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Review Article

Diabesity: An Emerging Epidemic and Advances in Treatment

Dr. Saqib Salah Aufi[a]*, Dr. Kaniz Hasnin[b]

[a]Medical Officer, Rajshahi Diabetic Association General Hospital. Rajshahi, Bangladesh

[b]Principal Nutrition Officer, Rajshahi Diabetic Association General Hospital, Rajshahi, Bangladesh

Correspondence to:

Dr. Saqib Salah Aufi
Medical Officer, Rajshahi Diabetic Association General Hospital. Rajshahi, Bangladesh
Email: draufisalah@gmail.com

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Abstract: ***Background*:** Diabesity, the coexistence of obesity and type 2 diabetes mellitus (T2DM), has emerged as a significant global public health issue. Characterized by shared pathophysiology, including insulin resistance and chronic inflammation, diabesity substantially increases the risk of complications such as cardiovascular disease and non-alcoholic fatty liver disease (NAFLD). ***Objectives:*** This paper reviews the interconnection between obesity and T2DM, emphasizing recent advancements in management, including pharmacological treatments, surgical interventions, and innovative technologies. ***Methods:*** A systematic review was conducted using databases such as PubMed, Scopus, and Cochrane Library to identify studies published in the past decade. Key areas of focus included GLP-1 receptor agonists, SGLT-2 inhibitors, bariatric surgery, microbiome-targeted therapies, and artificial intelligence applications in diabesity management. ***Results:*** Pharmacological advancements, such as GLP-1 receptor agonists (e.g., semaglutide) and dual-action agents (e.g., tirzepatide), significantly improved weight loss and glycemic control. SGLT-2 inhibitors demonstrated additional cardiovascular and renal benefits. Bariatric surgery provided long-term metabolic improvements for severe cases, while emerging technologies like wearable devices and microbiome research offered promising personalized treatment approaches. ***Conclusions:*** The integration of advanced pharmacological treatments, surgical interventions, and innovative technologies has revolutionized diabesity management. Public health strategies focusing on early intervention, prevention, and equitable healthcare access are critical to addressing this epidemic. Future research should focus on long-term efficacy, cost-effectiveness, and region-specific strategies to combat diabesity.

Keywords: Diabesity, T2DM, Insulin resistance, GLP-1 receptor agonists, Bariatric surgery.

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Introduction

Diabesity, a term coined to describe the synergistic coexistence of obesity and type 2 diabetes mellitus (T2DM), has emerged as one of the most significant public health challenges of the 21st century. Both conditions are chronic, non-communicable diseases (NCDs) with overlapping pathophysiological mechanisms, making their co-occurrence a growing concern. The global prevalence of obesity has nearly tripled since 1975, while T2DM affects an estimated 537 million adults as of 2021, a number projected to rise to 783 million by 2045.[1, 2] These staggering figures underscore the urgent need to address the diabesity epidemic comprehensively. Obesity, particularly central adiposity, is a major risk factor for T2DM, primarily due to its role in promoting insulin resistance. Excess visceral fat releases pro-inflammatory cytokines and free fatty

acids, disrupting insulin signaling and contributing to chronic hyperglycemia.[3, 4] This bidirectional relationship between obesity and T2DM amplifies the risk of complications such as cardiovascular disease, non-alcoholic fatty liver disease (NAFLD), and chronic kidney disease.[5] Southeast Asia, with its rapid urbanization, changing dietary habits, and sedentary lifestyles, is witnessing a disproportionate rise in diabesity, making it a regional hotspot for this dual epidemic.[6]

Despite advancements in medical science, the management of diabesity remains complex. Traditional treatment approaches, such as lifestyle modifications and monotherapy for diabetes or obesity, often fall short in achieving long-term control. However, recent innovations in pharmacological therapies, surgical interventions, and emerging technologies like artificial intelligence and microbiome research offer promising new strategies for managing diabesity effectively.[7] This paper aims to explore the pathophysiology, epidemiology, and recent advancements in diabesity treatment, with a particular focus on pharmacological and surgical approaches, as well as the role of innovative technologies. By addressing these aspects, this review seeks to provide a comprehensive understanding of diabesity and propose pathways for improved patient outcomes and public health strategies.

Literature Review

The dual epidemic of obesity and type 2 diabetes mellitus (T2DM), collectively termed "diabesity," has garnered significant attention in recent years. This section explores the existing literature on the interrelationship between obesity and T2DM, gaps in current research, and recent advancements in treatment approaches.

The Pathophysiological Link Between Obesity and Diabetes

The relationship between obesity and T2DM is well-documented, with insulin resistance serving as a critical connecting mechanism. Obesity, particularly visceral adiposity, promotes the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which impair insulin signaling pathways.[3, 7] Free fatty acids released by excess fat deposits further exacerbate insulin resistance and beta-cell dysfunction, eventually leading to hyperglycemia and T2DM. The term "diabesity" emphasizes the metabolic interdependence of obesity and T2DM, highlighting the need for integrated treatment approaches. Studies suggest that individuals with a higher body mass index (BMI) are significantly more likely to develop T2DM, with the risk increasing exponentially in cases of central obesity.[7, 8] Despite these insights, the molecular mechanisms underlying this association remain incompletely understood, particularly the role of ectopic fat deposition and gut microbiota dysbiosis.

Epidemiological Trends

Globally, the prevalence of obesity and T2DM has risen alarmingly. The International Diabetes Federation (IDF) estimates that 537 million adults had diabetes in 2021, with the number projected to reach 783 million by 2045. Concurrently, the World Health Organization (WHO) reports a near tripling of global obesity rates since 1975. Southeast Asia has become a hotspot for diabesity, driven by rapid urbanization, dietary shifts, and sedentary lifestyles. Approximately 65.9 million individuals in India and 88.5 million in China live with diabetes, with obesity being a key contributor.[8, 9]

Current Treatment and Strategies for Diabesity

Diabesity, the concurrent epidemic of obesity and type 2 diabetes mellitus (T2DM), requires a multifaceted treatment approach to address its complex pathophysiology. Current strategies focus on three primary domains: pharmacological therapies, surgical interventions, and lifestyle modifications. Recent advancements have introduced innovative technologies and precision medicine approaches that enhance management outcomes.

1. Pharmacological Therapies

Pharmacological advancements have significantly improved the management of diabesity. Key drug classes include:

GLP-1 Receptor Agonists

Glucagon-like peptide-1 (GLP-1) receptor agonists, such as semaglutide and liraglutide, are among the most effective pharmacological options. These drugs enhance insulin secretion, delay gastric emptying, and promote satiety, resulting in both

glycemic control and significant weight loss. Clinical trials report an average weight loss of 10-15% and HbA1c reduction of 1-2%.[10] Semaglutide, approved for chronic weight management, has demonstrated weight reductions exceeding 15% in many patients, making it a cornerstone therapy for diabesity.[11]

SGLT-2 Inhibitors

Sodium-glucose co-transporter-2 (SGLT-2) inhibitors, such as empagliflozin and dapagliflozin, lower blood glucose by increasing urinary glucose excretion. These drugs also provide cardiovascular and renal benefits, reducing hospitalization for heart failure and slowing the progression of chronic kidney.[12, 13] Their weight-reducing properties complement their glycemic effects, making them valuable in diabesity management.

Dual and Triple-Action Drugs

Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist, has shown superior outcomes compared to monotherapies. Studies indicate a mean weight loss of over 20% and significant improvements in insulin sensitivity and glycemic control.[14] The development of triple-agonist therapies targeting GLP-1, GIP, and glucagon pathways is underway, promising even greater efficacy in treating diabesity.

2. Surgical Interventions

Bariatric surgery remains the most effective treatment for severe obesity and associated metabolic disorders, including T2DM:

Gastric Bypass and Sleeve Gastrectomy

These procedures result in substantial and sustained weight loss, with patients typically losing 20-35% of their baseline weight. Long-term studies indicate remission of diabetes in up to 60% of cases, along with reductions in cardiovascular risk factors.[15] Gastric bypass surgery, in particular, enhances insulin sensitivity and reduces hepatic glucose production, providing durable metabolic improvements.[10]

Metabolic Surgery for T2DM

Bariatric procedures are increasingly recognized as metabolic surgeries due to their profound effects on glucose homeostasis. Guidelines now recommend surgery for patients with BMI ≥35 kg/m² and poorly controlled diabetes despite optimal medical therapy.[1]

3. Lifestyle Modifications

Behavioral interventions remain a cornerstone of diabesity management, particularly for prevention and early-stage disease:

Dietary Interventions

Caloric restriction and macronutrient-focused diets, such as low-carbohydrate and Mediterranean diets, improve both weight and glycemic control.[16] High-protein and low-glycemic index diets have shown efficacy in enhancing satiety and stabilizing blood sugar levels.[17]

Physical Activity

Regular exercise improves insulin sensitivity, facilitates weight loss, and reduces cardiovascular risk. Aerobic exercise, resistance training, and combined regimens are particularly effective in managing diabesity.[18, 19]

Behavioral Support

Structured lifestyle programs, such as the Diabetes Prevention Program (DPP), emphasize goal-setting, self-monitoring, and motivational strategies to sustain long-term behavioral changes.[20-22]

4. Emerging Technologies and Precision Medicine

Artificial Intelligence (AI) and Wearables

AI-powered tools analyze patient data to optimize treatment plans, while wearable devices like continuous glucose monitors and fitness trackers improve adherence to lifestyle interventions. These technologies offer real-time feedback and personalized recommendations, enhancing patient engagement and outcomes.[7]

Microbiome-Targeted Therapies

The gut microbiota plays a pivotal role in metabolic health. Dysbiosis has been linked to insulin resistance and obesity. Probiotics, prebiotics, and dietary interventions aimed at modulating gut flora are being investigated for their potential to improve diabesity outcomes.[8-9]

Gene Therapy and Stem Cell Research

Advances in genetic and stem cell research hold promise for reversing diabetes and its complications. Islet cell transplantation and regenerative therapies are being explored as long-term solutions.[23]

Challenges and Future Directions

While advancements in pharmacological and surgical interventions have transformed diabesity management, challenges remain. High costs, limited accessibility, and disparities in healthcare infrastructure hinder the widespread adoption of these strategies, particularly in low- and middle-income countries (LMICs). Future research should focus on developing cost-effective therapies, understanding regional variations in diabesity, and integrating innovative technologies into routine care.

Gaps in Current Literature

Despite these advancements, gaps remain in understanding the long-term efficacy and safety of emerging therapies. Limited data exist on the region-specific factors influencing diabesity prevalence and management, particularly in culturally diverse regions like Southeast Asia. Additionally, the high cost of advanced treatments poses challenges to their widespread adoption.

Methodology

This review adopts a systematic and narrative approach to synthesize recent advancements in the understanding and treatment of diabesity. The methodology followed includes a structured process of data collection, selection, and analysis to provide a comprehensive perspective on the topic.

Data Sources and Search Strategy

Primary data were collected from peer-reviewed journals, clinical trials, and meta-analyses available in databases such as PubMed, Scopus, and Cochrane Library. The search was conducted using keywords including "diabesity," "type 2 diabetes mellitus and obesity," "GLP-1 receptor agonists," "SGLT-2 inhibitors," "bariatric surgery," "microbiome therapies," and "artificial intelligence in diabesity management." Boolean operators (AND/OR) were used to refine searches, ensuring the inclusion of relevant literature. Articles published between 2013 and 2023 were prioritized to capture the most recent advancements.

Inclusion Criteria

Articles published in English.
Studies focusing on the relationship between obesity and T2DM.
Research discussing recent pharmacological, surgical, and technological advancements.
Population studies addressing the prevalence and management of diabesity in specific regions, particularly Southeast Asia.

Exclusion Criteria

Non-peer-reviewed articles or opinion pieces.
Studies with small sample sizes or weak methodological designs.
Research focusing solely on obesity or diabetes without addressing their interrelation.

Data Extraction and Synthesis

Data extraction was performed systematically, focusing on study objectives, methodology, findings, and limitations. Extracted data were organized into thematic categories, including pharmacological advancements, surgical interventions, and emerging technologies. Relevant data were then synthesized to highlight trends, gaps, and the clinical relevance of findings.

Analytical Approach

A qualitative analysis was conducted to interpret the findings of included studies. Comparative analysis methods were applied to evaluate the efficacy of pharmacological therapies such as GLP-1 receptor agonists and SGLT-2 inhibitors. The impact of bariatric surgery on long-term metabolic outcomes was assessed through meta-analyses. Emerging technologies, including artificial intelligence and microbiome-targeted therapies, were critically reviewed for their potential in personalized diabesity management.

Limitations of the Methodology

While this review provides a broad synthesis of current research, certain limitations must be acknowledged:
The exclusion of non-English studies may result in the omission of relevant findings from non-English-speaking regions. A reliance on secondary data sources limits the ability to conduct direct experimental validation.

Regional disparities in study representation may affect the generalizability of findings, particularly in under-researched areas like rural Southeast Asia.

Conclusion

Summary of Main Findings and Significance

This review highlights the critical interplay between obesity and type 2 diabetes mellitus (T2DM), emphasizing the global health burden of diabesity. Key findings include the transformative potential of pharmacological advancements such as GLP-1 receptor agonists and SGLT-2 inhibitors, which have demonstrated significant efficacy in improving weight loss, glycemic control, and overall metabolic health. Bariatric surgery has been identified as a cornerstone treatment for severe cases, providing durable improvements in metabolic outcomes and reduced mortality risks. Additionally, emerging technologies such as artificial intelligence, wearable devices, and microbiome-targeted therapies offer promising avenues for personalized and preventive care. These advancements collectively underscore the importance of integrated and multidisciplinary approaches to managing diabesity.

Restating the Research Question and Hypothesis

The primary research question of this review was whether recent advancements in diabesity treatment can effectively address the dual burden of obesity and T2DM. The findings support the hypothesis that innovative pharmacological therapies, surgical interventions, and technological innovations significantly enhance clinical outcomes and offer viable solutions for managing diabesity. However, challenges related to accessibility, cost, and long-term sustainability remain.

Practical Implications and Applications

The implications of this research are profound, both clinically and at a public health level.

Clinical Applications

The integration of advanced pharmacological treatments and surgical options provides healthcare professionals with robust tools to address severe cases of diabesity. Emerging technologies enable personalized interventions, enhancing treatment adherence and long-term efficacy.

Public Health Strategies

Policymakers must focus on prevention through community-based programs, lifestyle interventions, and early screening initiatives. Addressing socioeconomic disparities is critical to ensure equitable access to advanced therapies, particularly in resource-constrained settings like Southeast Asia.

Future Directions

Collaborative efforts among healthcare providers, researchers, and policymakers are essential to combat the diabesity epidemic effectively. Prioritizing cost-effective and region-specific solutions will be key to mitigating its global impact. By leveraging the synergy of innovative treatments and preventive strategies, the growing burden of diabesity can be managed effectively, improving quality of life and reducing the associated healthcare costs globally.

Author Declaration or Disclosure Statement

The author acknowledges that this manuscript is derived from their previously published book, titled '[Diabetes and Obesity: A Comprehensive Guide to Health and Wellness Evidence-Based Approaches for Prevention and Management], ISBN-978-6208065980, with significant modifications, updates, and additional analysis to align with the academic standards and scope of this journal. The content has been synthesized and expanded to incorporate recent advancements and findings in the field of diabesity management.

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