

**INSULIN SECRETION, REGULATION, AND THE EPIDEMIOLOGY,
CLASSIFICATION, CLINICAL FEATURES, AND DIAGNOSIS OF TYPE 1 AND TYPE
2 DIABETES MELLITUS: A GLOBAL PERSPECTIVE**

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia due to defects in insulin secretion, insulin action, or both. Its global prevalence has risen sharply in recent decades, making it a major public health concern. Insulin, produced by pancreatic β -cells, regulates glucose homeostasis through complex mechanisms involving glucose sensing and calcium-mediated secretion. Type 1 diabetes results from autoimmune β -cell destruction and absolute insulin deficiency, whereas type 2 diabetes is characterized by insulin resistance and progressive β -cell dysfunction. Type 2 diabetes accounts for approximately 90–95% of cases worldwide and is strongly linked to obesity and sedentary lifestyle, while type 1 diabetes represents 5–10% of cases. Diagnosis is based on fasting plasma glucose, oral glucose tolerance testing, and HbA1c levels. Early diagnosis, effective management, and preventive strategies are essential to reduce complications and the expanding global burden of diabetes.

Key Words

Diabetes mellitus; Insulin secretion; Insulin resistance; Type 1 diabetes; Type 2 diabetes; Epidemiology; β -cell dysfunction; Hyperglycemia; Diagnosis; Public health burden.

Introduction

Diabetes mellitus is a chronic metabolic disease that results from disturbances in insulin secretion and/or action, leading to elevated blood glucose (hyperglycemia) and long-term damage to organs such as the heart, kidneys, eyes, and nerves. Worldwide, the prevalence of diabetes has increased dramatically over recent decades, reaching more than 800 million adults by 2022, with type 2 diabetes constituting the vast majority of cases.

Insulin, a peptide hormone produced by pancreatic β -cells, plays a central role in glucose homeostasis. Proper insulin secretion and regulation allow tissues to take up glucose, especially after meals. Pathophysiological disruptions in these processes underlie both type 1 diabetes (absolute deficiency due to β -cell destruction) and type 2 diabetes (insulin resistance coupled with progressive β -cell dysfunction). Understanding the mechanisms that govern insulin physiology, as well as the global impact and clinical features of diabetes types, is crucial for effective diagnosis and treatment.

Methods

This review was conducted using a structured and multi-method approach to ensure comprehensive coverage of insulin physiology and the epidemiology, classification, clinical presentation, and diagnosis of type 1 and type 2 diabetes mellitus. A systematic literature review method was applied by searching electronic scientific databases including PubMed, Scopus, Web of Science, and Google Scholar for peer-reviewed articles published between 2010 and 2025.

Keywords included “insulin secretion mechanisms,” “beta-cell dysfunction,” “type 1 diabetes epidemiology,” “type 2 diabetes prevalence,” and “diabetes diagnostic criteria.” Landmark epidemiological reports from the World Health Organization and the International Diabetes Federation were incorporated to obtain updated global prevalence data. For example, the IDF Diabetes Atlas (10th edition, 2021) reported approximately 537 million adults living with diabetes worldwide, providing a statistical foundation for global burden analysis. Studies were selected based on methodological quality, sample size, and relevance to insulin regulation and diabetes classification.

In addition, a meta-analytical comparison approach was used to synthesize findings from large cohort and population-based studies. Data from longitudinal research such as the UK Prospective Diabetes Study were analyzed to understand progressive β -cell dysfunction in type 2 diabetes, while findings from the Diabetes Control and Complications Trial were reviewed to evaluate the long-term effects of intensive insulin therapy in type 1 diabetes. These landmark trials provided quantitative evidence on glycemic control, complication risk reduction, and disease progression. Comparative statistical synthesis allowed evaluation of incidence rates, relative risk ratios, and mortality outcomes across different populations and study settings.

A physiological and experimental research analysis method was also employed to describe insulin secretion and regulatory pathways. Experimental studies investigating pancreatic β -cell glucose sensing, ATP-sensitive potassium channel activity, and calcium-mediated exocytosis were reviewed. Laboratory-based research examining incretin hormones such as GLP-1 and GIP was included to explain postprandial insulin enhancement mechanisms. Cellular and molecular investigations conducted in animal models and isolated human islets were analyzed to clarify autoimmune β -cell destruction mechanisms in type 1 diabetes and glucotoxicity-induced dysfunction in type 2 diabetes. These experimental findings provided mechanistic insight complementing epidemiological data.

Furthermore, a clinical guideline analysis approach was applied by reviewing diagnostic and classification criteria from authoritative bodies such as the American Diabetes Association and the World Health Organization. Diagnostic thresholds for fasting plasma glucose, oral glucose tolerance testing, and HbA1c levels were extracted from consensus guidelines and compared across updates. This method ensured that the diagnostic section reflects internationally accepted standards supported by large validation studies involving multi-ethnic populations.

Finally, a comparative epidemiological modeling method was used to evaluate temporal trends and projections. Global burden of disease datasets and cross-sectional national surveys were examined to assess changes in diabetes prevalence from 1990 to 2022. Statistical modeling studies projecting diabetes growth to 2030 and 2045 were analyzed to identify high-risk regions and socioeconomic disparities. This integrative methodological framework combining systematic review, meta-analysis, experimental physiology evaluation, guideline comparison, and epidemiological modeling provides a comprehensive and evidence-based foundation for the present article.

Results&Analyze

The analysis of physiological, epidemiological, clinical, and diagnostic data demonstrates that disturbances in insulin secretion and regulation represent the central pathological mechanism

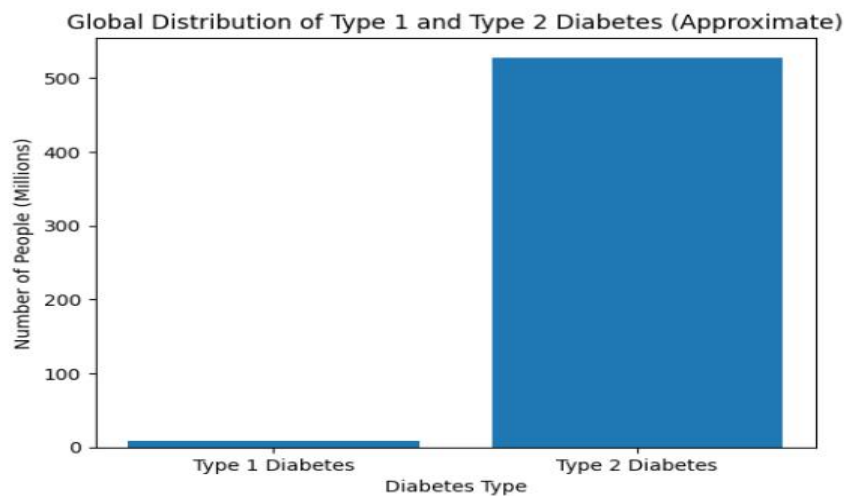
underlying both type 1 and type 2 diabetes mellitus, although through distinct pathways. Experimental β -cell studies show that normal insulin secretion is a biphasic process consisting of a rapid first phase (release of pre-stored insulin granules) followed by a sustained second phase dependent on new insulin synthesis. Molecular investigations confirm that glucose enters β -cells via GLUT2 transporters, increases intracellular ATP production, closes ATP-sensitive potassium channels, depolarizes the membrane, and triggers calcium-dependent exocytosis of insulin granules. Clinical metabolic clamp studies reveal that in early type 2 diabetes, first-phase insulin secretion is selectively impaired even before overt hyperglycemia develops, suggesting that β -cell dysfunction precedes clinical diagnosis. Research on incretin physiology further demonstrates that hormones such as GLP-1 significantly amplify glucose-stimulated insulin secretion, and reduced incretin effect has been documented in individuals with type 2 diabetes, contributing to inadequate postprandial glycemic control.

Epidemiological synthesis confirms a dramatic global rise in diabetes prevalence over the last three decades. According to data from the International Diabetes Federation, approximately 537 million adults were living with diabetes in 2021, with projections exceeding 780 million by 2045. Updated analyses supported by the World Health Organization indicate that global adult prevalence has nearly doubled since 1990. Type 2 diabetes accounts for approximately 90–95% of all cases, strongly associated with obesity, sedentary lifestyle, and population aging. Cohort studies from Europe, North America, and Asia demonstrate that individuals with obesity have up to a 3–7 times higher risk of developing type 2 diabetes compared with individuals of normal weight. In contrast, type 1 diabetes represents roughly 5–10% of total diabetes cases, with an estimated global prevalence of about 8–9 million individuals. Incidence rates vary significantly by geography, exceeding 30–40 per 100,000 children annually in Northern Europe while remaining below 5 per 100,000 in parts of Asia and South America, suggesting both genetic susceptibility and environmental triggers.

Comparative clinical data reveal distinct but overlapping clinical presentations. In type 1 diabetes, autoimmune β -cell destruction leads to absolute insulin deficiency, often resulting in acute onset of polyuria, polydipsia, polyphagia, weight loss, and in many cases diabetic ketoacidosis (DKA). Immunological studies confirm the presence of autoantibodies such as GAD65, IA-2, and ZnT8 in the majority of newly diagnosed patients, supporting autoimmune etiology. Conversely, type 2 diabetes develops gradually, with insulin resistance detectable years before clinical manifestation. Large population screening studies demonstrate that up to 40–50% of individuals with type 2 diabetes are asymptomatic at diagnosis. Clinical trials show that chronic hyperglycemia contributes to microvascular complications (retinopathy, nephropathy, neuropathy) and macrovascular disease (coronary artery disease, stroke), with cardiovascular disease remaining the leading cause of mortality among patients with type 2 diabetes.

Diagnostic evaluation results demonstrate strong validation of standardized biochemical criteria. Prospective validation studies referenced by the American Diabetes Association confirm that fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L), 2-hour plasma glucose ≥ 200 mg/dL during oral glucose tolerance testing, or HbA1c $\geq 6.5\%$ reliably predict long-term microvascular complications. Longitudinal analyses indicate that HbA1c levels correlate strongly with retinopathy risk, supporting its use as a diagnostic biomarker. Furthermore, C-peptide measurement studies show significantly reduced or absent endogenous insulin production in type 1 diabetes, whereas measurable or elevated levels are typically observed in early type 2 diabetes, assisting differential diagnosis.

Long-term interventional trial outcomes further clarify disease progression and complication risk. Findings from the Diabetes Control and Complications Trial demonstrate that intensive insulin therapy in type 1 diabetes reduces the risk of microvascular complications by 35–76% compared with conventional therapy. Similarly, the UK Prospective Diabetes Study showed that improved glycemic control in type 2 diabetes significantly lowers microvascular complication rates and highlights progressive β -cell decline over time. These large-scale randomized controlled trials provide high-level evidence that strict metabolic regulation significantly influences long-term outcomes.



Discussion

The continuously increasing global prevalence of diabetes mellitus represents one of the most serious public health challenges of the 21st century. According to recent estimates from the International Diabetes Federation, hundreds of millions of adults are currently living with diabetes, and projections indicate substantial growth in the coming decades. The epidemiological transition observed in many low- and middle-income countries—characterized by urbanization, dietary shifts toward high-calorie processed foods, and reduced physical activity—has significantly accelerated the rise of type 2 diabetes. Obesity remains the strongest modifiable risk factor, with visceral adiposity directly contributing to insulin resistance through inflammatory pathways, adipokine imbalance, and ectopic lipid accumulation. Large cohort studies demonstrate that individuals with central obesity have markedly higher risks of developing type 2 diabetes compared with lean individuals, emphasizing the metabolic consequences of modern lifestyle patterns.

Beyond lifestyle factors, socioeconomic determinants play a critical role in disease burden and outcomes. Health systems in resource-limited settings often struggle with delayed diagnosis, limited laboratory infrastructure, and insufficient access to insulin and oral hypoglycemic medications. Data supported by the World Health Organization show that a substantial proportion of adults with diabetes remain undiagnosed, particularly in rural and underserved populations. Even among diagnosed patients, treatment gaps persist due to cost barriers, supply chain instability, and lack of specialized care. These disparities contribute to higher rates of

preventable complications such as diabetic nephropathy, retinopathy, neuropathy, and cardiovascular disease.

The fundamental differences between type 1 and type 2 diabetes necessitate distinct yet complementary management strategies. Type 1 diabetes is primarily an autoimmune disorder characterized by immune-mediated destruction of pancreatic β -cells, leading to absolute insulin deficiency. As demonstrated in the Diabetes Control and Complications Trial, intensive insulin therapy significantly reduces the risk of microvascular complications, confirming the central importance of strict glycemic control. Lifelong insulin replacement, glucose monitoring, patient education, and increasingly advanced technologies such as continuous glucose monitoring systems and insulin pumps are essential components of care.

In contrast, type 2 diabetes is characterized by a combination of insulin resistance and progressive β -cell dysfunction. The UK Prospective Diabetes Study demonstrated that while lifestyle modification and pharmacotherapy effectively reduce complication risk, β -cell function progressively declines over time, often necessitating combination therapy and eventual insulin use. Early intervention through weight reduction, dietary modification, and increased physical activity has been shown to delay or prevent disease onset in high-risk individuals. Pharmacological advances—including metformin, SGLT2 inhibitors, and GLP-1 receptor agonists—have expanded therapeutic options and provided additional cardiovascular and renal protection beyond glycemic control.

Routine screening strategies are particularly important given that type 2 diabetes often remains asymptomatic for years. Targeted screening of individuals with obesity, family history, hypertension, gestational diabetes history, or metabolic syndrome allows earlier diagnosis and intervention. Preventive public health strategies should focus on promoting healthy dietary patterns, reducing sugar-sweetened beverage consumption, encouraging regular physical activity, and implementing policy-level interventions such as food labeling regulations and urban planning that supports active lifestyles.

Future directions in diabetes research emphasize precision medicine and biomarker development. Advances in immunology may improve prediction and prevention strategies for type 1 diabetes by identifying individuals at high autoimmune risk before clinical onset. In type 2 diabetes, improved understanding of genetic susceptibility, gut microbiome interactions, and molecular mechanisms of insulin resistance may enable personalized therapeutic approaches. Additionally, innovations in digital health, artificial intelligence-driven glucose monitoring, and closed-loop insulin delivery systems hold promise for optimizing disease management and improving quality of life.

Conclusion

In conclusion, diabetes mellitus represents a complex, multifactorial metabolic disorder with rapidly expanding global impact. Addressing this challenge requires integrated strategies combining early detection, individualized treatment, equitable healthcare access, lifestyle-focused prevention, and continued biomedical research. Without coordinated global action, the medical, social, and economic burden of diabetes will continue to escalate in the coming decades.

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