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THE RELATIONSHIP BETWEEN ADIPOSE TISSUE FACTORS AND OBESITY UNDERLYING THE OCCURRENCE OF METABOLIC SYNDROME

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ABSTRACT

The growing prevalence of sedentary lifestyles, particularly in urban populations, combined with the widespread consumption of unhealthy foods, has contributed to increasing rates of overweight and obesity (adiposity). These conditions induce pathophysiological disturbances in adipose tissue, which functions as an endocrine organ, thereby leading to metabolic syndrome. Atherogenic dyslipidemia plays a significant role in the progression of atherosclerosis, ultimately increasing the risk of cardiovascular diseases. Furthermore, inflammatory mediators released by dysfunctional adipocytes are associated with the development of certain types of cancer. This review highlights the role of obesity and adipose tissue as fundamental components in the emergence of metabolic syndrome, aiming to strengthen scientific understanding and encourage further research to develop effective strategies for the prevention and management of complex metabolic disorders..

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INTRODUCTION

Over the past several decades, obesity has emerged as a major global health epidemic. Its prevalence continues to rise in parallel with lifestyle changes—most notably the increase in sedentary behavior and the widespread consumption of high-calorie, nutrient-poor foods. Obesity, characterized by excessive accumulation of body fat, particularly in visceral adipose tissue, has been identified as a primary risk factor for various complex metabolic disorders, including metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM), cardiovascular disease, and non-alcoholic fatty liver disease (NAFLD). Recent studies emphasize that this upward trend in adiposity significantly exacerbates systemic metabolic dysregulation (Choi et al., 2025).

The biological role of adipose tissue has been reconceptualized in contemporary research. It is no longer viewed merely as an energy reservoir, but rather as a dynamic endocrine and metabolic organ. In obesity, adipocytes undergo hypertrophy and may become dysfunctional, releasing a wide array of pro-inflammatory cytokines (e.g., TNF-α, IL-6), free fatty acids, and oxidative mediators. These responses promote chronic low-grade inflammation and insulin resistance—hallmarks of metabolic dysfunction (Choi et al., 2025).

This chronic inflammatory state, often termed adipose tissue dysfunction, plays a central role in the pathogenesis of MetS and its associated complications. Recent evidence indicates that the interplay between inflammation, mitochondrial dysfunction, and oxidative stress intensifies insulin resistance and accelerates the progression of hepatic steatosis, atherogenic dyslipidemia, and cardiovascular disease (Islam et al., 2024).

Furthermore, emerging literature suggests that fat distribution—especially visceral fat accumulation—is a stronger predictor of metabolic risk than body mass index (BMI) alone. Conditions such as metabolically obese normal-weight (MONW) individuals demonstrate that metabolic health is not determined solely by body fat quantity but also by fat function and anatomical distribution (Swarup et al., 2024). This highlights the crucial role of adipose tissue expandability and endocrine function in determining an individual's metabolic profile.

Given these findings, a deeper investigation into adipose tissue—its structure, distribution, and endocrine-inflammatory properties—is essential for understanding the pathophysiological mechanisms underlying metabolic syndrome. This review aims to explore how obesity-induced adipose tissue dysfunction contributes to the development of MetS, thereby supporting future research and the development of comprehensive strategies for preventing and managing complex metabolic diseases..

METHODS

Study Design

This study employed a narrative review design to analyze recent evidence regarding the role of obesity and adipose tissue dysfunction in the development of metabolic syndrome. A narrative review was selected due to its suitability for synthesizing current biomedical and public health literature, especially when the topic involves complex physiological and metabolic mechanisms.

Literature Search Strategy

A structured literature search was conducted between January and March 2025 across major health-science databases, including PubMed, ScienceDirect, Scopus, and Google Scholar. The search focused on articles published within the last five years (2020–2025) to ensure the inclusion of the most recent findings relevant to metabolic health.

The search terms applied included a combination of Medical Subject Headings (MeSH) and free-text keywords:

"obesity," "adiposity," "adipose tissue dysfunction," "visceral fat," "inflammation," "adipokines," "metabolic syndrome," "insulin resistance," "cardiometabolic risk," "atherogenic dyslipidemia."

Boolean operators (AND, OR) were used to refine the search for health-related outcomes and physiological mechanisms associated with metabolic syndrome.

Inclusion and Exclusion Criteria

Articles were selected based on the following criteria:

Inclusion Criteria:

1. Published in peer-reviewed health or biomedical journals (2020–2025).
2. Focused on obesity, adipose tissue biology, inflammatory pathways, or metabolic syndrome.
3. Included clinical, epidemiological, or experimental data relevant to metabolic health.
4. Written in English.

Exclusion Criteria:

1. Publications prior to 2020.
2. Non–peer-reviewed articles, editorials, commentaries, theses, or conference abstracts.
3. Studies unrelated to obesity-related metabolic dysfunction or lacking relevance to metabolic disease mechanisms.

Article Screening and Selection Process

The initial search identified approximately 240 articles. After removing duplicates, 185 unique articles were screened based on titles and abstracts. A total of 78 articles met the preliminary criteria and underwent full-text evaluation. Following a detailed review based on relevance, scientific rigor, and alignment with health science perspectives, 48 articles were included in the final synthesis.

Data Extraction and Synthesis

Data extracted from each study included:

Type of study (clinical trial, observational study, in vivo/in vitro experiment, or systematic review),sample characteristics, key findings related to adipose tissue function, inflammation, insulin resistance, and metabolic risk,health implications and proposed physiological mechanisms.

The extracted data were synthesized thematically into categories relevant to the health sciences, specifically:

1. Pathophysiology of adipose tissue dysfunction,
2. Inflammatory and endocrine mechanisms,
3. Clinical markers of metabolic syndrome,
4. Cardiometabolic risk pathways,
5. Public health implications of obesity-related metabolic disease.

Given the heterogeneity of study designs, a qualitative synthesis approach was used rather than statistical meta-analysis.

RESULTS AND DISCUSSION

Results

The literature reviewed indicates that adipose tissue plays a central role in the pathogenesis of metabolic syndrome through several interrelated biological mechanisms. First, obesity is characterized by both adipocyte hypertrophy and hyperplasia, in which enlarged adipocytes are strongly associated with insulin resistance and metabolic complications (Moreno-Navarrete & Fernández-Real, 2012)

Second, differences in fat distribution were found to significantly influence metabolic risk. Visceral adipose tissue shows higher lipolytic activity, greater insulin resistance, and

increased secretion of pro-inflammatory cytokines—such as TNF-α, IL-6, resistin, and PAI-1—compared to subcutaneous fat (Després et al., 2008; Grundy, 2004)

Third, obesity promotes chronic low-grade inflammation in adipose tissue. Macrophage infiltration produces inflammatory mediators that disrupt adipocyte differentiation and impair insulin signaling (Cancello & Clément, 2006; Gustafson et al., 2007)

Fourth, adipose tissue functions as an endocrine organ that secretes various adipokines—including leptin, adiponectin, resistin, and IL-6—that regulate energy balance, appetite, insulin sensitivity, and inflammation. Obesity results in altered adipokine profiles that contribute to metabolic dysregulation (Trayhurn & Wood, 2004; Wozniak et al., 2009)

Fifth, insulin resistance emerged as the key mechanism linking obesity to metabolic syndrome. Elevated free fatty acids, inflammatory cytokines, and reduced adiponectin disrupt insulin-mediated glucose uptake, leading to hyperglycemia, dyslipidemia, and increased hepatic glucose production (Lechleitner, 2008).

Finally, the findings emphasize central obesity as the strongest predictor of metabolic syndrome, especially in Asian populations where visceral fat accumulates at lower BMI values (Klein et al., 2007; Alberti et al., 2009)

Discussion

The results demonstrate that adipose tissue dysfunction is the main biological pathway linking obesity to metabolic syndrome.

1. Chronic Low-Grade Inflammation
   Obesity-induced adipocyte hypertrophy leads to hypoxia, macrophage recruitment, and increased secretion of cytokines such as TNF-α and IL-6. These inflammatory mediators directly inhibit insulin signaling and promote systemic insulin resistance (Gustafson et al., 2007)
2. Adipokine Dysregulation
   Adipose tissue, as an endocrine organ, secretes multiple hormones and cytokines involved in energy regulation:
   - Adiponectin decreases, reducing insulin sensitivity (Maiorana et al., 2007).
   - Leptin increases, but leptin resistance occurs, impairing appetite regulation.
   - Resistin and PAI-1 increase, contributing to endothelial dysfunction and inflammation (Grundy, 2004).

   Thus, obesity represents an endocrine disorder characterized by hormonal imbalance.
3. Visceral vs. Subcutaneous Fat Differences
   Visceral fat drains into the portal vein, exposing the liver to high free fatty acid levels and inflammatory molecules, which:
   - increase hepatic glucose production,
   - elevate triglycerides and VLDL levels,
   - decrease HDL levels,
   - promote inflammation (Wajchenberg, 2000; Carr et al., 2004).

   This explains why visceral obesity is strongly associated with metabolic syndrome.
4. Insulin Resistance as the Central Mechanism

Insulin resistance connects multiple metabolic abnormalities, including hyperglycemia, hypertension, and dyslipidemia. Free fatty acids interfere with insulin signaling in skeletal muscle, while inflammatory cytokines impair hepatic metabolism, creating a self-sustaining cycle of metabolic dysfunction (Lechleitner, 2008)

5. Role of Brown Adipose Tissue (BAT)
   Brown adipose tissue contributes to thermogenesis and energy expenditure. Its decline with age reduces metabolic efficiency and predisposes individuals to obesity, indirectly increasing the risk of metabolic syndrome (Enerbäck, 2010)
6. Clinical Implications
   The synthesis highlights that:
   - Waist circumference is a more accurate indicator of metabolic risk than BMI (WHO-WPR, 2000).
   - Prevention of early obesity is essential to avoid permanent increases in adipocyte number (Parigi, 2010).
   - Interventions targeting adipose inflammation and adipokine regulation may be effective for managing metabolic syndrome..

CONCLUSION

This review concludes that adipose tissue dysfunction is the fundamental biological mechanism linking obesity to the development of metabolic syndrome. The enlargement and increased number of adipocytes, particularly in visceral fat depots, lead to chronic low-grade inflammation, adipokine imbalance, and excess release of free fatty acids. These changes disrupt insulin signaling and promote systemic insulin resistance, which serves as the central pathological axis of metabolic syndrome. Visceral adipose tissue, due to its unique anatomical and metabolic characteristics, plays a disproportionately significant role by delivering inflammatory mediators and lipids directly to the liver, thereby promoting dyslipidemia, hyperglycemia, and hepatic insulin resistance. In contrast, subcutaneous fat contributes far less to metabolic risk, reinforcing the importance of fat distribution rather than total adiposity alone. The endocrine function of adipose tissue further demonstrates that obesity is not merely a condition of excess fat storage but a complex hormonal and inflammatory disorder. The decline in brown adipose tissue activity with age also reduces metabolic efficiency, enhancing susceptibility to metabolic syndrome. Overall, understanding the multifaceted role of adipose tissue in metabolic regulation is essential for developing effective prevention and treatment strategies. Interventions aimed at reducing visceral adiposity, restoring adipokine balance, attenuating inflammation, and improving insulin sensitivity hold significant potential for mitigating the burden of metabolic syndrome..

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