Journal of Endocrinology, Diabetes and Metabolic Complications (JEDMC)

OLITES PUBLISHERS
A Global Approach For Research

Open Access

Review Article

Dysregulation: Understanding the Hidden Imbalance Behind Modern Metabolic Disease Metabolic

Skotheim D, Daigavane R, Momeni E, Trincado W, Romanello Y
Centre for Diabetes Research, Iran
***Corresponding Author:** Daigavane R, Centre for Diabetes Research, Iran
Citation: Daigavane R (2026). Metabolic Dysregulation: Understanding the Hidden Imbalance Behind Modern Metabolic Disease V2(2)

Received date: August 08, 2026: **Accepted date:** August 17, 2026: **Published date**: August 22,2026
Keywords metabolic dysregulation, insulin resistance, metabolic syndrome, mitochondrial dysfunction, inflammation, glucose metabolism, lipid metabolism, MASLD, metabolic health

Abstract
Metabolic dysregulation refers to a disruption in the body's ability to maintain normal energy production, glucose regulation, lipid metabolism, hormonal signaling, and cellular homeostasis. Rather than representing a single disease, it is a broad biological state that can contribute to conditions such as insulin resistance, type 2 diabetes, obesity, metabolic syndrome, cardiovascular disease, and metabolic dysfunction-associated steatotic liver disease (MASLD). At its core, metabolic dysregulation reflects an imbalance between energy intake, energy utilization, nutrient storage, and cellular signaling. Increasing evidence suggests that insulin resistance, chronic low-grade inflammation, mitochondrial dysfunction, abnormal lipid handling, oxidative stress, and altered adipose-tissue biology interact in a self-reinforcing cycle. Understanding these interconnected mechanisms provides a more comprehensive perspective on metabolic disease and highlights the importance of prevention, early detection, physical activity, nutritional quality, adequate sleep, and individualized clinical management.

Introduction
Human metabolism is a highly coordinated network that continuously adjusts energy production and storage according to nutritional intake, physical activity, hormonal signals, and cellular demands. Under healthy conditions, glucose, fatty acids, amino acids, and other nutrients are appropriately processed to provide energy while maintaining stable internal conditions.

Metabolic dysregulation develops when these regulatory systems become persistently disturbed. The disturbance may initially be subtle—for example, reduced insulin sensitivity or altered lipid handling—before progressing to measurable abnormalities such as elevated blood glucose, increased triglycerides, hypertension, central adiposity, or hepatic fat accumulation. This is important because metabolic disease rarely develops through one pathway alone. Insulin resistance, inflammation, oxidative stress, mitochondrial changes, adipose-tissue dysfunction, and abnormal lipid metabolism can influence one another, creating a biological feedback loop. Reviews of metabolic syndrome have identified insulin resistance, systemic inflammation, oxidative stress, and mitochondrial dysfunction as important interconnected components of this process

What Is Metabolic Dysregulation
Metabolic dysregulation can be described as a persistent disturbance in normal metabolic homeostasis. It can affect several physiological systems simultaneously:

- **Glucose metabolism:** impaired glucose uptake and abnormal blood-glucose regulation.
- **Insulin signaling:** reduced cellular responsiveness to insulin.
- **Lipid metabolism:** increased circulating triglycerides, abnormal lipid storage, and ectopic fat accumulation.
- **Energy metabolism:** inefficient utilization or storage of nutrients.
- **Adipose-tissue function:** abnormal expansion and altered secretion of signaling molecules.
- **Mitochondrial function:** impaired energy **production and increased oxidative stress.**
- **Inflammatory signalling:** persistent low-grade inflammation that interferes with metabolic pathways

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

Insulin Resistance: A Central Mechanism

Insulin is essential for coordinating glucose and lipid metabolism. It promotes glucose uptake in insulin-sensitive tissues, supports glycogen synthesis, influences lipid storage, and suppresses excessive glucose production by the liver.

In insulin resistance, cells respond inadequately to insulin. The pancreas may initially compensate by producing more insulin, resulting in hyperinsulinemia. Over time, compensation may become insufficient, contributing to impaired glucose tolerance and eventually type 2 diabetes

Lipid Dysregulation and Lipotoxicity

Lipids are essential for energy storage, cellular membranes, and signaling. However, abnormal accumulation of lipids in tissues that are not designed for large-scale lipid storage can become harmful.

Lifestyle and Metabolic Resilience

Metabolic health is influenced by both biological and environmental factors. Nutrition, physical activity, sleep, stress, alcohol exposure, medications, genetics, age, and socioeconomic conditions can all contribute to metabolic outcomes

Regular physical activity can improve insulin sensitivity and glucose utilization, while appropriate nutrition can help regulate energy balance and lipid metabolism. Adequate sleep and effective stress management may also support normal hormonal and metabolic regulation

Conclusion

Metabolic dysregulation is best understood as a network-level disturbance rather than a single abnormal laboratory value or disease. Insulin resistance, abnormal lipid metabolism, adipose-tissue dysfunction, inflammation, oxidative stress, and mitochondrial changes can interact to disrupt metabolic homeostasis.

References

1. Russo MP, Grande-Ratti MF, Burgos MA, Molaro AA, Bonella MB. Prevalence of diabetes, epidemiological characteristics and vascular complications. Arch Cardiol Mex. 2023;93(1):30-36
2. Dzaye O, Dudum R, Reiter-Brennan C, Kianoush S, Tota-Maharaj R, Cainzos-Achirica M, Blaha MJ. Coronary artery calcium scoring for individualized cardiovascular risk estimation in important patient subpopulations after the 2019 AHA/ACC primary prevention guidelines. Prog Cardiovasc Dis. 2019 Sep-Oct;62(5):423-430.
3. Szypowska A, Zatońska K, Szuba A, Regulska-Ilow B. Dietary Inflammatory Index (DII)® and Metabolic Syndrome in the Selected Population of Polish Adults: Results of the PURE Poland Sub-Study. Int J Environ Res Public Health. 2023 Jan 06;20(2)
4. Nakamura-Ishizu, A.; Ito, K.; Suda, T. Hematopoietic stem cell metabolism during development and aging. Dev. Cell 2020, 54, 239–255.
5. Tommasi, S.; Pabustan, N.; Li, M.; Chen, Y.; Siegmund, K.D.; Besaratinia, A. A novel role for vaping in mitochondrial gene dysregulation and inflammation fundamental to disease development. Sci. Rep. 2021, 11, 22773
6. Cao, H.; Tadros, V.; Hiramoto, B.; Leeper, K.; Hino, C.; Xiao, J.; Pham, B.; Kim, D.H.; Reeves, M.E.; Chen, C.S.; et al. Targeting tki-activated nfkb2-mif/cxcls-cxcr2 signaling pathways in flt3 mutated acute myeloid leukemia reduce blast viability. Biomedicines 2022, 10, 1038.

Journal of Endocrinology, Diabetes and Metabolic Complications (JEDMC)

DOI:10/JEDMC/2026/019

.

Journal of Endocrinology, Diabetes and Metabolic Complications (JEDMC)