accelerate the formation of atherosclerotic plaques, leading to coronary artery disease and cerebrovascular events.

Non-Alcoholic Fatty Liver Disease. Non-alcoholic fatty liver disease (NAFLD) is another frequent comorbid condition. Clinical investigations suggest that up to 60–70% of individuals with type 2 diabetes develop fatty liver infiltration. Insulin resistance increases hepatic lipid accumulation, which may progress to steatohepatitis, fibrosis, and eventually cirrhosis.

Chronic Kidney Disease. Chronic kidney disease is a well-recognized complication of diabetes and is closely associated with metabolic syndrome. Hyperglycemia damages the glomerular filtration barrier, resulting in proteinuria and progressive renal dysfunction. Epidemiological studies show that around 30–40% of diabetic patients develop diabetic nephropathy during the course of the disease.

Obstructive Sleep Apnea. Obesity, a key component of metabolic syndrome, is strongly linked to obstructive sleep apnea. Recurrent episodes of hypoxia during sleep increase sympathetic nervous system activity and worsen insulin resistance, thereby contributing to poor glycemic control.

Clinical Research Findings. Several recent clinical studies have investigated the interaction between metabolic syndrome and diabetes in different populations. A multicenter observational study involving more than 10,000 patients with type 2 diabetes reported that approximately 72% met the criteria for metabolic syndrome. These patients showed significantly higher levels of triglycerides, blood pressure, and waist circumference compared with diabetic individuals without metabolic syndrome. Another longitudinal study evaluated the risk of cardiovascular events over a 10-year period in patients with metabolic abnormalities. The findings revealed that individuals with both metabolic syndrome and diabetes experienced

nearly a threefold increase in cardiovascular complications compared with those without metabolic syndrome. Clinical trials examining lifestyle interventions also demonstrated promising results. Patients who achieved moderate weight reduction (5–10% of body weight) through dietary modification and physical activity showed significant improvements in insulin sensitivity and lipid profiles.

Conclusion. Metabolic syndrome and diabetes mellitus frequently coexist and share common pathophysiological mechanisms, particularly insulin resistance and chronic inflammation. The presence of these disorders significantly increases the risk of multiple comorbid conditions, including cardiovascular disease, fatty liver disease, and chronic kidney disease.

Epidemiological and clinical evidence indicates that the combination of metabolic syndrome and diabetes leads to substantially higher morbidity and mortality. Therefore, early identification, comprehensive risk assessment, and integrated management strategies are essential for improving patient outcomes.

Future research should focus on identifying novel biomarkers, improving preventive strategies, and developing personalized therapeutic interventions to address the growing global burden of metabolic diseases.

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