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THE PATHOPHYSIOLOGICAL RELATIONSHIP BETWEEN OBESITY AND TYPE 2 DIABETES MELLITUS

Aziza Samariddinova
University: Samarkand State Medical University
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ABSTRACT:

Obesity is the primary etiological factor in the development of Type 2 Diabetes Mellitus (T2DM). This relationship is mediated through insulin resistance, chronic low-grade inflammation, and deleterious changes in adipokine secretion. Understanding this nexus is critical for clinical intervention and long-term management of metabolic syndrome.

Adipose Tissue as an Endocrine Organ

Modern physiology no longer views adipose tissue merely as an energy reservoir. It is a complex endocrine organ that secretes signaling molecules called adipokines. In obese individuals, the hypertrophy of adipocytes leads to an imbalance:

• Reduced Adiponectin: A hormone that normally enhances insulin sensitivity.

• Increased Resistin and TNF-α: Cytokines that promote insulin resistance by interfering with the insulin receptor signaling pathway.

The Role of Free Fatty Acids (FFAs) and Lipotoxicity

Obesity, especially visceral adiposity, results in an elevated flux of Free Fatty Acids (FFAs) into the portal circulation. This leads to:

• Ectopic Fat Deposition: Accumulation of lipids in the liver and skeletal muscle.

• Impaired Glucose Uptake: Intracellular lipid metabolites (like diacylglycerol) inhibit the translocation of GLUT4 transporters, thereby preventing glucose from entering the cells Beta-cell Exhaustion.The initial response to insulin resistance is compensatory hyperinsulinemia. However, the chronic stress of obesity, combined with glucotoxicity and lipotoxicity, eventually leads to the failure of pancreatic beta-cells. Once the beta-cells can no longer compensate for the resistance, clinical Type Diabetes manifests.

While obesity is the primary trigger, the relationship with diabetes is also influenced by:

• Genetics: Specific genes (like TCF7L2) can predispose an obese individual to beta-cell failure.

• Sedentary Lifestyle: Lack of physical activity reduces the expression of GLUT4 in muscles, exacerbating insulin resistance even further.

Conclusion

The link between obesity and T2DM is primarily driven by the metabolic dysfunction of adipose tissue. Weight management remains the most effective strategy for improving insulin sensitivity and potentially achieving diabetes remission.

Pro-inflammatory Cytokines and Chemokines

In obesity, the enlarged adipose tissue undergoes "remodeling," where macrophages (immune cells) infiltrate the fat. These macrophages secrete:

• TNF-alpha (Tumor Necrosis Factor): This is a key mediator that impairs insulin signaling in the liver and muscle.

• IL-6 (Interleukin-6): Elevated levels in obese patients are directly linked to increased glucose production in the liver, contributing to fasting hyperglycemia.

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