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Metabolic Syndrome Calling Models

Zikrillaev Farrux Abdurashitovich
Asia International University, Bukhara, Uzbekistan

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Abstract: Metabolic Syndrome is a collection of metabolic disorders that increase the risk of cardiovascular diseases, diabetes, stroke, and other health issues. These disorders include central obesity, hypertension, insulin resistance, and atherogenic dyslipidemia. In many countries, approximately 20-30% of the adult population suffers from MetS, and its prevalence depends on factors such as age, gender, ethnicity, and diagnostic criteria. By 2035, the prevalence of MetS is expected to increase to around 53% . This combination of metabolic disorders was first discussed by Dr. Reaven in 1988. At that time, this clinical condition was referred to by various names, such as "insulin resistance syndrome," "syndrome X," and "the deadly quartet" with hypertriglyceridemia. However, it is now most commonly known as metabolic syndrome and is increasingly recognized as a major cardiovascular risk factor.

Keywords: metabolic syndrome, biomarkes, dyslipidemia, hypertension.

Metabolic syndrome (MetS) is a serious health risk for individuals, and studying it presents challenges that require the development of animal models that mimic the disease. Mice and rats are the most commonly used models to study MetS. In recent years, the fruit fly Drosophila melanogaster has become an effective and economical model for studying metabolic disorders and obesity-related diseases. In this review, we discuss the various animal models used to study MetS, highlighting their advantages and limitations. Research has shown that both Drosophila and rodents share many metabolic similarities with humans, making them suitable for studying metabolic processes and testing preventive strategies for obesity and MetS.

The metabolic syndrome has received increased attention in the past few years. This statement from the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) is intended to provide up-to-date guidance for professionals on the diagnosis and

management of the metabolic syndrome in adults. The metabolic syndrome is a constellation of interrelated risk factors of metabolic origin—metabolic risk factors—that appear to directly promote the development of atherosclerotic cardiovascular disease (ASCVD).1 Patients with the metabolic syndrome also are at increased risk for developing type 2 diabetes mellitus. Another set of conditions, the underlying risk factors, give rise to the metabolic risk factors. In the past few years, several expert groups have attempted to set forth simple diagnostic criteria to be used in clinical practice to identify patients who manifest the multiple components of the metabolic syndrome. These criteria have varied somewhat in specific elements, but in general they include a combination of both underlying and metabolic risk factors.

The most widely recognized of the metabolic risk factors are atherogenic dyslipidemia, elevated blood pressure, and elevated plasma glucose. Individuals with these characteristics commonly manifest a prothrombotic state and a proinflammatory state as well. Atherogenic dyslipidemia consists of an aggregation of lipoprotein abnormalities including elevated serum triglyceride and apolipoprotein B (apoB), increased small LDL particles, and a reduced level of HDL cholesterol (HDL-C). The metabolic syndrome is often referred to as if it were a discrete entity with a single cause. Available data suggest that it truly is a syndrome, ie, a grouping of ASCVD risk factors, but one that probably has more than one cause. Regardless of cause, the syndrome identifies individuals at an elevated risk for ASCVD. The magnitude of the increased risk can vary according to which components of the syndrome are present plus the other, non–metabolic syndrome risk factors in a particular person.

Many investigations confirm that multiple cardiovascular risk factors of endogenous origin commonly aggregate in one individual. Although this aggregation was originally observed many years ago, more recently, several terms have been proposed to describe this clustering: metabolic syndrome, syndrome X, the “deadly quartet,” insulin-resistance syndrome, and hypertriglyceridemic waist. The term metabolic syndrome is most commonly used in the cardiovascular field. Although the metabolic syndrome is often referred to as a discrete entity, it is important to recognize, as noted earlier, that it is a syndrome and not a defined uniform entity. No single pathogenesis has been elucidated, nor may one exist. Thus, the syndrome could range from a cluster of unrelated risk factors to a constellation of risk factors linked through a common underlying mechanism. From a clinical standpoint, presence of the metabolic syndrome identifies a person at increased risk for ASCVD and/or type 2 diabetes mellitus. Eventually, a better understanding of the specific cause(s) of the syndrome may provide an improved estimate of risk of developing ASCVD or type 2 diabetes mellitus for individuals. For now, however, the presence of the syndrome is a more general indicator of higher risk for these conditions. Because of a documented high relative risk for ASCVD events and type 2 diabetes mellitus, the metabolic syndrome undoubtedly carries a relatively high lifetime risk for these disorders even when shorter-term (10-year) risk is in the low-to-moderate range.

Rodent models are widely used to study various aspects of Metabolic Syndrome (MetS), as they share many functional and metabolic similarities with humans. Among rodents, diet-induced obesity models are especially common. These animals are fed high-calorie diets to induce an obesity phenotype. The most commonly used diet is a high-fat diet (42-58% fat content). These diets have been shown to induce clinical features typical of MetS, such as insulin resistance and high blood pressure. Various studies, such as those by Avtanski et al. have shown that high-fat diets lead to insulin resistance and pro-inflammatory states in C57BL/6J mice**.** Additionally, research by Rahmuny et al. demonstrated the effects of high-fat diets on metabolic processes in rodents. Even animals fed low-fat diets reached similar levels of obesity, but with higher insulin resistance. N. Mamikutty et al. developed two models of Metabolic Syndrome (MS) induced by the consumption of 20% or 25% fructose solutions as drinking water, with normal intake of regular feed. This drinking regimen in 8-week-old Wistar rats from both groups led to the development of **sy**stolic hypertension**,** hypertriglyceridemia**,** and hyperglycemia**.** Adipocyte hypertrophy**,** increased body mass, and abdominal obesity in rats consuming the 20% fructose solution as

drinking water were more pronounced due to higher consumption of this water, and therefore, more calories.One of the promising methods for modeling Metabolic Syndrome (MS) induced by fructose consumption is the addition of fructose to the drinking water of experimental animals. Wistar rats**,** kept for 5 weeks on a standard diet (commercial feed), but drinking a 10% fructose solution as their drinking water, developed key signs of MS, such as hyperglycemia and visceral obesity**.** Additionally, they showed a tendency for increased body ma**ss** and elevated levels of total cholesterol and triglycerides in the serum.Many studies, including those examining fructose consumption**,** support its role in the development of Metabolic Syndrome (MetS). In mice, 11 weeks of fructose consumption resulted in the classic signs of MetS: increased body mass, elevated blood glucose, insulin, total cholesterol, and triglycerides (TAG), as well as increased systolic and diastolic blood pressure. Fructose consumption also raised the HOMA-IR index, suggesting the induction of insulin resistance.

Result. In a study by Oron-Herman et al. **,** fructose-enriched diets led to hyperinsulinemia, hypertriglyceridemia, hypercholesterolemia, hypertension, and insulin resistance in Sprague-Dawley rat**s**. Similarly, in male Wistar rats**,** consuming 30% sucrose led to the development of MetS features such as increased body weight, higher blood pressure, and elevated insulin, TAG, total cholesterol, and LDL levels. Results from Pang et al. indicated that a 78% sucrose-enriched diet significantly increased systolic blood pressure, insulin, and TAG levels in rats.

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