DOI: 10.21088/ip.2347.1506.13225.2

International Physiology
Volume 13 Number 2 July - December 2025

REVIEW ARTICLE

Global Epidemiology of Diabetes: The Role of Urbanization, Obesity, and Genetics

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HOW TO CITE THIS ARTICLE:

Amitava Khan. Global Epidemiology of Diabetes: The Role of Urbanization, Obesity, and Genetics. Int.Phy. 2025; 13(2): 69–81.

ABSTRACT

Diabetes mellitus (DM), particularly Type 2 Diabetes Mellitus (T2DM), has emerged as one of the most significant global public health challenges of the 21st century. As of 2021, an estimated 537 million adults worldwide are living with diabetes, and this number is projected to rise to 643 million by 2030 and 783 million by 2045, according to the International Diabetes Federation (IDF). The rapid urbanization of developing nations, increasing prevalence of obesity, and the complex interplay of genetic predisposition has contributed immensely to this escalating burden. Urban lifestyles, characterized by sedentary behavior, dietary transitions, and environmental stressors, play a pivotal role in diabetes onset. Obesity, especially central adiposity, has been identified as the strongest modifiable risk factor for T2DM. Furthermore, genetic susceptibility, influenced by ethnicity and family history, modulates individual risk and may explain population differences in prevalence and severity. This review aims to scrutinize the multifactorial nature of the diabetes epidemic, focusing on the intersection of urbanization, obesity, and genetic factors, while providing a comprehensive overview of the current epidemiological landscape, emerging trends, and global disparities in disease burden.

KEYWORDS

• Diabetes Mellitus • Urbanization • Obesity • Genetic Factors

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➢ **Received:** 09-07-2025 ➢ **Accepted:** 15-09-2025

INTRODUCTION

Diabetes mellitus (DM) is a complex, chronic metabolic disorder primarily characterized by persistent hyperglycemia elevated levels of glucose in the blood resulting from impairments in insulin production by the pancreas, defects in insulin action at the cellular level, or a combination of both. Insulin, a hormone produced by the β-cells of the pancreatic islets, plays a vital role in glucose metabolism by facilitating the uptake of glucose into cells for energy production and storage. When insulin function is compromised, either due to inadequate secretion or cellular resistance, glucose accumulates in the bloodstream, leading to a range of acute and chronic complications.

The implications of uncontrolled diabetes are profound and multifaceted, affecting nearly every organ system in the body. Individuals with diabetes face an elevated risk of developing a host of serious health conditions, including **cardiovascular diseases** (such as heart attacks and strokes), **nephropathy** leading to kidney failure, **retinopathy** which may result in blindness, **neuropathy**, and **peripheral vascular disease**, which significantly increases the risk of non-traumatic **lower-limb amputations**. These complications not only reduce the quality of life but also contribute to increased mortality among diabetic populations.

From a public health standpoint, the global rise in the prevalence of diabetes has emerged as a critical concern. According to the **International Diabetes Federation (IDF)**, as of 2021, over **537 million adults** worldwide are living with diabetes, a number projected to reach **643 million by 2030** and **783 million by 2045**, if current trends continue.[1] Notably, the burden of the disease is not evenly distributed across the globe. **Low-and middle-income countries (LMICs)** now account for nearly **80% of the global diabetes burden**, reflecting a dramatic epidemiological shift. In these countries, the healthcare systems are often under-resourced, and populations may have limited access to preventive, diagnostic, and therapeutic services, further exacerbating the impact of the disease.

Historically, diabetes was often labeled a "**disease of affluence**," primarily affecting individuals in high-income countries who had access to calorie-rich diets and sedentary lifestyles. However, this perspective has shifted significantly over the past few decades. Today, diabetes has permeated all **socioeconomic strata**, including the poorest and most vulnerable segments of society. This transition has been fueled by several interrelated global phenomena, including **accelerated urbanization**, the **globalization of food systems**, **migration from rural to urban areas**, and the widespread **adoption of sedentary behaviors** and **nutrient-poor, energy-dense diets**.

This review seeks to explore in detail the **three key drivers** that are propelling the worldwide diabetes epidemic:

1. **Urbanization**, which influences environmental and behavioral factors such as physical inactivity, access to processed foods, and psychosocial stress.
2. **Obesity**, a well-established modifiable risk factor for insulin resistance and type 2 diabetes, and
3. **Genetics**, which interacts with environmental exposures to shape individual susceptibility to the disease.

By examining the intricate interplay among these factors, this article aims to provide a comprehensive understanding of the underlying causes of the global diabetes crisis and offer insights into potential avenues for prevention and control.

Table 1: Global Epidemiology of Diabetes

Section	Key Points	Supporting Data/References
Global Epidemiology	Current Prevalence: 10.5% global adult prevalence in 2021; projected to rise to 783 million by 2045.	IDF Diabetes Atlas (2021)
	Regional Variations: Highest growth in SE Asia, Western Pacific, and Africa. India and China have >180 million combined cases. African prevalence to rise 134% by 2045.	IDF (2021), Anjana *et al.* (2017)
	Age & Gender: Rising T2DM among youth due to childhood obesity. Men develop diabetes at lower BMI than women due to visceral fat.	Mayer Davis *et al.* (2017), Huxley *et al.* (2008)

table cont....

Urbanization & Diabetes	Lifestyle Shifts: Urbanization → sedentary lifestyle, processed food, stress, air pollution → insulin resistance.	Popkin (1999), Drewnowski & Popkin (1997), Brook *et al.* (2010)
	Urban-Rural Disparities: Urban diabetes prevalence higher than rural (e.g., 11.2% vs. 5.2% in India). Rural rates rising due to urbanized behavior.	Anjana *et al*. (2017)
	Migration & Acculturation: Migrants adopt urban habits and face increased diabetes risk (e.g., South Asians in the UK, Latinos in the US).	Misra & Ganda (2007)
Obesity and T2DM	Pathophysiology: Visceral fat → free fatty acids, inflammation (TNF-α, IL-6), adipokine imbalance (↓adiponectin, ↑leptin/resistin) → insulin resistance.	Hotamisligil (2006)
	Epidemiological Link: 80–85% of T2DM patients are obese; risk ↑ 12% per 1 kg/m² BMI increase. Global obesity tripled since 1975.	WHO (2021), Colditz *et al.* (1990), CDC (2020)
	Global Trends: US, MENA region have highest obesity-diabetes rates. Asia shows T2DM at lower BMIs → “thin-fat” phenotype.	Yajnik (2014), CDC (2020), Ng et al. (2014)
	Childhood Obesity: >340 million children obese; early-onset T2DM increasing, progressing faster, with worse complications.	WHO (2016)
Genetics and Diabetes	Family History & Heritability: Risk ↑ with one diabetic parent; up to 70% risk with both. Shared genetics and lifestyle.	Meigs *et al.* (2000)
	Ethnic Susceptibility: South Asians → high visceral fat at low BMI. Pima Indians → highest prevalence. African-Americans → higher insulin secretion.	Knowler *et al.* (1978)
	Risk Genes & GWAS: >400 variants identified (e.g., TCF7L2, FTO, PPARG). Gene-environment interaction key to expression.	Mahajan *et al.* (2018), Pearson (2019)
	Epigenetics & Intrauterine: Fetal programming due to maternal malnutrition/obesity → future risk. Transgenerational effects.	Gluckman & Hanson (2008)
Interplay of Drivers	Thrifty Gene Hypothesis: Genes aiding fat storage in famine times now contribute to diabetes in modern high-calorie environments.	Neel (1962)
	Urban-Genetic Synergy: Urbanization activates latent genetic risks. E.g., South Asians in UK.	Hu (2011), Misra & Ganda (2007)
	Obesity Amplifies Genetic Risk: Obese individuals with TCF7L2 variants have higher T2DM risk than lean carriers.	Florez (2017)
Public Health Implications	Prevention: Urban planning, sugar taxes, food labeling, early screening in high-risk groups.	WHO, IDF, Popkin (1999)
	Obesity Management: School programs, community support, GLP-1 agonists, bariatric surgery.	WHO, Colditz *et al.* (1990)
	Precision Medicine: Genetics to guide personalized therapy. Equity, affordability must be addressed.	Pearson (2019), Florez (2017)

1. Global Epidemiological Trends

1. Current Prevalence and Projections

The International Diabetes Federation (IDF) 2021 Atlas reports a global diabetes prevalence of 10.5% among adults aged 20–79 years.[2] The number of adults with diabetes has risen by over 250% since 1980, from approximately 108 million to over 537 million.[3] The disease is projected to affect 783 million by 2045 if current trends continue, with the majority of new cases expected in LMICs.[4]

2. Regional Variation

The **prevalence of diabetes** varies widely across different regions of the world, influenced by a combination of demographic, economic, and lifestyle-related factors. In the **South-East Asia and Western Pacific** regions, the burden of diabetes is growing at an alarming rate, largely fueled by rapid urbanization, economic development, and the associated lifestyle transitions. These regions are undergoing significant demographic shifts, with large populations migrating from rural to urban areas, leading to reduced physical activity and increased consumption of processed and calorie-dense foods. Notably, **India and China**, the two most populous nations globally, are at the epicenter of this trend. Together, they currently account for over **180 million cases of diabetes**, making them critical focal points in the global diabetes landscape.[5] The sheer scale of these populations means that even modest increases in prevalence translate into tens of millions of new cases, posing immense challenges to public health systems that are already strained.

In contrast, **Africa**, while currently experiencing a lower overall prevalence of diabetes estimated at around **4.5%** is projected to undergo the most dramatic relative increase in the coming decades. The **International Diabetes Federation (IDF)** predicts that the prevalence in Africa will rise by an astonishing **134% by the year 2045**, making it the region with the **highest anticipated growth rate.**[6] Several factors contribute to this projected surge, including ongoing urbanization, economic development, dietary changes, and a lack of widespread awareness and screening programs. Compounding these challenges, many African nations face significant limitations in healthcare infrastructure, access to medication, and chronic disease management resources, which may hinder early diagnosis and effective intervention. The anticipated rise in diabetes cases across the continent could therefore place additional burdens on already overextended healthcare systems and deepen health inequities.

In the more economically developed regions of **North America and Europe**, diabetes prevalence is already relatively high, with current estimates exceeding **10%** of the adult population. This high burden is closely linked to **sedentary lifestyles**, **high rates of obesity**, and **aging populations**, all of which are well-established risk factors for type 2 diabetes. In these regions, lifestyle-related behaviors such as physical inactivity, high consumption of saturated fats and refined sugars, and chronic stress contribute significantly to the disease burden. Additionally, the demographic trend of aging populations increases vulnerability to chronic diseases, including diabetes. While these regions often have more robust healthcare systems and better access to treatment and education, the high baseline prevalence and associated complications result in substantial healthcare costs and economic loss due to productivity declines and disability. The presence of a large aging diabetic population also places increased demand on long-term care services and highlights the urgency of implementing preventive strategies that target both younger and older age groups. Overall, while the burden of diabetes is truly global, the nature of its spread and the challenges associated with it are region-specific, shaped by a complex interplay of socioeconomic development, demographic trends, and public health infrastructure. Tailored strategies that reflect the unique realities of each region will be essential to effectively curb the growing global diabetes epidemic.

3. Age and Gender Distribution

While age has traditionally been recognized as a major risk factor for type 2 diabetes mellitus (T2DM), with prevalence typically increasing in individuals over the age of 45, recent epidemiological trends have revealed a concerning shift. A growing number of younger adults, and even adolescents, are being diagnosed with type 2 diabetes, particularly in rapidly urbanizing areas. This emerging pattern is strongly associated with increasing rates of childhood and adolescent obesity, driven by lifestyle factors such as reduced physical activity, excessive screen time, consumption of calorie-dense, nutrient-poor foods, and a decline in outdoor play and physical education.[7] Urban environments, with their abundance of fast food outlets, limited green spaces, and reliance on motorized transportation, have contributed to a more sedentary way of life for youth, further compounding the risk. The early onset of type 2 diabetes is particularly alarming, as it exposes individuals to the harmful effects of hyperglycemia over a longer period, significantly raising the risk of developing complications such as cardiovascular disease, nephropathy, and neuropathy at younger ages, and placing increased strain on healthcare systems.

In addition to age and lifestyle, biological sex differences also play a significant role in diabetes risk. Research indicates that men are more likely to develop T2DM at lower body mass indices (BMI) compared to women. This disparity is believed to stem from differences in fat distribution and metabolic sensitivity. Men tend to accumulate visceral fat—fat stored around internal organs in the abdominal cavity which is more metabolically active and strongly associated with insulin resistance and inflammation. On the other hand, women typically develop diabetes at higher levels of adiposity, partly because they accumulate more subcutaneous fat, which is considered less harmful metabolically. Additionally, hormonal factors, particularly levels of estrogen, play a protective role in premenopausal women by improving insulin sensitivity and modulating lipid profiles. However, this advantage diminishes after menopause, contributing to an increase in diabetes risk among older women.[8] These sex-specific differences have important implications for both prevention and treatment strategies, underscoring the need for tailored approaches that take into account gender, body composition, and hormonal status when assessing diabetes risk and implementing public health interventions.

2. Urbanization and Diabetes

Urbanization, defined as the demographic shift from rural to urban living, is a major driver of diabetes prevalence.

1. Urban Living and Lifestyle

Urbanization has emerged as a powerful force reshaping the global landscape, influencing not only the physical environment but also the health behaviors and disease profiles of populations. While **urban areas** often offer enhanced access to healthcare services, educational opportunities, and economic advancement, they also create environments that inadvertently promote **unhealthy lifestyle choices,** contributing significantly to the rising burden of **type 2 diabetes mellitus (T2DM).**

One of the most significant consequences of urbanization is the rise of **sedentary lifestyles**. In modern cities, economic activities are increasingly centered around **white-collar, desk-bound jobs**, and daily routines often involve **prolonged sitting**, whether in offices, schools, or during commutes. The widespread availability and reliance on **motorized transportation** including cars, buses, and trains has dramatically reduced opportunities for **incidental physical activity** such as walking or cycling. Urban planning in many developing regions often lacks pedestrian-friendly infrastructure, further discouraging active transport. This reduction in physical movement contributes to decreased energy expenditure, which over time leads to weight gain, insulin resistance, and ultimately, an increased risk for T2DM.[9] Furthermore, the limited time and resources for recreational physical activity in densely populated urban settings add another layer of complexity to maintaining an active lifestyle.

Urbanization also drives profound **dietary transformations**, often referred to as the **"nutrition transition."** Traditional diets rich in whole grains, legumes, fruits, and vegetables are increasingly being replaced by **energy-dense, ultra-processed foods** that are high in refined carbohydrates, trans fats, saturated fats, added sugars, and sodium. The proliferation of **fast food chains, supermarkets stocked with processed snacks**, and aggressive **marketing of sugary beverages**, particularly to children and adolescents, have made unhealthy foods not only easily accessible but often more affordable than healthier alternatives. This shift in dietary patterns has been strongly correlated with the rise in obesity and metabolic disorders in urban populations.[10] Additionally, the culture of convenience and time constraints associated with urban living further encourages dependence on pre-packaged and takeaway meals, many of which are nutrient-poor and high in glycemic load factors that accelerate metabolic dysfunction and increase diabetes risk.

Moreover, urban environments expose individuals to a variety of **environmental and psychosocial stressors** that can further exacerbate the risk of metabolic disease. High levels of air pollution, common in densely populated and industrialized urban centers, have been linked to **systemic inflammation** and **oxidative stress**, which play a role in insulin resistance and beta-cell dysfunction. Chronic exposure to pollutants such as particulate matter (PM2.5) and nitrogen dioxide (NO_2) has been associated with increased incidence of T2DM, independent of other risk factors[11] Beyond physical pollutants, urban dwellers often experience heightened levels of **psychological stress**, driven by socioeconomic pressures, job insecurity, overcrowding, and social isolation. This stress can activate the **hypothalamic-pituitary-adrenal (HPA) axis**, leading to elevated cortisol levels that negatively impact glucose metabolism. Compounding these issues, the scarcity of green spaces and safe recreational areas in many urban settings deprives residents of restorative environments that could otherwise buffer stress and promote physical activity. Taken together, these factors **reduced physical**

activity, unhealthy dietary patterns, and chronic exposure to stress and pollution form a syndemic environment in urban areas that fosters the development and progression of type 2 diabetes. While urbanization is often viewed as a marker of progress, its unintended health consequences underscore the urgent need for **urban health policies** that promote active lifestyles, ensure access to nutritious foods, reduce environmental hazards, and support mental well-being.

2. Urban–Rural Disparities

Studies have shown consistently higher diabetes prevalence in urban areas compared to rural ones. For example, in India, urban diabetes prevalence is estimated at 11.2%, while rural areas report around 5.2%.[12] This trend is replicated globally, although rural areas are beginning to catch up due to urbanization of behavior and environment.

3. Migration and Acculturation

Rural-to-urban migrants often experience a significant rise in diabetes risk within years of relocation. Similarly, international migrants to high-income countries such as South Asians in the UK or Latinos in the US show elevated diabetes risk due to both acculturation stress and mismatch between genetics and lifestyle.[13]

3. Obesity as a Principal Risk Factor

Obesity is the most significant modifiable risk factor for T2DM.

1. Pathophysiological Link

The relationship between **obesity** and **type 2 diabetes mellitus (T2DM)** is deeply rooted in complex pathophysiological mechanisms, particularly involving **visceral or abdominal adiposity**. Unlike subcutaneous fat, which is located beneath the skin, visceral fat surrounds internal organs and is metabolically active in a way that profoundly impacts glucose metabolism. The accumulation of visceral fat plays a central role in the development of **insulin resistance**, a hallmark feature of T2DM, by interfering with multiple physiological pathways.

One of the primary mechanisms through which visceral obesity contributes to insulin resistance is by increasing the levels of **free fatty acids (FFAs)** in the bloodstream. Adipocytes in visceral fat depots are highly lipolytic, meaning they break down stored fat at a higher rate, releasing FFAs into circulation. These FFAs are taken up by muscle and liver cells, where they **disrupt normal insulin signaling pathways**. In skeletal muscle, FFAs inhibit glucose uptake by interfering with insulin receptor substrate (IRS) phosphorylation, while in the liver, they promote gluconeogenesis and impair insulin-mediated suppression of glucose production. This **lipotoxic environment** decreases insulin sensitivity, creating a state where insulin is present but unable to exert its biological effects effectively.

In addition to elevated FFAs, **chronic low-grade inflammation** originating from expanded adipose tissue significantly contributes to insulin resistance. As adipocytes enlarge and become dysfunctional, they recruit and activate immune cells, particularly **macrophages**, which secrete pro-inflammatory cytokines such as **tumor necrosis factor-alpha (TNF-α)**, **interleukin-6 (IL-6)**, and **C-reactive protein (CRP)**. These inflammatory mediators interfere with insulin receptor signaling and promote oxidative stress within insulin-responsive tissues. The persistent activation of inflammatory pathways perpetuates a cycle of insulin resistance and further adipocyte dysfunction, forming a critical link between obesity and metabolic disease.

Another important dimension of this pathophysiological connection involves the **dysregulation of adipokines**, which are bioactive peptides secreted by adipose tissue that modulate metabolic processes. In obesity, the balance of adipokines is disrupted. For instance, levels of **adiponectin**, an insulin-sensitizing and anti-inflammatory adipokine, are typically reduced, while levels of **leptin** and **resistin** are elevated. Although leptin normally functions to regulate appetite and energy balance, in obese individuals, leptin resistance may develop, reducing its effectiveness and contributing to further weight gain. **Resistin**, which is increased in obesity, has been shown to impair glucose uptake and promote insulin resistance. The altered profile of these adipokines reflects a shift in adipose tissue from a metabolically beneficial to a **pro-diabetic state**, further linking obesity to the pathogenesis of T2DM.[14]

Therefore, **visceral obesity** is far more than a passive storage site for excess calories it acts as an **endocrine organ** that actively contributes to metabolic dysfunction. Through the release of FFAs, promotion of chronic inflammation, and disruption of adipokine signaling, abdominal fat creates an internal environment highly conducive to the development of insulin resistance and, ultimately, type 2 diabetes. Understanding these mechanisms is essential for designing effective strategies aimed at obesity prevention and management as a cornerstone of diabetes control.

2. Epidemiological Evidence

The global rise in **obesity** has emerged as one of the most critical public health challenges of the 21st century, and it is intimately linked to the surge in **type 2 diabetes mellitus (T2DM)**. According to the **World Health Organization (WHO)**, more than **1.9 billion adults** worldwide are currently classified as **overweight**, and of these, over **650 million individuals are obese** a staggering figure that has nearly tripled since 1975.[15] This epidemic of excess body weight is not confined to high-income countries; it has become increasingly prevalent in **low and middle-income countries (LMICs)**, especially in urban areas where dietary and lifestyle changes are most pronounced. The widespread adoption of **sedentary behaviors** and the increased availability of **calorie-dense, processed foods** have driven this dramatic rise in obesity rates across populations.

Obesity, particularly **central (abdominal) obesity**, is now recognized as the **strongest modifiable risk factor** for the development of T2DM. It is estimated that **80% to 85%** of individuals with type 2 diabetes are either overweight or obese, underscoring the profound influence of excess adiposity on metabolic dysfunction. Adipose tissue, particularly when accumulated viscerally, contributes to insulin resistance through multiple mechanisms, including chronic low-grade inflammation, lipid toxicity, and hormonal imbalances, all of which impair the body's ability to regulate glucose effectively.

The strength of the relationship between body weight and diabetes risk has been clearly demonstrated in large-scale epidemiological studies. Notably, findings from the **Nurses' Health Study**, a long-term prospective cohort study involving over 120,000 female nurses in the United States, provided compelling evidence linking **body mass index (BMI)** with diabetes incidence. The study found that for **each 1 kg/m² increase in BMI**, the risk of developing type 2 diabetes increased by approximately **12%**, even after adjusting for other lifestyle and demographic factors such as age, physical activity, and family history.[16] This linear relationship highlights how even modest increases in weight can substantially elevate an individual's risk of diabetes, emphasizing the critical need for preventive measures that address weight management across the lifespan.

Together, these findings reinforce the central role of **obesity prevention and treatment** in any comprehensive strategy to curb the global diabetes epidemic. Public health initiatives must prioritize efforts to promote healthy eating, encourage physical activity, and create supportive environments that make it easier for individuals to maintain a healthy weight. Without addressing the obesity crisis head-on, efforts to reverse the diabetes epidemic will remain limited in their impact.

3. Global Obesity-Diabetes Nexus

The burden of **obesity and type 2 diabetes mellitus (T2DM)** varies significantly across different global regions, reflecting a combination of cultural, genetic, environmental, and socioeconomic influences. In the **United States**, the obesity epidemic has reached alarming proportions, with more than **42% of adults classified as obese**, according to the Centers for Disease Control and Prevention (CDC). Closely aligned with this trend is the high prevalence of diabetes, affecting approximately **11.3% of the adult population.**[17] The obesogenic environment in the U.S. marked by a high availability of fast food, widespread sedentary behavior, and socioeconomic disparities contributes substantially to the rising incidence of T2DM. Moreover, the increasing prevalence of childhood obesity in the U.S. suggests that the burden of diabetes may shift even more toward younger age groups in the coming decades, raising concerns about long-term health outcomes and economic strain on healthcare systems.

In the **Middle East and North Africa (MENA)** region, the situation is similarly dire, if not more so. Countries such as **Saudi Arabia, Kuwait, Qatar, and the United Arab Emirates** report some of the **highest rates of obesity and diabetes globally.**[18] Rapid economic growth, urbanization, and lifestyle modernization in the region have led to decreased physical activity, increased consumption of energy-dense traditional and Westernized foods, and a cultural preference for car travel over walking. These changes, combined with genetic predisposition and limited public health infrastructure for prevention, have created a perfect storm for metabolic diseases. In many MENA countries, **over 30% of the adult population is obese**, and diabetes prevalence exceeds **15% in some age groups**, contributing to substantial morbidity and mortality. Furthermore, limited awareness, under diagnosis, and late presentation of diabetes complications exacerbate the regional health crisis, despite rising income levels.

The scenario in **Asia**, while distinct, is equally complex. Interestingly, many Asian populations, including those in **India, China, Japan, and Southeast Asia**, develop T2DM at significantly **lower body mass indices (BMIs)** compared to Western populations. This phenomenon has led researchers to describe the **"Asian phenotype"**, characterized by a tendency toward higher **visceral adiposity** and **ectopic fat deposition** even in individuals who appear lean by conventional BMI standards.[19] Despite having a BMI within what would be considered a "normal" range by Western definitions, many Asians accumulate fat around internal organs, particularly the liver and pancreas, which contributes to insulin resistance and early beta-cell dysfunction. This unique metabolic profile has significant public health implications, as traditional BMI cutoffs may fail to identify at-risk individuals in Asian populations. Consequently, several countries in Asia have adopted **lower BMI thresholds** for obesity and diabetes screening. The high diabetes burden in Asia, particularly in **India and China**, is further compounded by dietary transitions, declining physical activity, and limited access to healthcare in rural areas, underscoring the need for region-specific prevention and intervention strategies.

Together, these regional examples highlight the **global diversity** in how obesity and diabetes manifest, shaped by a complex interplay of genetic, cultural, and socioeconomic factors. A one-size-fits-all approach is unlikely to be effective; instead, **tailored public health strategies** that consider regional nuances, lifestyle behaviors, and metabolic risk profiles are crucial to combating the escalating diabetes epidemic worldwide.

4. Childhood Obesity

Childhood obesity has emerged as one of the most urgent and alarming public health issues of our time, with far-reaching implications for the future burden of chronic diseases, particularly **type 2 diabetes mellitus (T2DM)**. According to the **World Health Organization (WHO)**, more than **340 million children and adolescents aged 5–19 years** were classified as **overweight or obese** in 2016, and this number continues to rise rapidly across both high-income and low to middle-income countries.[20] This surge is largely attributed to a combination of factors including the proliferation of energy-dense, nutrient-poor foods; increased screen time and digital device use; reduced levels of physical activity in schools and neighborhoods; and broader sociocultural shifts that promote sedentary lifestyles. Alarmingly, children living in urbanized environments are particularly vulnerable, as they are more likely to be exposed to fast food advertising, have limited access to safe outdoor play areas, and live in households with busy caregivers who may rely on processed convenience foods.

The implications of childhood obesity extend far beyond weight gain alone. One of the most serious consequences is the **emergence of early-onset type 2 diabetes**, which was previously rare in children but is now increasingly being diagnosed in pediatric and adolescent populations. Unlike adult-onset T2DM, which typically progresses more gradually, **early-onset T2DM tends to follow a more aggressive clinical course**, characterized by **rapid beta-cell decline**, **greater insulin resistance**, and an earlier onset of **microvascular and macrovascular complications**, including nephropathy, retinopathy, and cardiovascular disease. Furthermore, managing diabetes in children and adolescents poses unique challenges. Hormonal fluctuations during puberty, lower adherence to medication regimens, psychosocial stress, and a lack of tailored pediatric diabetes care models often make **glycemic control more difficult** to achieve in this age group.

Early-onset T2DM also poses a significant **economic and societal burden**, as affected individuals are likely to live longer with the disease, increasing their cumulative risk for long-term complications and healthcare costs. Moreover, childhood obesity and its metabolic consequences often persist into adulthood, establishing a **lifelong trajectory of poor health**, reduced productivity, and diminished quality of life. The growing prevalence of childhood obesity underscores the urgent need for **preventive interventions**, including school-based nutrition and physical activity programs, public health campaigns targeting families and communities, and policy measures that regulate food marketing to children and improve access to healthy foods. Without decisive action, this pediatric health crisis threatens to undermine decades of progress in controlling chronic diseases and reducing premature mortality.

4. The Role of Genetics in Diabetes

While lifestyle factors are critical, genetics also play a major role in diabetes risk.

1. Heritability and Family History

Genetic predisposition plays a crucial role in the development of **type 2 diabetes mellitus (T2DM),** and a **positive family history** is one of the strongest known risk factors for the disease. Individuals with one diabetic parent face a markedly increased risk, but this risk rises dramatically when **both parents are affected**. Studies suggest that the **lifetime risk of developing T2DM in individuals with two diabetic parents can be as high as 70%**, indicating a strong **heritable component** to the disorder.[21] This familial clustering of diabetes is attributed to the inheritance of genes that influence **insulin secretion, insulin sensitivity**, and **glucose metabolism**. These genes may affect pancreatic β-cell function, insulin receptor activity, adipocyte regulation, and inflammatory pathways, all of which play a role in the development and progression of diabetes.

However, the influence of family history is not purely genetic. Families often share similar **environments, dietary habits,** and **lifestyle patterns**, which can amplify inherited susceptibility. For example, children raised in households with high-calorie diets, limited physical activity, and sedentary behaviors may adopt these habits, further increasing their risk of developing T2DM. This **gene-environment interaction** is especially important in the context of modern lifestyles, where environmental triggers such as poor diet, obesity, and physical inactivity are ubiquitous and may unmask underlying genetic vulnerabilities.

In recent years, advances in **genomic research** have identified a number of specific genetic loci associated with increased diabetes risk. These include variations in genes such as **TCF7L2, FTO, KCNJ11**, and **PPARG**, which are involved in various aspects of glucose homeostasis and insulin action. While the presence of these gene variants does not guarantee disease onset, it can **significantly elevate risk**, particularly when combined with adverse environmental factors. Importantly, individuals with a family history of diabetes are often diagnosed at a **younger age**, experience **more severe disease progression**, and have a **higher likelihood of complications**, emphasizing the need for early screening and targeted preventive strategies.

Understanding the role of **heritability and family history** in diabetes is essential for identifying high-risk individuals and implementing timely interventions. Lifestyle modification programs, particularly those that begin early in life, can significantly delay or prevent disease onset even in genetically predisposed individuals. Therefore, while genetics may load the gun, it is often **environment and behavior that pull the trigger** highlighting the importance of proactive health education and lifestyle support for individuals with a family history of diabetes.

2. Ethnic Differences

Ethnicity plays a significant role in determining susceptibility to **type 2 diabetes mellitus (T2DM)**, with clear differences in genetic predisposition, body composition, and metabolic response observed across populations. South Asians, including individuals from India, Pakistan, Bangladesh, Sri Lanka, and Nepal, exhibit a notably higher risk for insulin **resistance and T2DM**, even at **lower body mass indices (BMIs)** compared to Caucasian populations. This paradoxical risk is attributed to the so-called **"thin-fat phenotype,"** characterized by increased **visceral adiposity, hepatic fat**, and **low lean muscle mass**, despite having a normal or modest BMI. South Asians also exhibit higher postprandial glucose levels and earlier beta-cell dysfunction, making them highly vulnerable to diabetes at a younger age and with fewer visible signs of obesity.

In contrast, **African-Americans** typically demonstrate **higher insulin secretion** in response to glucose, a compensatory mechanism that initially protects against hyperglycemia. However, over time, this adaptive response appears to lead to **accelerated beta-cell exhaustion and dysfunction**, contributing to a disproportionately high burden of T2DM in this group. Moreover, African-Americans tend to have greater muscle mass and less visceral fat than other high-risk groups, suggesting that their diabetes risk is more strongly linked to **impaired insulin action at the cellular level** rather than fat distribution alone.

Among **Native American populations**, particularly the **Pima Indians of Arizona**, the prevalence of type 2 diabetes is among the highest recorded in the world. Studies have shown that up to **50% of Pima adults** over the age of 35 have diabetes, a staggering statistic that reflects the interplay of **strong genetic predisposition and environmental transitions**. Historically, the Pima maintained physically active lifestyles and consumed traditional diets, but over the past few decades, shifts toward Westernized diets rich in fats and sugars and reduced physical activity have triggered an explosive rise in obesity and diabetes. These ethnic disparities underscore the importance of **tailored prevention strategies** and screening protocols that consider cultural, genetic, and metabolic differences across populations.[22]

3. Genetic Studies and Risk Loci

The genetic basis of type 2 diabetes has been extensively studied through **genome-wide association studies (GWAS)**, which have now identified more than **400 genetic variants** that contribute to increased susceptibility to T2DM. These variants are located in genes that influence a wide array of metabolic pathways, **including insulin secretion, glucose regulation, adipogenesis, and inflammatory responses**. Among the most significant is the **TCF7L2 gene**, which has demonstrated the **strongest and most consistent association** with T2DM across multiple ethnic groups. Variants in TCF7L2 are believed to impair insulin secretion by affecting pancreatic beta-cell function and incretin signaling, making it a key target in diabetes genetics.

Another important gene is **FTO (fat mass and obesity-associated gene)**, which is primarily linked to obesity. Although FTO does not directly cause diabetes, its influence on body weight makes it an **indirect but important contributor** to diabetes risk. Individuals with risk variants in FTO tend to have higher caloric intake, increased fat mass, and a higher likelihood of obesity, thereby increasing their risk of insulin resistance and T2DM.

The **PPARG gene**, which encodes the peroxisome proliferator-activated receptor gamma, is also noteworthy. It plays a central role in **adipocyte differentiation, lipid metabolism**, and **insulin sensitivity**. Certain PPARG variants are associated with improved insulin action, and this gene is the pharmacological target of **thiazolidinediones**, a class of drugs used to improve insulin sensitivity in patients with T2DM.

Despite the identification of these and hundreds of other risk loci, it is important to note that the **effect size of individual genetic variants is typically modest**, explaining only a small fraction of overall disease risk. This has led to the growing recognition that **gene-environment interactions** the complex interplay between genetic makeup and external factors such as diet, activity levels, and stress are central to the development of diabetes. In other words, while a genetic predisposition may increase susceptibility, environmental and behavioral factors often determine whether the disease is ultimately expressed.[23]

4. Epigenetics and Intrauterine Environment

Beyond inherited DNA sequences, **epigenetic modifications** have emerged as a powerful mechanism influencing individual susceptibility to type 2 diabetes. **Epigenetics** refers to changes in **gene expression** that occur **without altering the underlying DNA sequence**, often through mechanisms such as **DNA methylation, histone modification, and non-coding RNA activity.** These changes can be **influenced by environmental exposures**, especially during critical periods of development such as **fetal life**, infancy, and early childhood.

The **intrauterine environment** is particularly important in shaping long-term metabolic health. For example, **poor maternal nutrition, gestational diabetes**, **maternal obesity**, and intrauterine growth restriction have all been linked to alterations in fetal gene expression that predispose the offspring to insulin resistance, obesity, and beta-cell dysfunction later in life. This phenomenon is often referred to as **"fetal programming"** or the **"Developmental Origins of Health and Disease" (DOHaD)** hypothesis. Studies have shown that infants exposed to hyperglycemia in utero as seen in mothers with poorly controlled gestational diabetes are more likely to develop obesity and type 2 diabetes in adolescence or adulthood.

Moreover, these **epigenetic changes can be transgenerational**, meaning that the metabolic consequences of poor maternal health can persist across multiple generations, even if the genetic code remains unchanged. For instance, a grandmother's nutritional status during pregnancy can affect not only her child but also her grandchild's metabolic risk profile. This underscores the importance of **maternal health** and **prenatal care** in diabetes prevention strategies.

In summary, the growing body of evidence from epigenetic and intrauterine studies highlights that **diabetes risk begins long before clinical symptoms appear**, and may even be shaped before birth. Addressing these early-life influences offers a valuable opportunity for **preventive interventions** that can alter disease trajectories at both individual and population levels.[24]

5. Interplay of Urbanization, Obesity, and Genetics

These three drivers urbanization, obesity, and genetics do not operate in isolation.

The global diabetes epidemic cannot be attributed to a single factor. Instead, it arises from the **complex interplay of urbanization, obesity, and genetics**, which together form a syndemic a set of synergistic epidemics that exacerbate each other. These three drivers do not operate in isolation. Rather, they intersect and amplify one another, creating a fertile ground for the development of **type 2 diabetes mellitus (T2DM)**, particularly in populations undergoing rapid socioeconomic and lifestyle transitions.

1. The Thrifty Gene Hypothesis

One of the earliest and most influential attempts to explain the genetic predisposition to diabetes in the context of modern lifestyles is the **Thrifty Gene Hypothesis**, proposed by geneticist **James Neel** in 1962.[25] According to this theory, certain human populations historically experienced repeated cycles of **feast and famine**, during which individuals with genes favoring **efficient energy storage** particularly in the form of fat had a **survival advantage**. These so called "**thrifty genes**" allowed individuals to store more calories during times of abundance to survive during subsequent food shortages. While these genetic traits may have conferred evolutionary benefits in ancient or pre-industrial societies, they have become **maladaptive** in modern environments characterized by **continuous food availability**, **sedentary behavior**, and **energy-dense diets**. The same genes that once protected against starvation now predispose individuals to **obesity, insulin resistance**, and **type 2 diabetes**, particularly in populations that have undergone rapid economic and nutritional transitions, such as Indigenous communities and some ethnic minorities.

2. Urban-Genetic Synergy

A particularly important concept in the modern context is that of **urban-genetic synergy**. Individuals who carry genetic risk factors for diabetes such as variants in **TCF7L2, FTO**, or PPARG may remain metabolically healthy in **traditional rural settings**, where diets are simpler, physical activity is higher, and energy balance is maintained. However, when these individuals **migrate to or are born into urban environments**, where processed foods are readily accessible and sedentary lifestyles are the norm, the **expression of their genetic predisposition is amplified**. In essence, urbanization acts as an environmental switch that **activates latent genetic risk**. For example, studies among South Asian migrant populations in Western countries have shown that their diabetes risk increases significantly after relocation, even if their body mass index (BMI) remains relatively low. This emphasizes the urgent need to consider both **genetic background and environmental context** when designing diabetes prevention and intervention programs.

3. Obesity Amplifies Genetic Risk

The interaction between **genetic susceptibility** and **obesity** is particularly critical. Research has shown that **obesity does not act independently** but rather **intensifies the effect of pre-existing genetic risk factors**. For instance, individuals who carry high-risk alleles of the **TCF7L2** gene one of the strongest genetic predictors of T2DM are significantly **more likely to develop diabetes if they are also obese**, compared to lean carriers of the same gene variant.[26] Obesity exacerbates insulin resistance, triggers chronic inflammation, and disrupts adipokine signaling, thereby **magnifying the pathogenic potential of**

genetic variants. This synergy underscores the importance of **weight management as a core strategy** for reducing diabetes risk, especially in genetically vulnerable populations. It also points to a future where **genetic screening** may help identify high-risk individuals who would benefit most from intensive lifestyle interventions.

6. Public Health Implications

Given the multifactorial origins of the diabetes epidemic, **comprehensive public health strategies** are essential. Interventions must address not only individual behaviors but also the broader **social, environmental, and policy-level determinants** of health. An integrated approach that combines urban design, education, regulation, and medical intervention can help curb the growing burden of T2DM.

1. Prevention Strategies

Prevention remains the most cost-effective and sustainable approach to reducing the burden of type 2 diabetes. **Urban planning** plays a critical role in shaping lifestyle behaviors. Cities should be designed to **encourage physical activity** by incorporating **walkable neighborhoods, safe cycling paths, accessible public transportation,** and **green spaces** that promote recreational activity. These environmental modifications can help reduce sedentary behaviors and promote active living. In parallel, **nutritional policies** can reshape dietary behaviors. Measures such as **taxing sugar-sweetened beverages**, implementing **front-of-pack food labeling**, and **regulating fast food advertising**, especially to children, have shown promise in shifting consumption patterns. Moreover, **early screening and education campaigns** targeted at **high-risk groups**, such as those with a family history or from high-prevalence ethnic communities, can facilitate **early detection** and **behavioral change** before the onset of disease.

2. Addressing Obesity

Addressing obesity is central to diabetes prevention. **School based interventions**, including improved nutrition education, healthier school meals, and daily physical education, can instill lifelong healthy habits in children. Community-based weight loss programs that provide peer support, behavioral counseling, and structured exercise can also help adults manage weight more effectively. For individuals with **severe obesity** or those at **very high risk, pharmacological therapies** such as GLP-1 receptor agonists (e.g., semaglutide) or **bariatric surgery** may be necessary. These interventions have been shown to not only reduce body weight but also improve glycemic control and in some cases, even **remit diabetes**. However, equitable access to these treatments remains a challenge, particularly in low-resource settings.

3. Precision Medicine and Genetics

The evolving field of **precision medicine** offers exciting possibilities for diabetes care by tailoring prevention and treatment strategies based on **individual genetic profiles**. By integrating genomic data with clinical and lifestyle information, it may be possible to identify **subgroups of patients** who are more likely to benefit from specific medications, dietary interventions, or behavioral therapies. For instance, certain genetic variants may predict better response to metformin, sulfonylureas, or lifestyle modification. Additionally, research into **pharmacogenomics** how genes affect drug metabolism and efficacy is advancing, though it remains in the early stages of implementation.[27] As this field matures, it may enable clinicians to offer **more personalized, effective, and efficient care**, especially for high-risk populations. However, challenges related to data privacy, affordability, and infrastructure must be addressed to ensure equitable adoption.

CONCLUSION

The global diabetes epidemic reflects a complex web of interrelated factors, primarily urbanization, obesity, and genetics. Addressing this crisis requires integrated, multidisciplinary efforts spanning public health policy, individual behavior change, and biomedical research. A nuanced understanding of the drivers of diabetes can help develop tailored interventions for different regions, populations, and risk profiles. The urgency is clear: without decisive action, diabetes will continue to surge, disproportionately affecting the most vulnerable communities worldwide.

Conflict of Interest: None

Funding: None

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