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Is Obesity a Precursor to Type 2 Diabetes Mellitus ? A Review Exploring Risk Factors, Lipid Profile Alterations, and Pathophysiological Links

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Abstract

Addressing a question like -is obesity a leading risk factor to type2 diabetes, raises global health concern and brings about a thought to relook at the significant risk factor for the development of type 2 diabetes mellitus (T2DM) by obesity, plus other complications. The intricate interplay between excess adiposity, insulin resistance, and metabolic dysfunction underscores the progression from obesity to T2DM. This review examines the multifactorial links between these conditions, focusing on risk factors such as genetic predisposition, chronic inflammation, and environmental influences. The main aim of this review was also to examine the role of dysregulated lipid metabolism and its impact on the lipid profile, which serves as a critical biomarker in predicting T2DM risk. Key alterations, including elevated triglycerides, reduced high-density lipoprotein (HDL), and increased low-density lipoprotein (LDL) levels, these parameters are explored in the context of their contribution to insulin resistance and β-cell dysfunction. The review further highlights the pathophysiological mechanisms, including adipokine imbalance and pro-inflammatory cytokine secretion, that exacerbate metabolic disturbances. Understanding these interrelationships is vital for identifying high-risk individuals which may be useful for novel strategic treatment options and for personalised interventions to mitigate the burden of obesity-related T2DM.

Keywords: Obesity, Diabetes Melletus, Lipid Profile, Cytokines, Insulin Resistance, Pathophysiology, B-Cell Dysfunction, Gut Dysbiosis.

Introduction

The prevalence of obesity and type 2 diabetes individuals has shown an enormous increase globally in all age groups and in both sexes. It is estimated that approximately two-thirds of adult populations in the US are either obese or overweight [1]. This highlights the severity of the obesity epidemic. According to a study published from 2017 to 2020, in the United States, 42.4% of adults are obese, and the proportion of younger obese individuals is 20.9% [2].

Globally, the prevalence of obesity is higher among women than men. Approximately, 14% of men and 20% of women are expected to develop obesity by 2030. Moreover, the Western Pacific region has shown the highest incidence of childhood obesity [3]. On the other hand, the prevalence of diabetes mellitus (both type 1and 2) has increased exponentially, with a percentage of 10.5% population affected on a global level. The frequency of diabetes among youth is also on the rise [3] . The countries with the highest prevalence of type 2 diabetes are – China (88.5 million), India (65.9 million) and US (28.9 million). The populations in these countries are believed to be the reason for such high incidences of diabetes [1]. On a global level, the number of adults with type 2 diabetes has increased to 422 million in 2014 compared to just 108 million in 1980 [4].

To proceed with the complicated etiology of the coexisting human pathologies like obesity and T2DM, we first describe what these terms stand for

Obesity: Obesity is a chronic condition characterized by excessive fat accumulation in specific areas of the body, organs (referred to as ectopic fat), or throughout the body. It is a progressive, recurring health issue that arises from various factors and can result in significant metabolic and psychological health impacts [1]. Obesity is defined as an energy imbalance, with more calories consumed than those burned causing weight gain and leading to metabolic disturbances [4]. The World Health Organization (WHO) categorizes adult weight status based on Body Mass Index (BMI): "overweight" is defined as a BMI from 25.0 to 29.9, and "obesity" is classified as a BMI of 30 or higher. Obesity is further divided into severity classes: Class I (BMI 30.0–34.9), Class II (BMI 35.0–39.9), and Class III (BMI 40 or above) [5].

Table 1: Standard Ranges of Body Mass Index and Corresponding Weight Status Categories.

However, there are significant individual variations in body fat percentage for a given BMI, which can be due to variations in factors such as sex, ethnicity, and age [5]. Adiposity risk assessment includes measurements such as BMI, height, weight, waist circumference, and body fat percentage. Obesity is diagnosed using BMI cutoffs and considering body weight, fat distribution patterns, and levels of visceral fat [1]. Obesity is considered the leading cause of preventable death as it increases the risk of metabolic syndrome (MetS), marked by central adiposity, high blood sugar, elevated triglycerides, low HDL, and hypertension. It also leads to insulin resistance, chronic inflammation, and endothelial dysfunction, raising the risk of heart disease, stroke, type 2 diabetes, and other chronic conditions [4]. In 2016, the WHO reported that obesity-related comorbidities—including hypertension, dyslipidaemia, type 2 diabetes mellitus, fatty liver disease, heart disease, and certain cancers—were responsible for approximately 3.4 million deaths among adults aged 18 and older [6].

Type 2 Diabetes: Diabetes is a metabolic disorder characterized by constantly elevated blood sugar levels [1]. Obesity is one of the significant contributors to the growing prevalence of Type-II Diabetes. T2DM is primarily characterized by diminished insulin secretion from pancreatic β-cells and increased insulin resistance in peripheral tissues. These dysfunctions lead to elevated fatty acid levels, impair glucose uptake in muscle cells, and increased fat breakdown and glucose production in the liver. Type 2 diabetes is the result of multiorgan insulin resistance along with a decline in insulin secretion by beta cells [7]. The intricate connection in pathophysiology of obesity and type 2 diabetes has led to the development of the term 'diabesity', indicating that major populations of type 2 diabetic patients are obese or overweight [1].

Type 2 diabetes is detected when glycated haemoglobin is (HbA1C) ≥ 6.5%, or fasting blood glucose is ≥ 126 mg/dL, or 2-hour post prandial blood glucose levels are ≥ 200 mg/dL [1].

Diabetes is diagnosed based on plasma glucose levels—either fasting plasma glucose (FPG), two-hour plasma glucose during a 75 g oral glucose tolerance test (OGTT), or glycated haemoglobin (HbA1c) concentrations—following the guidelines of the American Diabetes Association (ADA) and the World Health Organization (WHO) [8].

Table 2: Diagnostic reference values of FPG and HbA1c by WHO & ADA (Source Reference - 8)

Criteria	Fasting plasma glucose (FPG)	Glycated haemoglobin A1c (HbA1c)	Oral Glucose Tolerance Test OGTT (2h)
Prediabetes (ADA)	100-125 mg/dL	5.7-6.4%	140-199 mg/dL
Prediabetes (WHO)	110-125 mg/dL	Not Recommended	
Diabetes (ADA and WHO)	≥126mg/dL	≥6.5%	≥200 mg/dL

Legend ADA = American Diabetic Association; WHO= World Health Organization

Role of liver: In the interplay of these two conditions (Obesity and T2DM), we have one more parameter to consider that is the liver. The liver is central not only to T2DM but also an important organ that plays its role as a source of gluconeogenesis and as a target of damage from hyperinsulinemia. Several liver injury biomarkers, including alanine aminotransferase (ALT), γ-glutamyl transferase (GGT), ferritin, plasminogen activator inhibitor - 1 (PAI-1), tissue plasminogen activator antigen (tPA antigen), C reactive proteins (CRP), and triglycerides, are elevated in individuals with dysglycemia before a diabetes diagnosis is established [9]. Additionally, lipid abnormalities in individuals with diabetes, referred to as "diabetic dyslipidaemia," are commonly characterized by elevated total cholesterol (T-Chol) and triglycerides (Tg), reduced high-density lipoprotein cholesterol (HDL-C), and an increased presence of small, dense LDL particles [10]. The American Diabetes Association (ADA) suggests specific lipid targets for managing dyslipidaemia in patients with type 2 diabetes - HDL cholesterol level of at least 1.15 mmol/L (45 mg/dL) in men and 1.4 mmol/L (55 mg/dL) in women, an LDL cholesterol level below 2.6 mmol/L (100 mg/dL), and triglycerides below 1.71 mmol/L (150 mg/dL). These thresholds aim to minimize cardiovascular risks in diabetic individuals [11].

Trends Linking Obesity and Type 2 Diabetes

To understand the patterns and trends linking obesity and type 2 diabetes we must try to understand the influence of maternal health on childhood obesity and future diabetes risk. Maternal health plays a significant role in the offspring's susceptibility to obesity and predisposition to other metabolic disturbances like type 2 diabetes, cardiovascular diseases and even some infections and allergies. Here we'll be focussing on obesity and type 2 diabetes development risk. Gestational diabetes mellitus (GDM) has been observed to be associated with higher birthweight of the infant. The reason for this is that maternal hyperglycaemia leads to hyperglycaemia in the foetus, as glucose is easily transported across placenta, causing increased insulin secretion by the infant's pancreatic beta cells. This increase in insulin enhances foetal growth [12]. Additionally, there are evidence suggesting that maternal gestational diabetes mellitus leads to disturbances in hypothalamus, thus predisposing the foetus to obesity [13]. GDM effects on offspring's obesity risk extends into adolescence and beyond; Colorado Longitudinal Exploring Perinatal Outcomes among Children (EPOCH) study done on children aged 10 and 17 years exposed to maternal gestational diabetes mellitus (GDM) compared to unexposed individuals of the same age revealed that the exposed subjects had higher BMI and an increased visceral and subcutaneous adipose tissue [14]. Additionally, the development and function of pancreatic beta cells in offspring is affected by maternal hyperglycaemia, which along with gestational diabetes mellitus results in insulin resistance and/or other precursors of type 2 diabetes in the offspring [3]. Hence, factors that enhance childhood obesity and type 2 diabetes development risk in the offspring are due to higher maternal BMI before pregnancy, greater calorie intake, higher gestational weight gain and maternal hyperglycaemia (figure-1).

Figure 1: Effects Of Maternal Health in Shaping Childhood Obesity and Diabetes Risk

Shared Mechanisms Connecting Obesity to Type 2 Diabetes Mellitus

In the light of parameters described above it is obvious to evaluate the various pathways through which obesity leads to Type-II Diabetes mellitus are discussed below:

Insulin Resistance Pathways

Insulin resistance (IR) refers to reduced responsiveness of target peripheral tissues towards insulin hormone, impairing its ability to suppress glucose production and promoting uptake of glucose in the peripheral tissues, leading to hyperinsulinemia. IR is characterized by disruptions in insulin-mediated blood glucose regulation, abnormalities in glucose utilization, excessive lipid storage, and increased lipid breakdown in adipocytes [15]. All of these makes it difficult for the cells to take up glucose from the blood, thus leading to elevated blood glucose levels. Chronic increase in blood glucose is known as type-II diabetes.

Adipose Tissue Insulin Resistance

The outcome of altered adipogenesis and ineffective control of blood glucose levels, insulin resistance and their altered pathways as outcomes are summarised in Table-3 and 4.

Table 3: This table captures the sequence of events and relationships between different processes related to adipocytes that lead to insulin resistance

Factors	Outcomes	
1.Altered adipogenesis	1. Reduced ability of adipocytes to store and secrete lipids. ⇩ Ectopic fat accumulation in non-adipose sites. ⇩ Insulin resistance. 2. Adipocyte hypertrophy ⇩ Adipocyte Hypoxia ⇙ ⇘	
2. Obesity induced WAT accumulation	Reduced adiponectin (insulin sensitizing adipokine) ⇩ Increased susceptibility to insulin resistance	Infiltration of pro-inflammatory cytokines (TNF alpha, IL-1β, MCP-1, IL-6) ⇩ Systemic metabolic inflammation ⇩ Insulin resistance
	Decreased angiogenesis (blood vessel formation). ⇩ Inefficiency in storage of excess energy ⇩ Insulin resistance.	

Legends: WAT= White Adipose Tissue

Table 4: This table captures the various dysregulations common in obesity that leads to hyperglycaemia and eventually type 2 diabetes.

Factors	Outcomes
1. Ineffective regulation of insulin	Increased delivery of free fatty acid delivery to the liver. ⇩ Hepatic gluconeogenesis upregulation ⇩ Elevated basal and post prandial glycaemic levels.
2. Improper activation of AKT protein	Activates lipolytic enzymes ⇩ Enhances lipolysis. ⇩ Impaired translocation of GLUT-4 on membranes. ⇩ Inefficient glucose transport across membranes. ⇩ Hyperglycaemia.

3. Obesity induced increase in free fatty acid (FFA) levels	Higher circulating FFAs. ⇩ Decreased glucose metabolism ⇩ Skeletal muscles prefer lipids as energy source. ⇩ Accumulation of glucose in the body. (Hyperglycaemia) ⇩ Increased insulin release as a compensatory mechanism. (Hyperinsulinemia) ⇩ Prolonged hyperglycaemia and hyperinsulinemia lead to type 2 diabetes.

Legends: AKT= Protein Kinase B; FFA= Free Fatty Acid

Tables 3 and 4 present a flowchart outlining the relationships and processes involving adipocytes, adipogenesis, inflammation, insulin resistance, and obesity. Each step is logically connected to illustrate how one parameter influences the next.

In obese individuals, elevated levels of free fatty acids (FFAs), resulting from increased lipid oxidation, play a pivotal role in the onset of insulin resistance. Lipid overflow, characterized by excessive circulating FFAs, impairs glucose metabolism and shifts skeletal muscle energy preference toward fatty acid utilization (Figure 2). The consequent suppression of glucose metabolism downregulates glycogen synthase activity, thereby restricting glycogen-derived glucose utilization. Over time, this metabolic inflexibility leads to systemic glucose accumulation, eliciting a compensatory hyperinsulinemic response. Chronic hyperglycemia coupled with sustained hyperinsulinemia ultimately drives the pathophysiological progression to type 2 diabetes mellitus [1].

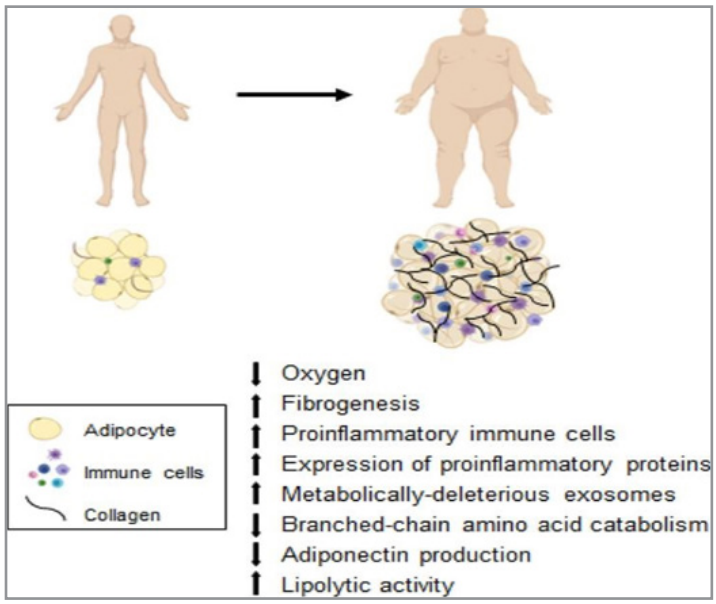

Figure 2: Adipose tissue Changes due to Metabolic Dysfunction – Source-Reference [7]

Hepatic Insulin Resistance

Once again, we focus on the role of the liver, which plays a crucial role in glucose production in the body, primarily through two processes: glycogenolysis and gluconeogenesis, which occur at nearly equal rates in healthy individuals. However, in people who are obese or have type 2 diabetes, there is a marked increase in gluconeogenesis compared to glycogenolysis. This heightened gluconeogenesis by the liver is a key factor contributing to high blood sugar levels during fasting. Furthermore, insufficient suppression of glucose production and gluconeogenesis by the liver after meals leads to elevated blood sugar levels post-meal in individuals with glucose intolerance [7].

Insulin is responsible for regulating glucose production in the liver. However, individuals with obesity often experience insulin resistance, which impairs the effectiveness of insulin. To compensate, their pancreatic beta cells produce more insulin, resulting in hyperinsulinemia. This can maintain normal fasting

and post-meal blood sugar levels temporarily. However, when hyperinsulinemia is no longer effective or when insulin secretion diminishes, as seen in type 2 diabetes, liver glucose production increases, resulting in systemic high blood sugar levels. Additionally, insulin resistance in adipose tissue prevents the proper suppression of fat breakdown, increasing the levels of free fatty acids in the liver. This further stimulates gluconeogenesis and worsens insulin resistance in the liver [7].

Skeletal Muscle Insulin Resistance

Skeletal muscle depends on free fatty acids to produce energy during basal conditions. After ingestion of a meal, there is a spike in glucose, which leads to increased secretion of insulin, which suppresses lipolysis, thereby reducing the availability of free fatty acids, and increasing glucose uptake by the muscles. It does so by binding to myocyte insulin receptor, which leads to a series of cascade intracellular signalling reactions aiding to the translocation of GLUT4 on to the plasma membrane, thereby facilitating the entry of glucose into the myocytes. However, in obese and diabetic patients, skeletal muscle insulin resistance impairs this glucose metabolism process due to reduced number and function of insulin receptors along with defects in post receptor insulin signalling, leading to suppressed glucose oxidation and glycogen synthesis in the muscle. Additionally, the increased accumulation of intra- and inter-myocellular lipids common in obesity and type 2 diabetes, impairs skeletal muscle insulin signalling, eventually causing insulin resistance in skeletal muscles. This results in decreased uptake of glucose by the muscles, aiding type 2 diabetes development [7].

Autophagy

Autophagy is a vital cellular process of disposing and eliminating toxic cellular components by the cells itself to maintain cellular quality and organ function. Dysregulated autophagy (enhanced or suppressed) leads to various metabolic disorders like obesity, type 2 diabetes and cancer. Autophagy is regulated by mechanistic target of rapamycin (mTOR) kinase and autophagy related protein (ATG) family [3]. In situations of overnutrition, common in obesity, mTOR gets hyperactivated, suppressing autophagy. On the contrary, adipose tissue shows enhanced autophagy, primarily as a compensatory anti-inflammatory mechanism to cope with increased inflammation of adipose tissue which is common in obesity. However, enhanced autophagy in adipose tissue promotes intracellular lipid disposal and reduced lipolysis and proteolysis, ultimately leading to accumulation of visceral fat and insulin resistance [3]. Additionally, adipose tissue expansion and chronic inflammation cause dyslipidaemia. All of these leads to insulin resistance making the cells less responsive to insulin. As a compensatory mechanism pancreas increases the secretion of insulin, leading to hyperinsulinemia. Prolonged hyperinsulinemia results in the onset of type 2 diabetes [3].

Pathophysiology of the Two Conditions

Inflammation Affecting Innate Immune System

Obesity leads to chronic low-grade inflammation, which triggers the activation of the innate immune system. This happens because the excess buildup of adipose tissue is perceived by the body as a stress signal. In addition, this inflammation is worsened by the uncontrolled release of pro-inflammatory cytokines from adipocytes and macrophages within the adipose tissue. These cytokines include TNF, interleukin-1β, IL-6, IL-8, leptin, resistin, and monocyte chemoattractant protein 1 (MCP1). At the same time, there is a decrease in anti-inflammatory cytokines like IL-10 and adiponectin due to tissue remodelling caused by adipocyte apoptosis. This balance between pro-inflammatory and anti-inflammatory signals leads to impaired insulin signalling and contributes to insulin resistance [3].

Chronic low-grade inflammation in the pancreatic islets gradually deteriorates beta cell mass and function, eventually causing diabetes. In the liver, inflammation leads to macrophage infiltration, which impairs hepatic insulin sensitivity and disrupts glucose metabolism. Inflammation also enhances lipolysis, increasing the delivery of free fatty acids and glycerol to the liver. This process promotes glucolipotoxicity and hyperglycaemia, further disrupting glucose homeostasis. Moreover, the activation of inflammatory pathways such as NF-κB and other protein kinases like inhibitor of NF-κB kinase subunit-β (IKK-β), IKK-ϵ, Jun N-terminal kinase (JNK), and protein kinase Cγ (PKCγ) interferes with insulin signalling. This interference leads to systemic metabolic dysfunction and Diabetes.

Beta Cell Dysfunction and Apoptosis

The development of type-II diabetes through obesity and insulin resistance occurs due to impaired glucose stimulated insulin secretion and loss of function in beta cells. This functional loss in beta cells is promoted by the dedifferentiation of beta cells to endocrine like progenitor cells and trans differentiation of beta cells to other cell types. Importantly, it is not possible for the newly generated beta cells to compensate for the loss of beta cells as the human pancreas is incapable of beta cell neogenesis or replication beyond the age of 30. Currently, various therapeutic strategies have been developed and are undergoing testing and validation to reverse this process by stimulating β-cell neogenesis and regeneration for the treatment of both T1DM and T2DM. Furthermore, prolonged hyperglycaemia and hyperlipidaemia, which are common in obesity induce glucolipotoxicity, exacerbating β-cell dysfunction by impairing insulin secretion and promoting β-cell apoptosis. Moreover, the chronic exposure to overnutrition and increased hormone synthesis and secretion in obesity causes endoplasmic reticulum stress (ER stress) which negatively impacts β-cell function and survival. To compensate for insulin resistance in peripheral tissues, the demand for insulin production rises, overloading the ER's protein-folding capacity. This results in the activation of the unfolded protein response (UPR) and PKR-like ER-associated kinase (PERK), which ultimately inhibit protein translation and contribute to insulin deficiency. Over time, this prolonged stress accelerates β-cell dedifferentiation and apoptosis, further exacerbating insulin deficiency. Despite the importance of short-term ER stress responses for maintaining β-cell homeostasis, chronic stress—particularly in the context of lipid overload—leads to irreversible β-cell loss. This progressive β-cell dysfunction and loss are critical in the pathogenesis of T2DM [3].

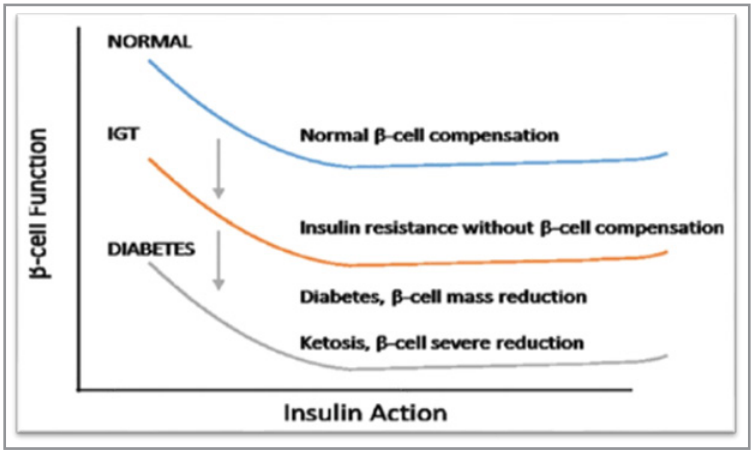

Figure 3: Decline of β-cell Function leading to Diabetes Legends: IGT = impaired glucose tolerance'– Source Reference-16

Gut Microbiome Dysregulation

The gut microbiome plays an essential role in regulating metabolism, adiposity, energy balance, and appetite signalling, all of which are crucial in the development of obesity and type-II diabetes mellitus (T2DM), with microbiome dysfunction contributing to energy imbalance, fat deposition, inflammation, insulin resistance, glucolipotoxicity, and endocrine signalling disruptions [3]. Larsen et al. reported that an alteration in composition of gut microbiome was observed in T2DM patients, particularly, lower levels of Firmicutes and increased Bacteroidetes and Proteobacteria, compared to control group [17]. A diverse microbiome is vital for maintaining health, with its composition shaped by factors such as diet, genetics, age, and medication [3]. Additionally, a reduction in microbiome diversity correlates with higher BMI, fat mass, inflammatory markers, and diminished insulin sensitivity and dyslipidaemia, all contributing to T2DM.Changes in microbiome composition also influence basal glycaemic levels and glycated haemoglobin (HbA1c) levels that promote T2DM development as shown in figure -4. These include modifications in gastrointestinal peptides, appetite control, fat storage, liver lipid metabolism, and glucose regulation. The microbiome's conversion of dietary nutrients into metabolites regulates both central and peripheral metabolic functions, impacting insulin signalling and inflammation, which are central to T2DM onset. Bile acids (BAs) are key signalling molecules that regulates metabolism by activating receptors in the gut, liver, and adipose tissue [3].

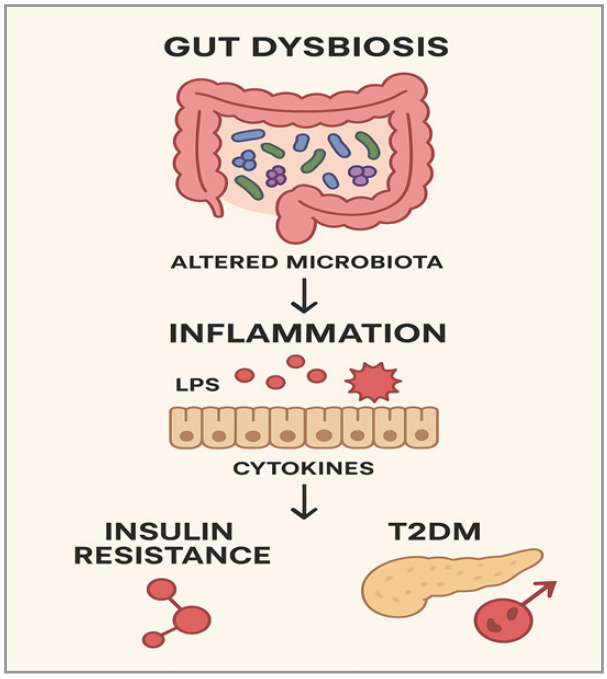

Figure 4: Altered microbiota causing T2DM and Insulin resistance:Legends: LPS = Lipopolysaccharide

The human gut harbours trillions of microorganisms—predominantly bacteria from the phyla Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. These microbes contribute to nutrient metabolism, immune modulation, and maintenance of gut barrier integrity. Dysbiosis, or the loss of microbial diversity and function, has emerged as a hallmark of metabolic disorders such as obesity and T2DM [18]. Obese individuals typically show an increased Firmicutes-to-Bacteroidetes ratio, accompanied by enrichment of energy-harvesting taxa such as Clostridium, Lactobacillus, and Eubacterium, and reduction of beneficial Bacteroides species. This compositional shift enhances the gut's ability to extract energy from indigestible polysaccharides, leading to increased caloric availability and adiposity [19].

Dysbiosis induces gut barrier dysfunction, allowing lipopolysaccharide (LPS) translocation into circulation—known as metabolic endotoxemia. LPS activates TLR4 signalling, leading to systemic low-grade inflammation characterized by increased IL-6 and TNF-α, cytokines strongly associated with insulin resistance and β-cell dysfunction. This establishes a chronic inflammatory milieu linking gut dysbiosis to obesity-induced insulin resistance [20].

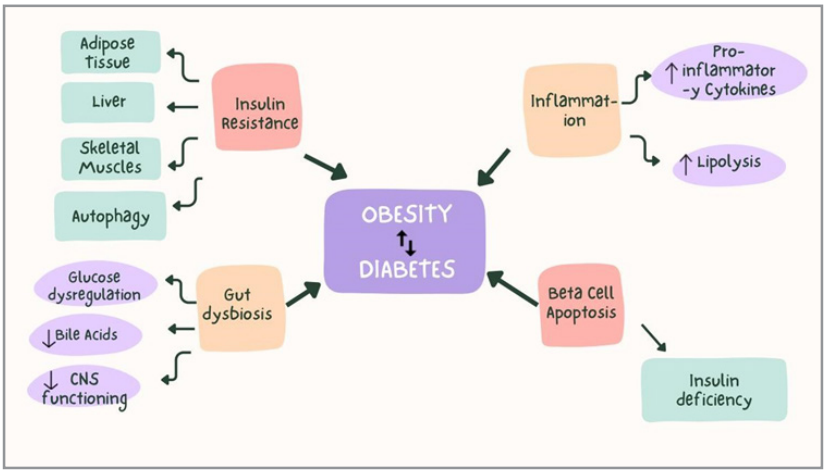

Figure 4: Common Factors leading to Obesity and Diabetes

The gut microbiome influences synthesis, modification and uptake of bile acids. These stimulate GLP-1 secretion and regulate genes involved in metabolism, energy balance, and inflammation. The gut microbiome and BAs have a bidirectional relationship, and disruptions in BA metabolism, along with dysbiosis, contribute to metabolic disorders such as obesity and T2DM [3].

Gene–Microbiome Interactions

Host genetic variants (e.g., TCF7L2, PPARG, FTO) may modulate gut microbiota composition and function. For example, FTO risk alleles correlate with reduced microbial diversity and altered butyrate synthesis [21]. Epigenetic changes induced by microbial metabolites—especially SCFAs acting as histone deacetylase inhibitors (HDACi)—affect genes regulating lipogenesis and insulin signalling [22]. Gut microbiome dysregulation represents a central mechanistic node linking diet, inflammation, and host metabolism in obesity and T2DM. Integrative multi-omics approaches (metagenomics, metabolomics, and epigenomics) are essential to unravel host–microbe crosstalk and to develop precision microbiota-based therapies for metabolic diseases [23]. The nervous system plays a critical role in regulating metabolic balance, particularly glycemia. The central nervous system (CNS) monitors blood glucose fluctuations throughout the day, while the autonomic nervous system (ANS), including the enteric nervous system (ENS) and the vagus nerve (VN), senses glucose variations along the gastrointestinal (GI) tract and portal vein during digestion. This coordination adjusts the release of glucose-regulating hormones and peptides to maintain metabolic homeostasis. Disruptions in the gut microbiome can impair ENS and VN functionality, leading to metabolic dysregulation [3].

Conclusion and Future Directions

Obesity plays a pivotal role in the pathogenesis of type 2 diabetes mellitus (T2DM), driven by complex interactions between metabolic, genetic, and environmental factors. Key contributors such as insulin resistance, chronic low-grade inflammation, and dysregulated lipid metabolism underline the progression from obesity to T2DM. Alterations in the lipid profile, including elevated triglycerides, reduced HDL, and increased LDL levels, serve as important biomarkers and mediators of this transition. These insights emphasize the urgent need for early identification and management of obesity to prevent or delay the onset of T2DM. Lifestyle modifications, personalized medical interventions, and public health strategies focusing on weight reduction and metabolic health optimization are critical in addressing this growing health crisis. The gut microbiome is now recognized as a crucial metabolic organ that interacts intricately with host genetics, diet, and immunity. Its dysregulation ("dysbiosis") is a key factor linking obesity and type 2 diabetes mellitus (T2DM) through multiple metabolic and inflammatory pathways. Future research should focus on unravelling the genetic and molecular mechanisms underlying obesity-induced T2DM. Studies exploring the role of novel biomarkers, including adipokines and inflammatory cytokines, could provide deeper insights into disease progression and therapeutic targets. Additionally, advancements in precision medicine, integrating genomics, metabolomics, and lipidomics, may offer personalized approaches to risk assessment and novel treatment strategies. Investigating the long-term impacts of emerging interventions such as anti-obesity pharmacotherapies, bariatric surgery, and gut microbiome modulation will further enhance our understanding of effective strategies to combat obesity-related T2DM. Collaborative efforts between clinicians, researchers, and policymakers are essential to address the dual burden of obesity and T2DM, ultimately improving global health outcomes.

Declarations

Conflict of Interest

All authors declare no conflict of interest.

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