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DETRIMENTAL EFFECTS OF DIETARY SUGAR ON HUMAN HEALTH: A DECADE OF EVIDENCE FROM 2015 ONWARD

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ABSTRACT

Excessive dietary sugar intake has emerged as a major contributor to the global burden of non-communicable diseases over the past decade. While naturally occurring, sugars are present in whole foods, high consumption of added sugars, particularly from sugar-sweetened beverages and ultra-processed products, has been strongly associated with adverse metabolic and systemic effects. This review synthesizes evidence published between 2015 and 2025 on the detrimental impact of sugar on human health. Mechanistically, chronic high sugar intake promotes hyperglycemia, insulin resistance, hepatic de novo lipogenesis, uric acid production, oxidative stress, and formation of advanced glycation end products. These processes contribute to obesity, type 2 diabetes mellitus, non-alcoholic fatty liver disease, and cardiovascular disorders. Emerging data also suggest associations with cognitive impairment, renal dysfunction, gut microbiota dysbiosis, reproductive hormonal imbalance, and increased cancer risk, largely mediated through chronic inflammation and metabolic disruption. Although observational and interventional studies vary in design and quality, the overall body of evidence supports a consistent link between excessive added sugar consumption and multi-organ dysfunction. Public health strategies aimed at reducing added sugar intake may therefore play a critical role in preventing metabolic and chronic diseases.

Continued research is needed to clarify dose–response relationships and long-term outcomes across diverse populations.

KEYWORDS: Added sugar; Insulin resistance; Non-alcoholic fatty liver disease; Oxidative stress; Cardiovascular disease; Chronic inflammation.

INTRODUCTION

Dietary sugar has become one of the most pervasive components of the modern diet and a leading factor in the global rise of non-communicable diseases. Sugar is present not only in obvious sources such as sweets and sugary drinks but also in a wide range of processed foods.[1] While sugars naturally occur in fruits and dairy, the primary public health concern is added or free sugars, those included during food processing, preparation, or at the table.[2] The World Health Organization recommends that free sugars make up less than 10 percent of total daily energy intake, and ideally less than 5 percent for additional health benefits.[3] Despite these guidelines, many populations worldwide exceed these limits substantially.

Global sugar consumption, measured both in total volume and per capita intake, continues to rise. Projections from the Food and Agriculture Organization and the Organization for Economic Co-operation and Development indicate that global sugar demand will grow by more than one percent per year over the next decade, reaching nearly 200-202 million tons by the early 2030s.[4] In many regions, population growth and rising incomes support this increase, especially in South and Southeast Asia and parts of Africa where per capita sugar intake is currently lower but on the rise.[4]

Excessive sugar intake has a direct link to a range of adverse health outcomes. The global burden of obesity has reached epidemic proportions, driven in part by high-calorie, low-nutrient diets rich in added sugars.[5] Although the exact contribution of sugar to obesity varies by region and individual dietary patterns, the trend is clear: as sugar consumption increases, so do rates of overweight and obesity.[6] The rise in obesity contributes to a parallel rise in type 2 diabetes and cardiovascular diseases.[7] These diseases are among the leading causes of death worldwide, responsible for more than 40 million deaths annually, or roughly 65 percent of all mortality.[8]

A growing body of evidence quantifies the impact of sugar-sweetened beverages (SSBs) — one of the most concentrated sources of added sugars in many diets — on global health.[9] A

recent analysis across 184 countries estimated that in 2020, SSB consumption was responsible for approximately 2.2 million new cases of type 2 diabetes and 1.2 million new cases of cardiovascular disease, and these figures represent nearly 10 percent of all new diabetes cases and more than 3 percent of new cardiovascular cases worldwide.[10] In terms of disability and mortality, sugar-related diseases accounted for millions of disability-adjusted life years (DALYs) and hundreds of thousands of deaths, underlining the extensive human and economic costs tied to high sugar intake.[11]

Dental health is also profoundly affected by sugar consumption. Tooth decay remains one of the most common preventable conditions globally, affecting an estimated 2.5 billion people at some point in their lives.[12] Free sugars are the primary dietary risk factor for dental caries, and evidence suggests that limiting sugar intake can significantly reduce the prevalence of this condition throughout the life course.[13]

Across regions, patterns of consumption and disease burden vary. In high-income countries and Latin America, SSB consumption and its attributable disease burden are particularly high, while lower but increasing consumption in parts of Asia and Africa suggests an emerging public health challenge.[14] Many governments are responding with policy measures such as taxes on sugary drinks, advertising restrictions, and reformulation targets for processed foods — interventions that have shown promise in some settings.[15] Recent news shows that several countries, including China, are considering or implementing fiscal policies aimed at reducing sugar intake to curb obesity and related diseases.[16]

Despite some signs of slowed growth in sugar consumption in parts of the world, largely due to public health efforts and shifting consumer preferences, the overall global trend remains upward. Without intensified interventions and public awareness, the continued rise in added sugar intake will likely drive further increases in metabolic diseases and healthcare costs worldwide.

METHODOLOGY

This review was conducted to synthesize evidence published over the ten-year period from 2015 to 2025 regarding the detrimental effects of excessive sugar consumption on human health. Although structured as a narrative review, a systematic search strategy was applied to enhance methodological rigor and transparency.

Literature Search Strategy

A comprehensive literature search was conducted using multiple electronic databases, including PubMed, Scopus, Web of Science, Cochrane Library, ScienceDirect, and Google Scholar, to ensure broad coverage of biomedical, clinical, and public health research. The search was limited to studies published between January 2015 and December 2025 and restricted to articles available in English.

The following keywords and combinations were used: “added sugar”, “dietary sugar”, “fructose metabolism”, “glucose metabolism”, “insulin resistance”, “non-alcoholic fatty liver disease”, “cardiovascular disease”, “oxidative stress”, “inflammation”, “cancer risk”, and “metabolic syndrome” were applied to refine the search strategy.

1. Types and Metabolism of Sugar

Dietary sugars are primarily consumed as monosaccharides, such as glucose and fructose, or as disaccharides like sucrose, which is composed of one glucose and one fructose molecule. Although both glucose and fructose provide energy, their metabolic pathways and physiological consequences differ significantly. **Figure 1** illustrates the distinct metabolic fates of glucose and fructose following ingestion and their differential effects on energy homeostasis and disease pathogenesis.

1.1 Glucose Metabolism: Glycolysis and Insulin Regulation

Glucose is the principal energy substrate for most tissues. After ingestion, it is absorbed from the intestine into the bloodstream, raising plasma glucose levels. This increase stimulates pancreatic β-cells to release insulin.[17] Insulin facilitates glucose uptake into insulin-sensitive tissues such as skeletal muscle and adipose tissue through translocation of GLUT4 transporters to the cell membrane.[18]

Once inside the cell, glucose undergoes glycolysis, a cytoplasmic pathway that converts glucose into pyruvate while generating ATP and reducing equivalents (NADH) .[19] Pyruvate subsequently enters the mitochondria and is converted into acetyl-CoA, which enters the tricarboxylic acid cycle for further energy production.[20] In conditions of excess glucose availability, insulin promotes glycogenesis in the liver and muscle and stimulates lipogenesis when glycogen stores are saturated.[21,22]

Chronic high glucose intake leads to persistent hyperglycemia and hyperinsulinemia. Over time, this may cause insulin resistance, characterized by reduced responsiveness of peripheral tissues to insulin.[23] Compensatory hyperinsulinemia further disrupts metabolic homeostasis and contributes to obesity, type 2 diabetes mellitus, and cardiovascular complications.[24]

1.2 Fructose Metabolism in the Liver

Fructose metabolism differs fundamentally from glucose metabolism. Unlike glucose, fructose uptake is largely insulin-independent.[25] After absorption, fructose is transported to the liver, where it is phosphorylated by fructokinase to form fructose-1-phosphate. This pathway bypasses phosphofructokinase-1, the key regulatory step in glycolysis.[26]

Because of this bypass, fructose metabolism is less tightly regulated. Rapid hepatic fructose metabolism generates intermediates that drive de novo lipogenesis, leading to triglyceride synthesis and hepatic fat accumulation.[27] Excessive fructose intake has been associated with increased very-low-density lipoprotein (VLDL) production, hypertriglyceridemia, and non-alcoholic fatty liver disease.[28] Additionally, fructose metabolism increases uric acid production, which may contribute to oxidative stress, endothelial dysfunction, and hypertension.[29]

1.3 Role of Insulin and Glycemic Load

Insulin plays a central role in maintaining glucose homeostasis. It regulates carbohydrate, lipid, and protein metabolism by promoting anabolic processes and inhibiting catabolic pathways.[30] Diets high in rapidly absorbable carbohydrates with a high glycemic index or glycemic load cause sharp postprandial spikes in blood glucose and insulin.[31] Repeated exposure to such spikes contributes to β-cell stress and progressive insulin resistance.[32]

Glycemic load reflects both the quality (glycemic index) and quantity of carbohydrates consumed. High-glycemic-load diets have been linked to increased risk of metabolic syndrome, cardiovascular disease, and certain cancers.[33] In contrast, diets rich in complex carbohydrates and dietary fiber produce slower glucose absorption and more stable insulin responses.[34]

1.4 Formation of Advanced Glycation End Products (AGEs)

Persistent hyperglycemia promotes non-enzymatic glycation of proteins, lipids, and nucleic acids, leading to the formation of advanced glycation end products (AGEs).[35] This process

begins with the reaction between reducing sugars and amino groups of proteins, forming unstable Schiff bases and Amadori products, which undergo further rearrangements to become irreversible AGEs.[36]

AGE accumulation alters protein structure and function, cross-links extracellular matrix proteins, and impairs enzymatic activity.[37] Binding of AGEs to their receptor (RAGE) activates intracellular signaling pathways, including NF-κB, which increases the production of pro-inflammatory cytokines and reactive oxygen species.[38] These processes contribute to endothelial dysfunction, vascular stiffness, nephropathy, retinopathy, and other chronic complications associated with prolonged hyperglycemia.[39]

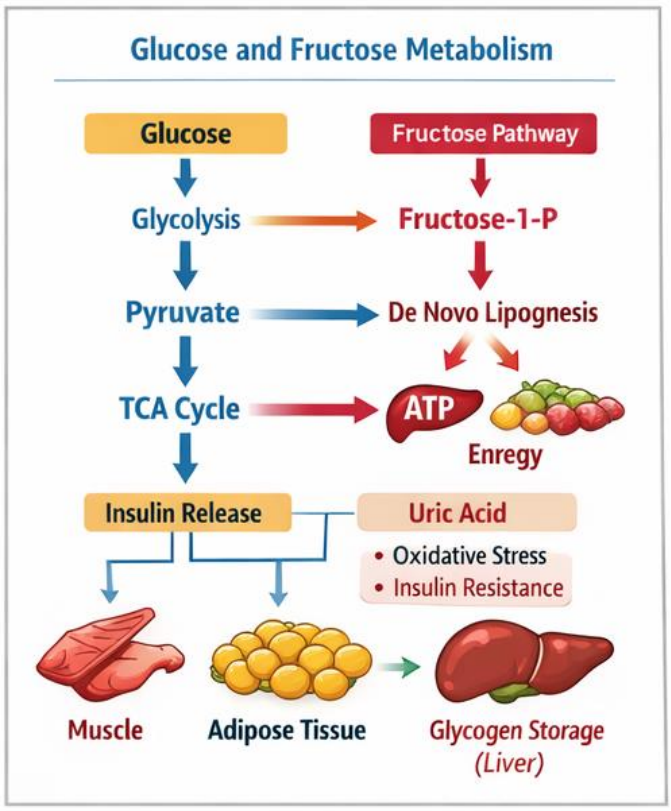

Figure 1: Comparative Metabolic Pathways of Dietary Glucose and Fructose.

2. Metabolic Disorders

Excessive sugar intake plays a central role in the development of metabolic disorders, particularly obesity and its related complications. The metabolic consequences of chronic high sugar consumption extend beyond simple caloric excess and involve complex hormonal, biochemical, and neuroregulatory mechanisms. **Table 1** summarizes the types of dietary

sugars, their primary metabolic pathways, the organ systems affected, key mechanistic pathways, and resultant health outcomes.

2.1 Obesity

Obesity arises from a sustained imbalance between energy intake and expenditure. High sugar consumption contributes significantly to caloric excess because added sugars provide energy without inducing proportional satiety.[40] Sugar-sweetened beverages are especially problematic, as liquid calories produce weaker satiety signals compared to solid foods, leading to incomplete compensatory reductions in subsequent food intake.[41] This promotes a positive energy balance and progressive weight gain.

Fructose, in particular, has distinct metabolic effects that favor adiposity. Unlike glucose, fructose metabolism in the liver bypasses phosphofructokinase-1, the major rate-limiting enzyme in glycolysis.[42] This bypass allows unregulated entry of fructose-derived intermediates into pathways that stimulate de novo lipogenesis.[43] As a result, excessive fructose intake enhances hepatic triglyceride synthesis and increases very-low-density lipoprotein secretion.[44] These triglycerides can accumulate in adipose tissue and ectopic sites, promoting visceral fat deposition, which is metabolically more harmful than subcutaneous fat.[45]

Chronic high sugar intake also influences hormonal regulators of appetite and energy balance. Leptin, a hormone secreted by adipocytes, signals satiety to the hypothalamus and helps regulate long-term energy homeostasis.[46] Persistent overconsumption of sugar, especially fructose, has been associated with leptin resistance.[47] In this state, circulating leptin levels may be elevated due to increased adiposity, but hypothalamic sensitivity to leptin is reduced.[48] Consequently, appetite suppression becomes impaired, and energy expenditure may decrease, perpetuating weight gain.[49]

In addition to leptin resistance, high sugar intake affects other appetite-regulating hormones. Fructose has been shown to produce a weaker stimulation of insulin and lower suppression of ghrelin compared to glucose.[50] Because insulin and leptin act as satiety signals in the central nervous system, reduced stimulation may result in increased hunger and higher subsequent caloric intake.[51] Alterations in dopamine signaling within the brain’s reward pathways may further enhance preference for sweet foods, reinforcing habitual overconsumption.[52]

Beyond adipose expansion, obesity induced by high sugar intake is often accompanied by chronic low-grade inflammation, adipocyte hypertrophy, and macrophage infiltration into adipose tissue.[53] These inflammatory processes contribute to systemic insulin resistance and increase the risk of progression to type 2 diabetes mellitus and cardiovascular disease.[54]

Overall, excessive sugar intake promotes obesity not only through increased caloric load but also through metabolic reprogramming, hormonal dysregulation, and central appetite signaling disturbances. Understanding these interconnected mechanisms is essential for clarifying how dietary sugars contribute to the global obesity epidemic and associated metabolic complications.

2.2 Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is one of the most significant metabolic consequences of chronic excessive sugar consumption.[55] It is characterized by persistent hyperglycemia resulting from a combination of insulin resistance and progressive pancreatic β-cell dysfunction.[56] While genetic predisposition plays a role, dietary patterns rich in added sugars and refined carbohydrates substantially increase disease risk.[57]

Frequent consumption of high-sugar foods and beverages leads to repeated postprandial spikes in blood glucose and insulin.[58] Over time, chronic hyperinsulinemia reduces insulin sensitivity in peripheral tissues such as skeletal muscle, liver, and adipose tissue.[59] In insulin-resistant states, glucose uptake by muscle declines, hepatic gluconeogenesis remains inappropriately elevated, and lipolysis in adipose tissue increases.[60] These disturbances collectively contribute to sustained hyperglycemia.

Fructose contributes to T2DM development through distinct hepatic mechanisms.[61] As discussed earlier, fructose metabolism bypasses key glycolytic regulatory steps and drives de novo lipogenesis.[62] The resulting accumulation of hepatic triglycerides promotes hepatic insulin resistance.[63] When the liver becomes insulin resistant, it fails to suppress glucose production adequately, further exacerbating fasting hyperglycemia.[64] Additionally, increased circulating triglycerides and free fatty acids impair insulin signaling in skeletal muscle, worsening systemic insulin resistance.[65]

Chronic exposure to elevated glucose levels also induces glucotoxicity, which directly damages pancreatic β-cells.[66] Persistent hyperglycemia increases oxidative stress within β-

cells, which are particularly vulnerable due to relatively low antioxidant defense capacity.[67] Excess reactive oxygen species impair insulin gene expression, reduce insulin secretion, and promote β-cell apoptosis.[68] Simultaneously, lipotoxicity from elevated free fatty acids further compromises β-cell function.[69] The combined effect of glucotoxicity and lipotoxicity accelerates β-cell exhaustion, marking the transition from compensated insulin resistance to overt diabetes.[70]

Another important mechanism involves the formation of advanced glycation end products (AGEs). Persistent hyperglycemia enhances non-enzymatic glycation of proteins, leading to AGE accumulation in pancreatic tissue and vascular structures.[71] Interaction of AGEs with their receptor (RAGE) activates inflammatory signaling pathways, including NF-κB, increasing pro-inflammatory cytokine production.[72] This chronic low-grade inflammation further disrupts insulin signaling and contributes to vascular complications associated with diabetes.[73]

Epidemiological studies consistently show a strong association between high intake of sugar-sweetened beverages and increased risk of T2DM, independent of body weight in some analyses.[74] This suggests that beyond its contribution to obesity, excessive sugar intake may exert direct diabetogenic effects. High glycemic load diets also increase β-cell demand, promoting earlier functional decline.

In summary, excessive sugar consumption contributes to the development of type 2 diabetes mellitus through multiple interconnected mechanisms, including systemic insulin resistance, hepatic fat accumulation, oxidative stress, inflammation, and progressive β-cell dysfunction. These pathophysiological changes underscore the critical importance of reducing added sugar intake in preventing diabetes and its long-term complications.

2.3 Metabolic Syndrome

Metabolic syndrome represents a cluster of interrelated metabolic abnormalities that significantly increase the risk of type 2 diabetes mellitus and cardiovascular disease.[75] It is typically defined by the presence of central obesity, hyperglycemia, hypertension, elevated triglycerides, and reduced high-density lipoprotein (HDL) cholesterol.[76] Excessive sugar intake contributes directly and indirectly to the development of this syndrome through multiple overlapping mechanisms.[77]

One of the primary drivers is visceral adiposity. High consumption of added sugars, particularly fructose, promotes hepatic de novo lipogenesis and increases circulating triglycerides.[78] These triglycerides are transported and deposited in abdominal adipose tissue, leading to central obesity, which is a core component of metabolic syndrome.[79] Visceral fat is metabolically active and releases free fatty acids, inflammatory cytokines such as TNF-α and IL-6, and adipokines that impair insulin signaling pathways.[80]

Insulin resistance is a central feature of metabolic syndrome and is strongly influenced by high sugar intake.[81] Chronic hyperglycemia and hyperinsulinemia reduce insulin receptor sensitivity in muscle and liver tissues.[82] As insulin becomes less effective at facilitating glucose uptake and suppressing hepatic glucose output, blood glucose levels rise.[83] At the same time, insulin resistance in adipose tissue enhances lipolysis, increasing circulating free fatty acids, which further aggravate hepatic and muscular insulin resistance.[84] This creates a self-perpetuating metabolic cycle.

Dyslipidemia is another key component. Fructose-driven lipogenesis elevates very-low-density lipoprotein (VLDL) production in the liver, increasing plasma triglyceride levels.[85] Elevated triglycerides often occur alongside reduced HDL cholesterol, a combination strongly associated with atherogenic risk.[86] Additionally, small dense low-density lipoprotein (LDL) particles, which are more prone to oxidation and arterial deposition, are frequently observed in individuals with high sugar intake and insulin resistance.[87]

Hypertension within metabolic syndrome may also be linked to excessive sugar consumption.[88] Fructose metabolism increases uric acid production, which can impair endothelial nitric oxide availability, reducing vasodilation.[89] Elevated uric acid levels have been associated with vascular stiffness, endothelial dysfunction, and activation of the renin-angiotensin system, all of which contribute to increased blood pressure.[90]

Chronic low-grade inflammation further integrates these metabolic abnormalities.[91] Enlarged adipocytes and infiltrating macrophages in visceral fat secrete pro-inflammatory mediators that activate intracellular signaling pathways such as NF-κB and JNK.[92] These pathways interfere with insulin receptor signaling and exacerbate systemic metabolic dysfunction.[93] Oxidative stress generated by hyperglycemia and lipid accumulation amplifies this inflammatory environment.[94]

Importantly, metabolic syndrome is not merely a collection of isolated risk factors but a pathophysiological state driven by interconnected metabolic disturbances. Diets high in added sugars accelerate these processes by promoting energy excess, hepatic lipid accumulation, insulin resistance, and inflammatory activation.[95] As a result, individuals with high sugar intake are at substantially greater risk of progressing to overt type 2 diabetes mellitus and cardiovascular disease.[96]

In summary, excessive sugar consumption contributes to the development and progression of metabolic syndrome through mechanisms involving visceral adiposity, insulin resistance, dyslipidemia, hypertension, oxidative stress, and chronic inflammation. Addressing high sugar intake is therefore a critical component in preventing the clustering of cardiometabolic risk factors that define this condition.

Table 1: Metabolic pathways and systemic effects of dietary sugars, detailing how different sugar types contribute to multi-organ damage through distinct metabolic mechanisms.

Sugar Type	Primary Metabolism	Affected Organs / Systems	Key Mechanisms	Health Outcomes	Ref
Glucose	Glycolysis → Pyruvate → TCA cycle; stimulates insulin release	Liver, Muscle, Adipose, Pancreas, Brain, Heart	Hyperglycemia, insulin release, elevated glycemic load	Obesity, Type 2 Diabetes, Cognitive impairment, cardiovascular disease	[97-100]
Fructose	Liver via fructokinase → Fructose-1-phosphate → Triose-phosphate → De novo lipogenesis	Liver, Heart, Pancreas, Kidney, Brain	Lipogenesis, uric acid generation, insulin resistance, AGE formation	NAFLD, NASH, Dyslipidemia, Hypertension, CKD, Cognitive deficits	[101-104]
Sucrose / Table Sugar	Cleaved into glucose + fructose; combined effects	Multiple organs (systemic)	Hyperglycemia, lipogenesis, inflammation, oxidative stress	Obesity, Cardiovascular disease, Metabolic syndrome, Cognitive decline, Cancer risk	[67,105-107]
Added Sugars / Sugar-sweetened beverages	High glycemic load, rapid absorption	Liver, Brain, Heart, Kidneys, Gut	Insulin spikes, chronic inflammation, oxidative stress, gut	Obesity, Diabetes, NAFLD/NASH, Cardiovascular disease, Cognitive impairment, Cancer	[74,108-110]

			microbiota dysbiosis	risk	

3. Cardiovascular System

Excessive dietary sugar has emerged as a significant and independent risk factor for cardiovascular disease (CVD), encompassing conditions such as coronary artery disease, hypertension, and heart failure. The harmful effects of sugar on the cardiovascular system result from a combination of metabolic, inflammatory, hemodynamic, and oxidative mechanisms. These mechanisms often act synergistically, amplifying the risk of vascular damage and adverse cardiac outcomes over time.

3.1 Dyslipidemia and Atherogenesis

High sugar intake, particularly from added sugars and sugar-sweetened beverages, promotes dyslipidemia, a central contributor to atherosclerosis.[111] Fructose is metabolized in the liver via pathways that bypass glycolytic regulation, stimulating de novo lipogenesis.[112] This process increases hepatic triglyceride production and enhances secretion of very-low-density lipoprotein (VLDL) particles into circulation.[113] Elevated triglycerides are often accompanied by an increase in small dense low-density lipoprotein (LDL) particles, which are highly atherogenic due to their susceptibility to oxidative modification and enhanced penetration into the arterial intima.[114] Concurrently, high sugar intake reduces high-density lipoprotein (HDL) cholesterol, impairing reverse cholesterol transport.[115] Together, these alterations accelerate plaque formation, increase arterial stiffness, and promote progression of atherosclerotic cardiovascular disease.

3.2 Hypertension

Dietary sugar contributes to elevated blood pressure through multiple mechanisms, with fructose playing a particularly important role.[116] Metabolism of fructose in the liver generates uric acid, which inhibits endothelial nitric oxide synthase (eNOS) activity, reducing nitric oxide bioavailability and impairing vasodilation.[117] Elevated uric acid also stimulates the renin-angiotensin-aldosterone system, promoting vasoconstriction and sodium retention.[118] These effects are compounded by obesity-induced increases in sympathetic nervous system activity.[119] Collectively, these mechanisms result in sustained hypertension, a leading risk factor for myocardial infarction, stroke, and other cardiovascular events.

3.3 Insulin Resistance and Endothelial Dysfunction

Persistent high sugar intake induces insulin resistance, which significantly impacts vascular health. Insulin normally promotes vasodilation through endothelial nitric oxide release, but insulin-resistant states reduce this response, leading to impaired vascular tone.[120] Moreover, chronic hyperglycemia accelerates the formation of advanced glycation end products (AGEs), which cross-link extracellular matrix proteins in the vasculature and interact with the receptor for AGEs (RAGE).[121] Activation of RAGE triggers intracellular signaling pathways, including NF-κB, increasing oxidative stress, promoting inflammatory cytokine release, and further compromising endothelial integrity.[122] Endothelial dysfunction is an early step in atherogenesis and contributes to vascular stiffness, impaired microvascular circulation, and a higher risk of thrombotic events.[123]

3.4 Inflammation and Oxidative Stress

Excess sugar intake also promotes systemic inflammation and oxidative stress, which are closely linked to cardiovascular risk.[124] Visceral adiposity, which is often increased in individuals consuming high levels of sugar, secretes pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6).[125] These cytokines exacerbate insulin resistance and directly affect endothelial cells, contributing to vascular dysfunction.[126] High glucose and fructose levels enhance reactive oxygen species (ROS) production in the liver, pancreas, and vascular endothelium, amplifying oxidative stress.[127] Oxidative stress damages lipids, proteins, and DNA in vascular tissues, accelerates plaque instability, and increases susceptibility to acute cardiovascular events such as myocardial infarction or stroke.[128]

3.5 Epidemiological Evidence

Population-level data support the mechanistic links between sugar consumption and cardiovascular disease.[111] The Global Burden of Disease Study 2019 highlighted that diets high in sugar-sweetened beverages contribute to millions of CVD-related deaths worldwide.[129] Longitudinal cohort studies demonstrate that individuals consuming more than 25% of their daily calories from added sugars have significantly higher risks of coronary heart disease and cardiovascular mortality compared to those consuming less than 10%.[130] Notably, these associations remain significant even after adjusting for total caloric intake and body mass index, indicating that sugar exerts direct cardiovascular effects beyond weight gain alone.[131]

4. Liver Damage

The liver plays a central role in sugar metabolism, particularly in the processing of fructose, which is increasingly consumed in the form of sugar-sweetened beverages and processed foods.[62,132] Chronic overconsumption of sugar, especially fructose, has profound implications for liver health, contributing to the development of non-alcoholic fatty liver disease (NAFLD).[133] NAFLD encompasses a spectrum of hepatic disorders ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and, in severe cases, hepatocellular carcinoma.[134] Recent global estimates indicate that approximately 25–30% of adults worldwide are affected by NAFLD, with prevalence rising sharply in populations with high dietary sugar consumption.[135]

4.1 Fructose Metabolism and Hepatic Lipogenesis

Fructose is primarily metabolized in hepatocytes through the enzyme fructokinase, which converts it into fructose-1-phosphate, bypassing the key regulatory enzyme phosphofructokinase in glycolysis.[136] This bypass leads to unregulated production of triose-phosphate intermediates that serve as substrates for de novo lipogenesis (DNL), resulting in enhanced synthesis of triglycerides.[136,137] These triglycerides can accumulate in the liver, causing hepatic steatosis, or are secreted as very-low-density lipoprotein (VLDL) into the circulation, contributing to hypertriglyceridemia and systemic metabolic disturbances.[138] Studies indicate that individuals consuming high amounts of fructose may have a 30–50% increase in hepatic DNL, which strongly correlates with intrahepatic fat accumulation.[78]

4.2 Hepatic Insulin Resistance

Fructose-induced fat accumulation in hepatocytes is a key driver of hepatic insulin resistance.[61] In this state, insulin fails to suppress gluconeogenesis, leading to persistent fasting hyperglycemia.[60] Moreover, the liver's impaired response to insulin exacerbates dyslipidemia and contributes to systemic insulin resistance, linking NAFLD closely with the pathogenesis of metabolic syndrome and type 2 diabetes mellitus.[139,140] Clinical studies have shown that individuals with NAFLD have a 2–3 times higher risk of developing T2DM, independent of overall obesity.[141]

4.3 Oxidative Stress and Inflammation

Chronic high sugar intake generates reactive oxygen species (ROS) within hepatocytes, creating a state of oxidative stress.[142] ROS damages cellular macromolecules, including lipids, proteins, and DNA, and triggers inflammatory signaling pathways such as NF-κB,

which upregulates pro-inflammatory cytokines like TNF-α, IL-6, and IL-1β.[143] This inflammatory environment promotes progression from simple steatosis to NASH, characterized by hepatocyte injury, ballooning degeneration, and immune cell infiltration.[144] Persistent oxidative stress also activates hepatic stellate cells, stimulating collagen deposition and fibrosis, which may progress to cirrhosis over time.[145]

4.4 Uric Acid and Liver Injury

Fructose metabolism also generates uric acid, which contributes to mitochondrial oxidative stress and impairs nitric oxide availability in hepatocytes.[101] Elevated uric acid levels have been implicated in worsening insulin resistance and promoting liver inflammation, creating a vicious cycle that accelerates NAFLD progression.[146] Epidemiological data suggest that individuals with hyperuricemia have a significantly higher prevalence of NAFLD compared to those with normal uric acid levels.[147]

4.5 Epidemiological and Clinical Evidence

The rising prevalence of NAFLD parallels global sugar consumption trends. Studies indicate that consumption of sugar-sweetened beverages is associated with a 55% higher risk of developing NAFLD over 5–10 years, independent of body mass index.[148] NASH, the progressive inflammatory form of NAFLD, is increasingly observed in younger populations, reflecting early exposure to high-sugar diets.[149] NAFLD is now one of the leading causes of liver-related morbidity worldwide and is projected to become the primary indication for liver transplantation within the next decade.[150]

4.6 Clinical Implications

Liver damage from excessive sugar intake has systemic metabolic consequences. Hepatic insulin resistance contributes to hyperglycemia, dyslipidemia, and increased cardiovascular risk.[151] Chronic inflammation and oxidative stress originating from the liver further exacerbate metabolic and vascular dysfunction.[152] Importantly, early intervention through dietary sugar reduction can reverse hepatic fat accumulation, improve insulin sensitivity, and prevent progression to NASH and fibrosis.[153] Lifestyle modification remains the cornerstone of management, highlighting the critical role of public health strategies to reduce sugar consumption globally.[154]

5. Neurological and Cognitive Effects

Excessive dietary sugar intake not only impacts metabolic and cardiovascular health but also has significant effects on the central nervous system (CNS).[77,155] Emerging evidence suggests that chronic high sugar consumption can alter brain structure and function, impair cognitive performance, and affect mood and behavior.[156,157] These effects are mediated through multiple mechanisms, including insulin resistance in the brain, neuroinflammation, oxidative stress, and dysregulation of neurotransmitter systems.[157]

5.1 Brain Insulin Resistance

Insulin is a critical regulator of neuronal energy metabolism, synaptic plasticity, and cognitive function.[158] High sugar intake, particularly from refined carbohydrates and sugar-sweetened beverages, leads to systemic hyperinsulinemia and peripheral insulin resistance, which may extend to the CNS.[159] Brain insulin resistance impairs glucose uptake by neurons and astrocytes, limiting energy availability in key regions such as the hippocampus and prefrontal cortex.[160] These areas are essential for learning, memory consolidation, and executive function.[161] Chronic insulin resistance in the brain has been linked to reduced synaptic plasticity, impaired long-term potentiation (LTP), and deficits in memory and attention in both animal models and human studies.[162]

5.2 Cognitive Impairment

Several animal studies have shown that diets high in sugar impair performance on tasks requiring spatial memory, object recognition, and learning.[163] In humans, high consumption of sugar-sweetened beverages is associated with decreased hippocampal volume, impaired verbal memory, and slower cognitive processing speed.[164] A meta-analysis of observational studies indicates that individuals with the highest sugar intake have a significantly higher risk of mild cognitive impairment and age-related memory decline.[165] Chronic hyperglycemia, insulin resistance, and associated inflammation appear to be central drivers of these cognitive deficits.[166]

5.3 Neuroinflammation and Oxidative Stress

High sugar diets increase oxidative stress and trigger neuroinflammatory pathways in the brain.[167] Excess glucose and fructose promote the formation of reactive oxygen species (ROS), which damage neuronal lipids, proteins, and DNA.[168] Moreover, the accumulation of advanced glycation end products (AGEs) in the CNS activates receptors for AGEs (RAGE) on neurons and glial cells, stimulating the release of pro-inflammatory cytokines such as

TNF-α and IL-6.[169] This chronic low-grade neuroinflammation contributes to synaptic dysfunction, neuronal loss, and impaired neurogenesis in regions critical for memory and learning.[124]

5.4 Dopamine Reward Pathway and Addiction-like Behavior

High sugar intake also affects brain reward circuits, particularly those mediated by dopamine in the mesolimbic pathway.[170] Repeated consumption of sugar-rich foods activates dopamine release in the nucleus accumbens, creating pleasurable sensations that reinforce feeding behavior.[171] Over time, this can lead to neuroadaptations similar to those seen in drug addiction, including reduced dopamine receptor sensitivity.[172] These changes increase sugar-seeking behavior, reduce satiety signaling, and may contribute to compulsive overeating, further exacerbating metabolic dysfunction.[173]

5.5 Alzheimer's Disease and Neurodegeneration

Emerging evidence suggests a link between high sugar consumption and increased risk of neurodegenerative diseases such as Alzheimer's disease (AD).[174,175] Chronic hyperglycemia and insulin resistance in the brain impair amyloid-beta clearance and promote tau hyperphosphorylation, hallmarks of AD pathology.[176] Some researchers refer to this phenomenon as "type 3 diabetes," highlighting the role of metabolic dysregulation in cognitive decline.[177] Epidemiological studies have found that individuals with high sugar intake, particularly from sugar-sweetened beverages, exhibit higher rates of cognitive decline and dementia later in life.[157]

5.6 Epidemiological Evidence

Population-based studies support the association between high sugar consumption and adverse neurological outcomes. For example, longitudinal studies in adults demonstrate that excessive intake of sugar-sweetened beverages is associated with poorer memory performance, reduced hippocampal volume, and higher incidence of mild cognitive impairment.[164] In children and adolescents, high sugar diets have been linked to attention deficits, behavioral problems, and impaired academic performance.[178] These findings underscore that sugar's effects on the brain may begin early in life and persist into adulthood.

6. Inflammation and Oxidative Stress

Excessive sugar intake triggers systemic inflammation and oxidative stress, which serve as central mechanisms linking metabolic, cardiovascular, hepatic, and neurological dysfunction.

Chronic consumption of high levels of glucose and fructose initiates a cascade of molecular events that disrupt cellular homeostasis, damage tissues, and accelerate the development of non-communicable diseases. **Figure 2** depicts how hyperglycemia and lipid accumulation trigger oxidative stress (ROS) and inflammation, which in turn worsen insulin resistance and directly promote damage to the liver, heart, brain, and kidneys.

6.1 Mechanisms of Sugar-Induced Inflammation

High dietary sugar promotes chronic low-grade inflammation through multiple pathways. Excess glucose and fructose elevate circulating free fatty acids and triglycerides, which stimulate pro-inflammatory signaling in adipocytes and hepatocytes.[179] Enlarged adipocytes secrete cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1), recruiting macrophages and perpetuating adipose tissue inflammation.[180] This inflammatory milieu impairs insulin signaling, contributing to insulin resistance in muscle, liver, and vascular tissues.[181]

Fructose metabolism specifically increases uric acid production, which can activate the NLRP3 inflammasome in immune cells.[182] Activation of this pathway further enhances the release of IL-1β and IL-18, reinforcing systemic inflammation.[183] Moreover, advanced glycation end products (AGEs) formed from persistent hyperglycemia interact with RAGE receptors on various cell types, triggering NF-κB-mediated transcription of pro-inflammatory genes.[184] This pathway is implicated in vascular inflammation, endothelial dysfunction, and organ-specific damage in the liver, pancreas, and brain.[185,186]

6.2 Oxidative Stress

Excess sugar intake enhances the production of reactive oxygen species (ROS), exceeding the antioxidant capacity of cells and causing oxidative stress. ROS can damage lipids, proteins, and DNA, impairing normal cellular function.[187] In the liver, oxidative stress contributes to the progression of NAFLD to non-alcoholic steatohepatitis (NASH) and fibrosis.[188] In the vascular system, ROS reduces nitric oxide bioavailability, promoting endothelial dysfunction, vasoconstriction, and hypertension.[189] In the central nervous system, oxidative stress disrupts neuronal integrity and synaptic function, contributing to cognitive decline.[190]

6.3 Cross-Talk Between Inflammation and Oxidative Stress

Inflammation and oxidative stress are tightly interconnected. Pro-inflammatory cytokines such as TNF-α activate NADPH oxidase and mitochondrial ROS production, while ROS

themselves further activate NF-κB and other inflammatory transcription factors.[191] This vicious cycle amplifies tissue damage across multiple organ systems, accelerating the progression of obesity, type 2 diabetes, cardiovascular disease, liver injury, and neurodegeneration.[192-194]

6.4 Epidemiological and Clinical Evidence

Epidemiological studies link high sugar consumption with elevated markers of systemic inflammation, such as C-reactive protein (CRP), IL-6, and TNF-α. Individuals consuming diets high in sugar-sweetened beverages consistently show higher inflammatory biomarker levels, independent of body weight.[195] Elevated oxidative stress markers, including malondialdehyde (MDA) and 8-hydroxy-2'-deoxyguanosine (8-OHdG), are also observed in populations with high sugar intake, confirming the biochemical impact at the cellular level.[196] These changes correlate with increased risk for metabolic syndrome, cardiovascular events, liver disease, and cognitive impairment.[197]

6.5 Clinical Implications

Targeting inflammation and oxidative stress is crucial for mitigating the systemic effects of high sugar intake. Reducing added sugar consumption decreases circulating cytokines, ROS production, and AGE formation, improving insulin sensitivity and vascular function.[124] Lifestyle interventions that combine dietary sugar restriction with antioxidant-rich foods and physical activity have been shown to lower inflammatory markers, reduce hepatic fat accumulation, and improve cognitive performance, highlighting the reversibility of sugar-induced damage when addressed early.[198]

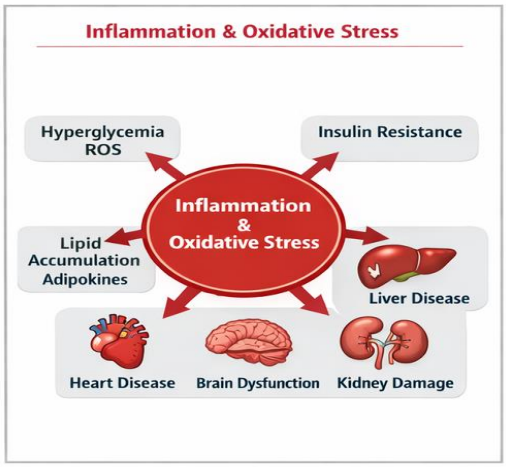

Figure 2: Central Role of Inflammation and Oxidative Stress in Sugar-Induced Organ Damage.

7. Cancer Risk

Emerging evidence suggests that excessive sugar intake may increase the risk of several types of cancer through both direct and indirect mechanisms. While sugar itself is not carcinogenic, chronic high sugar consumption contributes to metabolic and hormonal environments that favor tumor development and progression.

7.1 Mechanistic Links

Hyperinsulinemia and IGF-1: High sugar intake induces repeated spikes in blood glucose and insulin. Chronic hyperinsulinemia increases circulating levels of insulin-like growth factor 1 (IGF-1), which stimulates cell proliferation and inhibits apoptosis.[109] Elevated IGF-1 signaling is implicated in the development of breast, colorectal, and pancreatic cancers.[199]

Obesity and Adipokines: Sugar-induced weight gain and visceral adiposity alter adipokine secretion, increasing leptin and reducing adiponectin.[200] Leptin promotes angiogenesis, inflammation, and tumor cell proliferation, while low adiponectin removes a protective anti-proliferative signal.[201] These hormonal changes create a microenvironment conducive to tumor growth.

Chronic Inflammation: Excess sugar consumption promotes systemic inflammation, characterized by elevated TNF-α, IL-6, and CRP.[190] Chronic inflammation increases DNA damage, supports tumor initiation, and enhances progression through pro-angiogenic and immunosuppressive pathways.[203]

Advanced Glycation End Products (AGEs): Persistent hyperglycemia leads to AGE formation. AGEs bind to RAGE on cells, activating oxidative stress and NF-κB-mediated transcription, which can promote carcinogenesis, particularly in tissues like the liver, pancreas, and colon.[204]

7.2 Epidemiological Evidence

Observational studies indicate a correlation between high sugar-sweetened beverage consumption and increased risk of certain cancers. For example.

Colorectal cancer: High dietary glycemic load and excessive sugar intake are associated with a modest but significant increase in risk.[205]

Breast cancer: Elevated sugar intake, particularly in postmenopausal women, has been linked to higher incidence rates, potentially via insulin and IGF-1 signaling.[206,207]

Pancreatic cancer: Studies suggest a link between chronic high sugar consumption, hyperinsulinemia, and pancreatic tumor development.[208]

While sugar is rarely considered a direct carcinogen, its role in creating a pro-tumorigenic metabolic and inflammatory environment highlights the importance of moderation, particularly in populations at high risk for obesity-related cancers.

8. Other Organ Systems and Health Effects

Excessive sugar consumption affects multiple organ systems beyond metabolism, cardiovascular health, liver, and the brain. Its systemic effects are mediated through mechanisms such as glycation, inflammation, oxidative stress, and microbiome dysregulation, which together compromise overall health. **Figure 3** summarizes the primary detrimental health outcomes resulting from long-term high dietary sugar intake across various organ systems.

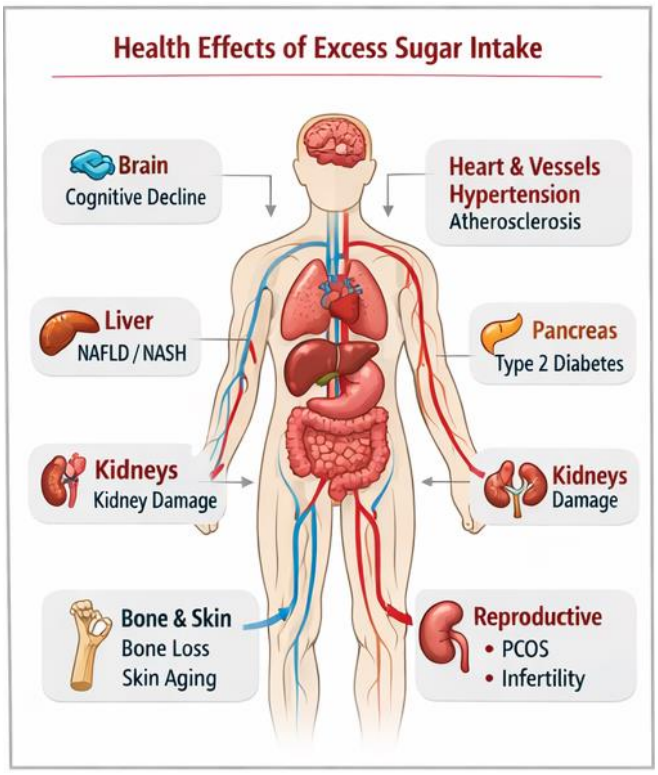

Figure 3: Multi-Organ Damage Associated with Chronic Excessive Sugar Consumption.

8.1 Renal System

High sugar intake, particularly fructose, contributes to chronic kidney disease (CKD) and other renal dysfunctions.[209] Fructose metabolism increases uric acid production, which can impair endothelial function in renal vasculature and promote hypertension.[210] Persistent

hyperglycemia also accelerates the formation of advanced glycation end products (AGEs) in renal tissues, damaging glomerular cells and the extracellular matrix.[211] Over time, these changes contribute to glomerulosclerosis, proteinuria, and progressive kidney injury. Epidemiological studies have linked sugar-sweetened beverage consumption to a 30–40% higher risk of CKD in adults, independent of body mass index.[212]

8.2 Gut Microbiota

Dietary sugar significantly impacts the composition and function of the gut microbiota, which plays a critical role in metabolism, immunity, and systemic inflammation.[124,213] Excess sugar promotes the growth of pathogenic bacteria while reducing beneficial commensals such as Bifidobacteria and Lactobacilli.[214] This dysbiosis increases gut permeability (“leaky gut”), allowing bacterial endotoxins such as lipopolysaccharides (LPS) to enter circulation and trigger systemic inflammation.[215] Altered microbiota has also been associated with insulin resistance, obesity, and metabolic syndrome, demonstrating the indirect systemic effects of sugar through gut-mediated pathways.[216]

8.3 Skeletal System

High sugar intake negatively affects bone health.[206] Elevated blood glucose increases urinary calcium excretion, reducing mineral availability for bone formation.[219] Additionally, chronic inflammation induced by excessive sugar impairs osteoblast activity and stimulates osteoclast-mediated bone resorption.[217] Children and adolescents consuming large amounts of sugary beverages are at higher risk for reduced bone mineral density, increasing susceptibility to fractures and osteoporosis later in life.[220]

8.4 Skin Health

Excessive sugar accelerates skin aging and contributes to dermatological conditions.[221] The non-enzymatic glycation of collagen and elastin fibers forms AGEs, which stiffen connective tissue, reduce skin elasticity, and promote wrinkling.[222] Sugar-induced systemic inflammation can exacerbate conditions such as acne and eczema.[223] Long-term high sugar intake may therefore contribute to both aesthetic and structural skin damage.[224]

8.5 Immune System

High sugar diets impair immune function by affecting leukocyte activity and increasing oxidative stress.[225] Hyperglycemia can reduce neutrophil chemotaxis, phagocytosis, and pathogen-killing capacity, making individuals more susceptible to infections.[226] Chronic

inflammation driven by sugar intake may also dysregulate adaptive immunity, impairing antibody responses and prolonging recovery from illness.[227]

8.6 Reproductive Health

Excess sugar consumption has been associated with hormonal imbalances and reproductive dysfunction.[228] Insulin resistance and hyperinsulinemia can disrupt ovarian steroidogenesis, contributing to conditions such as polycystic ovary syndrome.[229] In men, high sugar diets have been linked to impaired sperm quality and erectile dysfunction, highlighting the broader endocrine impact of sugar-induced metabolic derangements.[230]

Table 2 summarizes the organ-specific detrimental effects of chronic excessive sugar intake. Mechanisms include insulin resistance, oxidative stress, chronic inflammation, lipogenesis, uric acid production, and advanced glycation end-product formation.

Table 2: Organ-specific pathologies resulting from chronic excessive sugar intake, summarizing the effects, mechanisms, and clinical outcomes across all major body systems.

Organ / System	Effect of Excess Sugar	Mechanisms Involved	Clinical / Health Outcomes	Ref
Liver	Fat accumulation, inflammation	Fructose metabolism → de novo lipogenesis, ROS, uric acid, AGE formation	NAFLD, NASH, fibrosis, insulin resistance	[231,232]
Heart & Vessels	Atherosclerosis, hypertension	Dyslipidemia, endothelial dysfunction, chronic inflammation, oxidative stress	Coronary artery disease, stroke, hypertension	[233,234]
Pancreas	β-cell stress, insulin resistance	Chronic hyperglycemia, insulin overproduction	Type 2 diabetes, impaired glucose tolerance	[193,235]
Brain	Cognitive decline, memory impairment, reward pathway alteration	Brain insulin resistance, neuroinflammation, oxidative stress, dopamine dysregulation	Memory deficits, learning impairment, addiction-like eating behaviors	[164,236]
Kidneys	Glomerular damage, reduced filtration	Uric acid elevation, AGE formation, oxidative stress	Chronic kidney disease, proteinuria, hypertension	[237,238]
Gut / Microbiota	Dysbiosis, increased gut permeability	Altered microbiota composition, endotoxin leakage, inflammation	Metabolic syndrome, systemic inflammation	[213,239]
Bone & Skin	Reduced density, collagen glycation	Calcium excretion, inflammation, AGE-	Osteoporosis, fractures, premature	[240-242]

		mediated collagen crosslinking	skin aging	
Reproductive System	Hormonal imbalance, fertility issues	Insulin resistance, altered steroidogenesis	PCOS, reduced sperm quality, infertility	[243,244]
Cancer Risk	Tumor initiation and progression	Hyperinsulinemia, IGF-1 elevation, inflammation, ROS, AGEs	Increased risk of breast, colorectal, pancreatic cancers	[245,246]
Systemic Mediators	Chronic multi-organ damage	Inflammation, oxidative stress, insulin resistance, hormonal dysregulation	Multi-organ dysfunction, accelerated chronic disease development	[247,248]

9. Public Health Perspective and Recommendations

Excessive sugar consumption is a growing global public health concern, contributing to obesity, diabetes, cardiovascular disease, liver disorders, neurological dysfunction, and potentially cancer. Addressing sugar-related health risks requires a combination of population-level interventions, policy measures, and individual behavioral strategies.

9.1 Global Sugar Consumption Trends

Worldwide, sugar consumption has risen dramatically over the past few decades. According to the World Health Organization (WHO, 2023), the average global intake of free sugars exceeds 50 grams per day per person, far above the recommended limit of 25 grams (≈6 teaspoons) per day.[249] Sugar-sweetened beverages are a major contributor, especially in high-income countries, but increasingly in low- and middle-income countries where processed foods are more widely available.[14] Urbanization, increased availability of ultra-processed foods, and aggressive marketing have amplified sugar intake globally, particularly among children and adolescents.[250]

9.2 Health and Economic Implications

High sugar consumption is linked to the rising prevalence of obesity, type 2 diabetes, cardiovascular disease, and NAFLD, imposing significant healthcare costs.[251] The Global Burden of Disease Study 2019 estimated that diets high in sugar-sweetened beverages alone were responsible for over 180,000 deaths worldwide due to diabetes and cardiovascular complications.[252] Beyond morbidity and mortality, high sugar intake also contributes to reduced productivity, increased medical expenditure, and lower quality of life.[253]

9.3 Public Health Strategies

Policy Interventions

I. **Sugar taxes:** Several countries have implemented excise taxes on sugar-sweetened beverages, which have been shown to reduce consumption by 10–20% in some populations.[15]

II. **Labeling regulations:** Mandatory front-of-pack labeling of added sugars helps consumers make informed dietary choices.[254]

III. **Marketing restrictions:** Limiting advertising of high-sugar foods to children can reduce early-life exposure and prevent lifelong habits.[255]

Dietary Guidelines and Education

I. International health organizations recommend reducing added sugar intake to less than 10% of total daily calories, with an ideal target of 5% for additional health benefits.[256]

II. Public education campaigns highlighting the risks of excessive sugar consumption and promoting healthier alternatives, such as water, unsweetened beverages, fruits, and whole foods, are essential.[257]

III. School and workplace programs can promote sugar reduction by providing healthier food and beverage options and encouraging nutrition literacy.[258]

Behavioral and Individual Approaches

I. Gradual reduction of sugar in the diet is more sustainable than abrupt elimination.[259]

II. Encouraging consumption of fiber-rich foods, protein, and healthy fats can improve satiety and reduce sugar cravings.[99]

III. Monitoring sugar intake through food diaries or digital apps can help individuals track consumption and make informed adjustments.[98]

9.4 Future Directions

Research should focus on understanding sugar's organ-specific and systemic effects, developing population-specific dietary recommendations, and evaluating the long-term outcomes of policy interventions. Personalized nutrition strategies based on metabolic, genetic, and behavioral factors may enhance the effectiveness of sugar reduction initiatives.[97]

DISCUSSION

Over the ten-year period from 2015 to 2025, the scientific evidence linking excessive sugar consumption to adverse health outcomes has expanded substantially. Accumulating epidemiological, mechanistic, and clinical data consistently demonstrate that high intake of added sugars, particularly from sugar-sweetened beverages and ultra-processed foods, contributes to metabolic dysfunction, chronic inflammation, and increased risk of non-communicable diseases. The present review synthesizes these findings and highlights the biological plausibility underlying these associations.

One of the most consistently reported outcomes is the relationship between high sugar intake and obesity. Excess dietary sugar increases total caloric intake without proportionate satiety, thereby promoting positive energy balance.[108] Fructose-containing sugars, especially in liquid form, appear particularly problematic because fructose metabolism in the liver bypasses key regulatory steps of glycolysis, stimulating de novo lipogenesis.[260] This process enhances hepatic triglyceride synthesis, contributing to visceral adiposity and ectopic fat deposition.[261] Moreover, chronic high sugar intake has been linked to leptin resistance and impaired appetite regulation, reinforcing a cycle of overeating and weight gain.[262]

The metabolic consequences extend beyond adiposity. Strong evidence supports the association between high sugar intake and insulin resistance, a central defect in type 2 diabetes mellitus.[263] Repeated exposure to high glycemic loads induces frequent insulin surges, which over time may reduce insulin sensitivity in peripheral tissues.[264] Additionally, fructose-driven hepatic lipid accumulation exacerbates hepatic insulin resistance, promoting hyperglycemia.[265] Advanced glycation end products formed through chronic hyperglycemia further impair cellular function and contribute to microvascular and macrovascular complications.[266]

Cardiovascular risk is another major concern. Prospective cohort studies during the past decade have shown that higher consumption of added sugars correlates with elevated blood pressure, dyslipidemia, and increased cardiovascular mortality.[267] Mechanistically, sugar-induced hyperinsulinemia may activate the sympathetic nervous system and promote sodium retention, thereby increasing blood pressure.[268] Concurrently, hepatic overproduction of very-low-density lipoproteins contributes to hypertriglyceridemia, a recognized cardiovascular risk factor[269] Chronic low-grade inflammation and oxidative stress induced

by excessive sugar intake may also accelerate endothelial dysfunction and atherosclerotic progression.[270]

Emerging evidence has further explored the potential link between high sugar consumption and cancer risk. Although sugar does not directly "cause" cancer, hyperinsulinemia and elevated insulin-like growth factor-1 levels may create a pro-proliferative environment that facilitates tumor growth.[271] Obesity, a consequence of chronic excess sugar intake, is itself a well-established risk factor for multiple cancers.[272] Additionally, persistent inflammation and oxidative stress may contribute to DNA damage and tumorigenesis.[273] While causality remains complex and multifactorial, the biological mechanisms suggest plausible pathways connecting chronic high sugar intake to increased cancer susceptibility.

Neurological and cognitive outcomes have also received growing attention. Experimental and observational studies suggest that diets high in refined sugars may impair memory and cognitive performance, potentially through insulin resistance within the brain and increased neuroinflammation.[164] Some evidence indicates that excessive sugar intake may influence reward pathways similarly to addictive substances, reinforcing habitual consumption patterns.[172] These findings warrant further investigation, particularly in younger populations where dietary habits are established early.

Despite the strong associations observed, it is important to acknowledge limitations within the existing literature. Many epidemiological studies rely on self-reported dietary assessments, which are subject to recall bias and measurement error. Confounding factors such as physical activity, overall dietary patterns, and socioeconomic status may also influence observed outcomes. Furthermore, the heterogeneity of sugar sources complicates interpretation. Naturally occurring sugars in whole fruits, accompanied by fiber and phytonutrients, do not appear to exert the same detrimental metabolic effects as added sugars in processed foods.[274] Therefore, public health messaging must differentiate between intrinsic and added sugars.

Intervention studies provide more direct evidence, demonstrating that reducing added sugar intake improves body weight, glycemic control, and lipid profiles.[275] Policy-level interventions, including taxation of sugar-sweetened beverages and reformulation initiatives, have shown promising results in lowering population-level sugar consumption.[15] However,

global intake remains above recommended limits in many regions, particularly among adolescents and young adults.[276]

Collectively, the evidence from 2015 to 2025 underscores that excessive added sugar consumption is not merely a source of "empty calories" but a significant modifiable risk factor for metabolic and cardiovascular diseases. The mechanistic pathways involving insulin resistance, hepatic lipogenesis, inflammation, oxidative stress, and advanced glycation provide biological coherence to epidemiological findings. Future research should focus on long-term randomized controlled trials, dose-response relationships, and interactions between sugar intake and genetic or environmental modifiers.

In summary, the detrimental effects of high sugar consumption are multifaceted and interrelated, influencing metabolic, cardiovascular, oncological, and neurological health. Reducing added sugar intake at both individual and population levels remains a critical strategy for preventing non-communicable diseases and improving global health outcomes.

CONCLUSION

Excessive dietary sugar is a major threat to human health, affecting nearly every organ system. Chronic high intake contributes to obesity, type 2 diabetes, and metabolic syndrome through insulin resistance, hormonal imbalance, and dyslipidemia. It promotes cardiovascular disease, drives non-alcoholic fatty liver disease through fructose-induced lipogenesis and oxidative stress, and impairs brain function by disrupting insulin signaling and increasing neuroinflammation. Sugar also negatively impacts the kidneys, gut microbiota, immune function, and may increase cancer risk. Inflammation and oxidative stress are central mechanisms underlying these effects.

Rising global sugar consumption parallels the increase in chronic diseases, creating significant public health and economic burdens. Reducing added sugar intake through policy measures and healthier dietary choices is essential. Overall, limiting sugar consumption is a key modifiable strategy to protect long-term metabolic and systemic health.

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Competing Interests

None

Authors' contributions

Md. Al Amin: Project administration; supervision; conceptualization of the study; methodology; comprehensive literature search; writing—original draft, review, and editing; validation of references and information; Correspondence.

Md. Rezwan Hossain and Moazzema Binta Bashar: Literature collection and data extraction; critical analysis and interpretation of studies; manuscript review and editing.

Md. Ismail Kabir: Validation of references and information, visualization of figures and tables; writing—review and editing; resources; formal analysis of literature.

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