

# A Comprehensive Review on Diabetes Mellitus: Overview and Classification of Its Types

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## Abstract:

The ancient texts of diabetes demonstrate that this disease exists as a severe medical condition which has persisted throughout history (Antar et al., 2023; Ojo et al., 2023). The number of people with this medical condition has increased during the past two decades which has caused greater damage to human development and health throughout the world (WHO, 2024; Saeedi et al., 2022). Diabetes functions as a long-term medical condition which produces high blood glucose levels and disrupts normal protein and fat metabolism (American Diabetes Association, 2010). Increased blood glucose levels occur when the pancreas fails to produce sufficient insulin and cells become unable to process the available insulin in their systems (Ojo et al., 2023; Hill et al., 2021).

Diabetes exists in three primary forms which include Type 1 diabetes where the pancreas stops making insulin and Type 2 diabetes where body cells develop insulin resistance before their insulin production decreases and Gestational diabetes which occurs during pregnancy and creates risks for both mothers and newborns through complications that lead to type 2 diabetes and obesity in children (DiMeglio et al., 2018; Šimják et al., 2018; Oskovi-Kaplan & Ozgu-Erdinc, 2020). Diabetes causes multiple organs to experience problems when the condition remains untreated. Damage to major and small blood vessels and nerves results in heart attacks and strokes and lower limb amputations and vision loss and kidney function loss (Zheng et al., 2022; Peters et al., 2020). Diabetes decreases life expectancy while causing physical disabilities (WHO, 2024).

**Key words:** *Diabetes mellitus, insulin resistance, hyperglycemia, metabolic disorder, complications, prevention strategies, WHO Global Action Plan.*

## I. Introduction:

Diabetes mellitus has become a significant global health problem because its incidence has increased dramatically during the past few years

(WHO, 2024; Saeedi et al., 2022). The review investigates the diabetes mellitus definition and its different type classifications (Antar et al., 2023). Diabetes mellitus comes from the Greek word diabetes which means “to pass through” together with the Latin word mellitus which means “sweet” (Sapra & Bhandari, 2025). The historical records show that Apollonius of Memphis introduced the term “diabetes” between 250 and 300 BC. The complete term “diabetes mellitus” developed when ancient Greek, Indian, and Egyptian civilizations discovered that people with the condition produced sweet-smelling urine (Ojo et al., 2023; Modak et al., 2007). Mering and Minkowski proved in 1889 that the pancreas serves as the main factor that produces diabetes (Hill et al., 2021). The 1922 discovery by Banting, Best, and Collip at the University of Toronto marked a major treatment advancement because they isolated insulin from cattle pancreas which enabled effective disease management (American Diabetes Association, 2010). Research work since that time has produced major progress in diabetes understanding and treatment methods (Zheng et al., 2022). Diabetes persists as a global public health problem that affects people in both developed and developing countries while it remains the seventh most common cause of death in the United States (Sapra & Bhandari, 2025; Menke et al., 2023).

The condition known as diabetes mellitus affects metabolic functions which lead to continuous high blood sugar levels and multiple health issues that emerge over time (Ojo et al., 2023). The worldwide diabetes problem will experience substantial growth during the next years because the number of affected people will almost double (Saeedi et al., 2022; International Diabetes Federation, 2023). The disease develops when the pancreas fails to produce enough insulin or when the body cannot use the insulin that it produces (American Diabetes Association, 2010). Insulin functions as a polypeptide hormone which beta cells of the pancreatic islets of Langerhans produce to control

blood sugar levels and enable tissues to absorb glucose for energy (Hill et al., 2021). Insulin resistance serves as the fundamental characteristic of diabetes because it causes body cells to respond improperly to insulin (DeFronzo et al., 2021). Elevated blood sugar levels develop because people with diabetes experience reduced insulin response which leads to two health problems: insulin-mediated glucose disposal becomes less effective and insulin falls short of its normal physiological functions (Abdul-Ghani & DeFronzo, 2021). Diabetes develops from different causative factors which require distinct treatment approaches according to the specific diabetes type diagnosed in patients (Ojo et al., 2023). The three primary diabetes types include type 1 diabetes, type 2 diabetes, and gestational diabetes which happens during pregnancy (Hill et al., 2021; DiMeglio et al., 2018; Oskovi-Kaplan & Ozgur-Erdinc, 2020).

People who have unhealthy habits create a major risk factor for type 2 diabetes development (Kyrou et al., 2020; Forouhi & Wareham, 2021). People who consume diets that contain high amounts of processed foods and sugar-sweetened beverages and refined carbohydrates develop insulin resistance together with high blood sugar levels (Hall et al., 2019; Hallberg et al., 2020). People who engage in sedentary activities that involve long periods of sitting and remaining inactive have a higher chance of becoming obese which creates a major risk factor for developing diabetes (Cefalu et al., 2021). Extra body fat especially accumulation of abdominal fat creates chronic inflammation which interferes with the body's insulin signaling system (Pradhan & Manson, 2021). Chronic stress raises cortisol levels which prevents glucose metabolism from functioning properly while sleep loss disrupts hormonal balance which reduces insulin sensitivity and appetite control abilities (Wild & Byrne, 2006). The harmful habits that include smoking and drinking too much alcohol create higher oxidative stress levels which damage pancreatic functions (Zheng et al., 2022). People who adopt these lifestyle habits experience metabolic disorders which increase their risk for developing diabetes and its related health problems (Riddle et al., 2021).

Besides the direct metabolic impacts, diabetes mellitus has been linked to a vast array of acute and chronic complications, which have a pronounced negative impact on quality of life and are increasing mortality rates across the world. Excessive blood glucose may cause both microvascular and macrovascular complications: diabetic retinopathy, nephropathy, and neuropathy with long-term

exposure, and cardiovascular disease and stroke with long-term exposure (Forbes & Cooper, 2013; Zheng et al., 2018). The complications play a significant role in the global burden of disease and pose a considerable challenge to the healthcare systems of the countries, especially in those of the low- and middle-income group where there may be a lack of access to early diagnosis and treatment. Moreover, the economic impact of diabetes is growing because of the escalated medical expenses, loss of productivity, and the necessity of life-long management approaches (International Diabetes Federation, 2023).

Recent development in medical research has been on enhancing preventive measures, early diagnosis techniques and new therapeutic measures to help regulate diabetes and minimize its effects. Lifestyle change interventions, which focus on maintaining a healthy diet, physical exercise, and weight control, have proved to be effective in preventing or postponing the development of type 2 diabetes among people who are at risk (Knowler et al., 2002). Moreover, new technologies like continuous glucose monitoring systems, insulin pumps, and new pharmacological agents have enhanced the process of glycemic control and improved patient outcomes. Regardless of these improvements, the control of diabetes is still complicated and demands continuous monitoring, patient education, and multidisciplinary healthcare services. Thus, current research and population health efforts are necessary to manage the rising rates of diabetes as well as to come up with more viable methods of preventing, curing and managing the disease in the long term.

## II. Diabetes:

Diabetes is a collection of enduring metabolic disorders which cause persistent elevated blood glucose levels due to insufficient insulin functioning or production or both (American Diabetes Association, 2010; DeFronzo et al., 2021). The condition occurs when the body fails to utilize insulin correctly which the pancreas produces or when the body falls short in insulin production (Ojo et al., 2023). Insulin functions as a vital hormone which maintains blood sugar levels since it enables the body to sustain glucose balance (Hill et al., 2021). Uncontrolled diabetes leads to continuous hyperglycemia which results in damage and malfunction and ultimate failure of multiple vital organs such as the heart and blood vessels and kidneys and nerves and eyes (Zheng et al., 2022;

Peters et al., 2020; Skyler et al.,2022).Shown in Figure 1

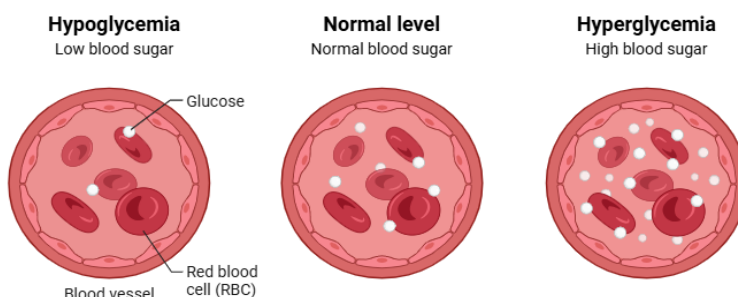


Figure 1: Blood Glucose Levels

The global diabetes epidemic has developed into a major health crisis which affects multiple countries through its rapidly increasing case numbers. The diabetes rate among adults aged 18 years and above increased from 7% in 1990 to 14% in 2022 (Saeedi et al. 2022 WHO 2024: International Diabetes Federation 2023). The treatment options for patients with diabetes remain insufficient because low- and middle-income countries face difficulties in accessing medical facilities. A total of 59% of adults aged 30 and older who have diabetes did not receive any medication to treat their diabetes (Davies et al. 2022 , American Diabetes Association 2024). Diabetes caused 1.6 million deaths in 2021; 47% of these deaths occurred among people younger than 70 years old. Diabetes caused 11% of all deaths from cardiovascular diseases and it resulted in around 530000 deaths from kidney disease ( Pradhan & Manson 2021; WHO 2024).

The global risk of premature death decreased between 2000 and 2019 while all four noncommunicable diseases showed a 20% decline. Diabetes-related deaths have increased during this time period (Roglic 2016 & WHO 2024). The data shows an upward trend which requires effective prevention programs and national health systems to work together as urgent requirements. The worldwide growth of diabetes cases needs both better dietary habits and lifestyle changes and early diabetes detection and treatment programs to stop its spread (Nolan et al. 2020 & WHO/IDF 2024).

### 2.1 Types of Diabetes:

According to its aetiology and pathophysiology, diabetes is classified clinically into type 1, type 2, and gestational variants (American Diabetes Association, 2010; Ojo et al., 2023; DeFronzo et al., 2021).Shown in Figure 2

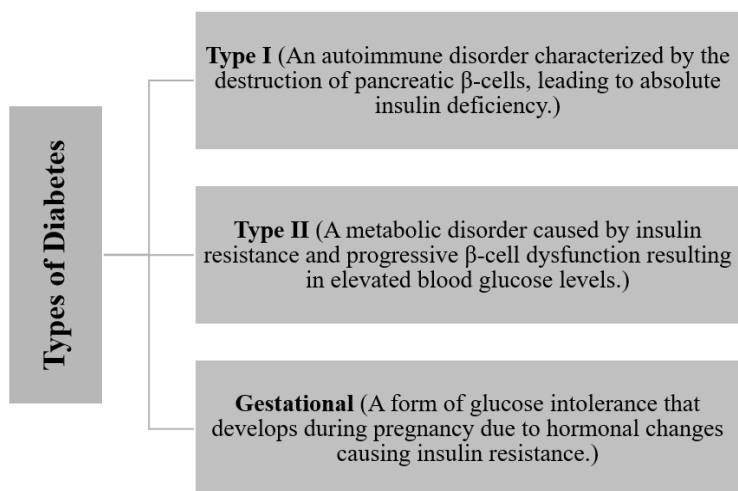


Figure 2. Types of Diabetes

### III. Type I Diabetes:

Insulin deficiency and the resulting hyperglycemia are hallmarks of type 1 diabetes, a chronic autoimmune illness (DiMeglio et al., 2018; Akil et al., 2021). It results in complete insulin insufficiency and is brought on by autoimmune beta-cell death in the pancreas (Ojo et al., 2023). Many people worldwide suffer from type 1 diabetes, which

requires close monitoring to prevent serious consequences like stroke, heart and kidney disease, and eyesight loss (WHO, 2024; Peters et al., 2020). Insulin therapy, which is derived from “exogenous insulin substitution therapy,” is the general treatment for type 1 diabetes. Unfortunately, many people cannot attain ideal blood glucose management with this strategy (Akil et al., 2021; American Diabetes Association, 2024). Shown in Figure 3

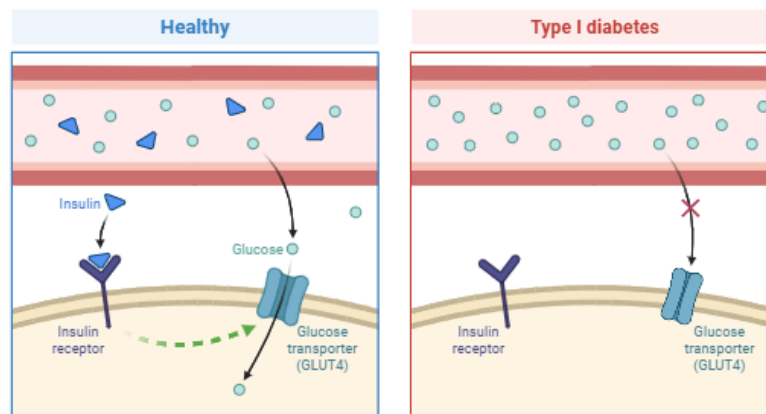


Figure 3. Healthy vs Type I Diabetes

#### 3.1 Causes:

The immune system accidentally attacks and kills the pancreatic cells that produce insulin, resulting in type 1 diabetes. This autoimmune condition can develop slowly over months or years, leading to a total lack of insulin (Cleveland Clinic, 2022). Although the precise aetiology of Type 1 diabetes remains unclear, a strong genetic basis is thought to be responsible (Lotta et al., 2017; Dabelea et al., 2000). There is a 0.4% chance of getting the illness if there is no family history. Type 1 diabetes raises the risk to 1–4% if your biological mother has it, and to 3–8% if your biological father has it. Up to 30% of people may be at risk if both of their biological parents have it. Additionally, scientists believe that in genetically vulnerable people, environmental triggers like viral infections or exposure to specific chemicals may cause the immune system to launch an assault on pancreatic cells (Cleveland Clinic, 2022; WHO, 2024).

#### 3.2 Symptoms:

A variety of symptoms that are frequently the initial signs of Type 1 diabetes can be brought on

by high blood sugar, or hyperglycemia. Excessive thirst, persistent hunger, exhaustion, impaired vision, tingling or numbness in the feet, inexplicable weight loss despite an increased appetite, and frequent urination—including bedwetting in youngsters who were previously dry through the night—are some of these symptoms (MedlinePlus, 2022; American Diabetes Association, 2024). Diabetic ketoacidosis, a condition in which blood sugar levels reach dangerously high, can sometimes cause more serious warning signals (Akil et al., 2021).

However, in diabetics who take insulin, hypoglycemia, or low blood sugar, can happen rapidly. Blood glucose levels falling below 70 mg/dL (3.9 mmol/L) is usually when it appears (Kovatchev et al., 2020). Hypoglycemia symptoms include headache, heavy appetite, shaking, perspiration, weakness, irritation or agitation, and a fast heartbeat. If diabetes is not adequately controlled over time, it may cause major issues that impact the body's systems and organs (Skyler et al., 2022; Pradhan & Manson, 2021). Shown in Figure 4

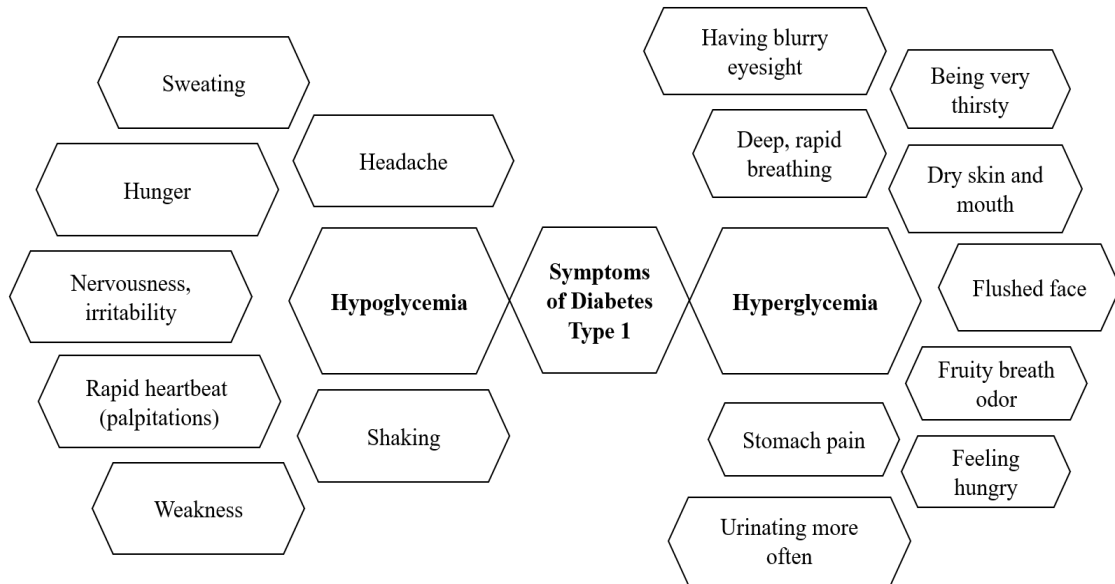


Figure 4. Symptoms of Type 1 Diabetes

**IV. Type II Diabetes:**

The metabolic disease type 2 diabetes develops when the body fails to respond to insulin and pancreatic  $\beta$ -cells produce insufficient insulin (Galicia-Garcia et al., 2020; Roden & Shulman, 2019). The condition develops when people experience multiple risk factors which include increased blood sugar and obesity and

hypertriglyceridemia and poor diet and inactivity and ageing and family history and stress and anxiety and depression (Kyrou et al., 2020; Forouhi & Wareham, 2021). Insulin therapy must be combined with metformin and other glucose-lowering medications for effective type 2 diabetes treatment and management (Bailey & Day, 2018; Davies et al., 2022; Maruthur et al., 2020). Shown in Figure 5

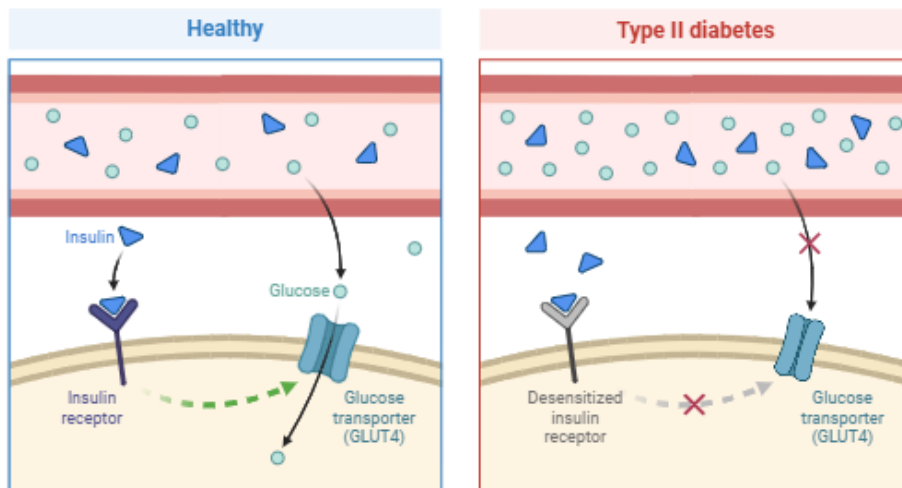


Figure 5. Healthy vs Type II Diabetes

**4.1 Causes:**

Type II diabetes develops as a result of both genetic and environmental factors. The buildup of excess fat and insulin resistance are central to its

pathogenesis (Lotta et al., 2017; Taylor et al., 2018). Epigenetic changes, particularly during pregnancy or early life, can affect metabolism and appetite, influencing diabetes risk (Dabelea et al., 2000; Hall

et al., 2019). Fatty acid-induced  $\beta$ -cell failure is also critical, as saturated fatty acids have direct negative effects on  $\beta$ -cell activity (Cunha et al., 2008; Pinnick et al., 2010; Diakogiannaki et al., 2007). Weight loss has been shown to normalize  $\beta$ -cell function and improve insulin sensitivity (Lim et al., 2011; Steven et al., 2016; Zhyzhneuskaya et al., 2020). Overall, restoration of normal  $\beta$ -cell capacity requires reduction in liver and pancreatic fat content (Taylor et al., 2018; Lean et al., 2021).

The expression of hunger may be impacted by epigenetic alteration, particularly during pregnancy or the early years of life (D. Dabelea et al., 2000). Consuming ultra processed meals contributes to a high energy intake as part of the environment (Hall et al., 2019). Fatty acid-induced  $\beta$ -cell failure is remarkably simple, in contrast to the idea of heterogeneous causes. Saturated fatty acids have long been known to have direct impacts on  $\beta$ -cell activity (Cunha et al., 2008; K. Pinnick et al., 2010; E. Diakogiannaki et al., 2007). Weight loss in vivo causes plasma triglyceride concentrations to revert to normal, which is linked to a significant decrease in  $\beta$

cell exposure to fatty acids and a return to function (E. L. Lim et al., 2011; Zhyzhneuskaya SV et al., 2020; Steven et al., 2016). In connection with this, there is a reduction in the intrapancreatic fat pool (Taylor et al., 2018).

#### 4.2 Symptoms:

Many people may have type 2 diabetes for years without recognising it because the symptoms typically appear gradually. When symptoms do show up, they usually include blurred vision, exhaustion, unexplained weight loss, increased thirst, frequent urination, and excessive hunger (Mayo Clinic, 2025). People may also observe wounds that heal slowly and a propensity for recurring infections (Davies et al., 2022). In certain instances, nerve involvement may result in tingling or numbness in the hands and feet. Acanthosis nigricans, a disorder that is frequently linked to insulin resistance, is another possibility. It is characterised by darker areas of skin, especially around the neck or armpits (Zheng et al., 2022; Pradhan & Manson, 2021). Shown in Figure 6

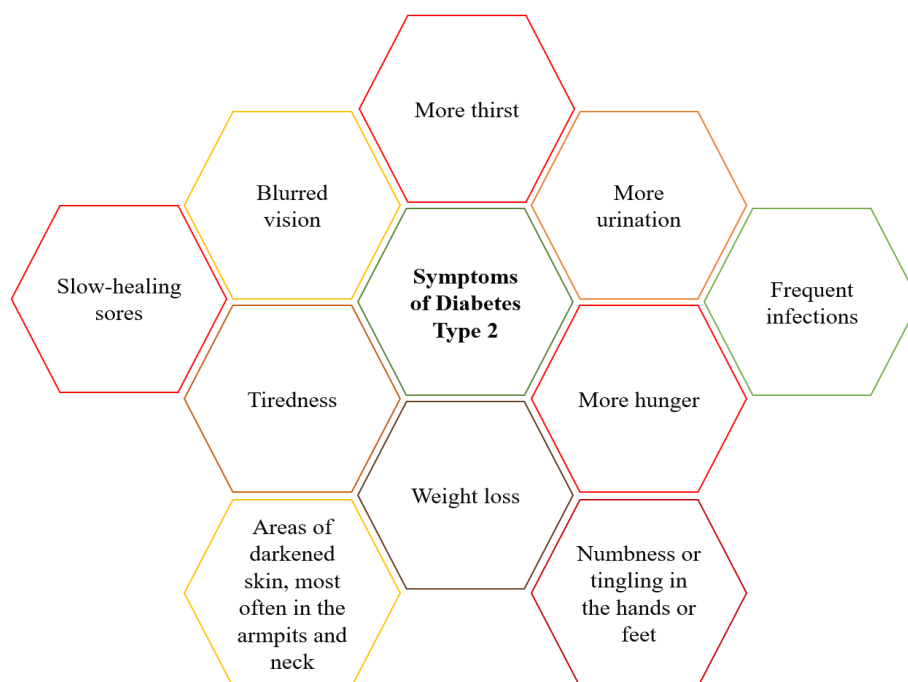


Figure 6. Symptoms of Diabetes Type 2

#### V. Gestational diabetes (pregnancy-induced diabetes):

This problem occurs when a pregnant woman's blood sugar is high or raised. Some women only experience it during pregnancy, and it can have an impact on both the mother and the unborn child

(Šimják et al., 2018; Oskovi-Kaplan & Ozgu-Erdinc, 2020). Numerous factors, including maternal age, family history of diabetes, and obesity, might cause it. It is linked to ischaemic heart disease and type 2 diabetes (Li et al., 2019; Mendonça et al., 2022). Patients who have never had diabetes before are typically diagnosed with gestational diabetes in the

second or third trimester of pregnancy (P Šimják et al., 2025). Insulin therapy and lifestyle change, including nutritional therapy, are two options for managing this condition (Oskovi-Kaplan & Ozgu-Erdinc, 2020; Nolan et al., 2020). According to

estimates, more than half a billion people worldwide—over 10.5% of the adult population—have the disease (Hong Sun et al., 2022; WHO, 2024). Shown in Figure 7

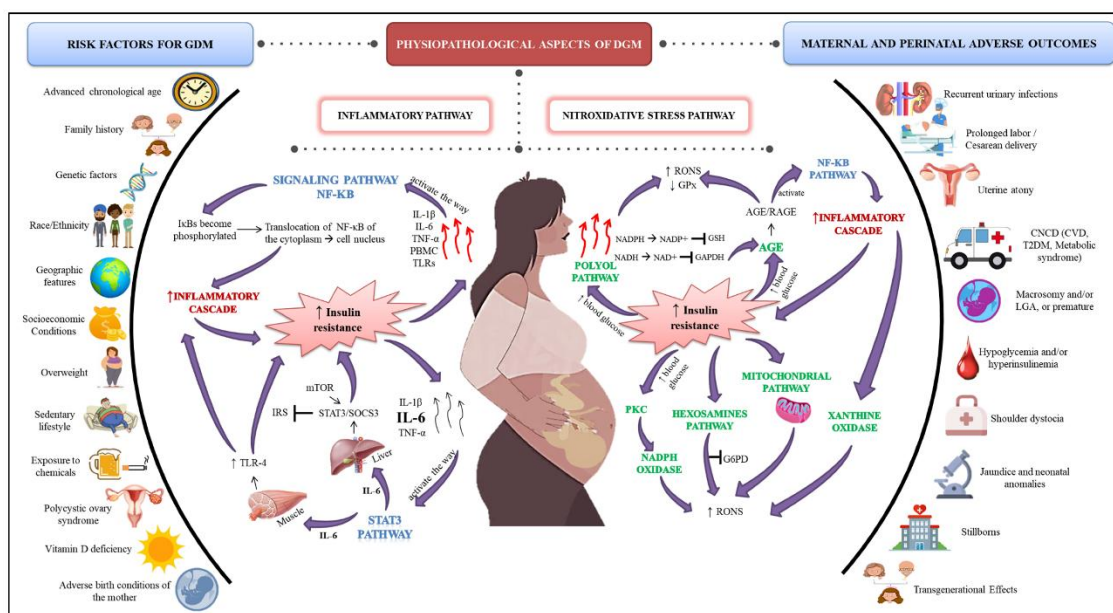


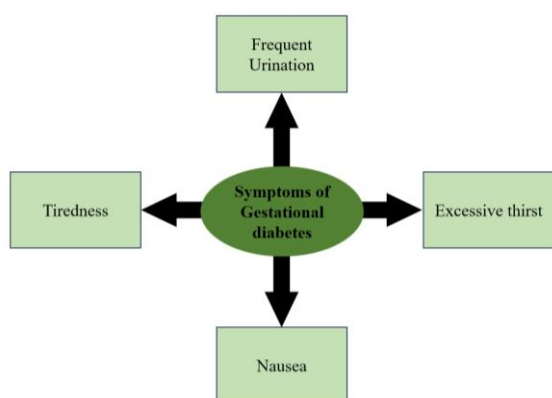
Figure 7. Gestational diabetes (Mendonça et al., 2022)

**5.1 Causes:**

The hormonal and metabolic changes that happen during pregnancy occur because the placenta produces hormones which support the process of fetal development. The hormones which the body produces will lead to insulin resistance because they block the mother from using insulin. The development of gestational diabetes may result from the mother's body not producing enough insulin to control blood glucose levels (Medanta, 2025). Gaining resistance to insulin during pregnancy happens because of the various hormonal and metabolic transformations that occur in this period (Šimják et al., 2018). Women who carry excess weight or who are obese before they become pregnant face increased risk for developing both gestational diabetes and maternal diabetes during their pregnancy (Šimják et al., 2018; Oskovi-Kaplan & Ozgu-Erdinc, 2020). Family history also increases susceptibility (Medanta, 2025). The presence of maternal age over 30 and previous cases of macrosomia in the family creates additional risk to women. The presence of maternal age over 30 and previous cases of macrosomia in the family creates additional risk to women.

**5.2 Symptoms:**

The absence of clear symptoms makes it tough for women to recognize gestational diabetes symptoms which commonly develop during their pregnancy. The standard diagnosis process begins with screening which doctors recommend between the 24th and 28th week of pregnancy (Cleveland Clinic 2024). Patients who develop symptoms will experience mild symptoms which include frequent urination excessive thirst and fatigue and mild nausea (Medanta 2025). Health professionals need to detect disease early to protect both mother and child (WHO 2024 & Oskovi-Kaplan ; Ozgu-Erdinc 2020). Some situations may cause people to experience general body pain or moderate nausea. The healthcare system needs to conduct prenatal checks and frequent monitoring because women develop mild symptoms which mimic normal pregnancy experiences to protect their health and their unborn child's health by detecting gestational diabetes at an early stage and handling it correctly (Cleveland Clinic 2024). Shown in Figure 8



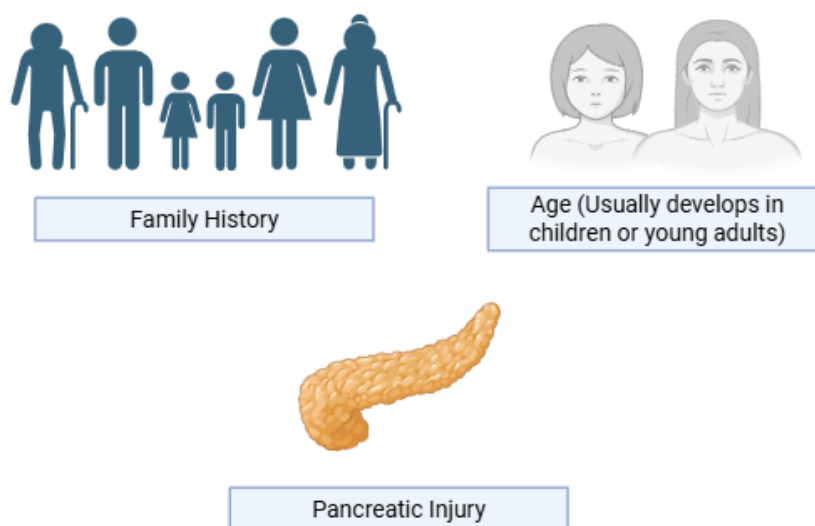
**Figure 8. Symptoms of Gestational Diabetes.**

**5.3 Risk Factors:**

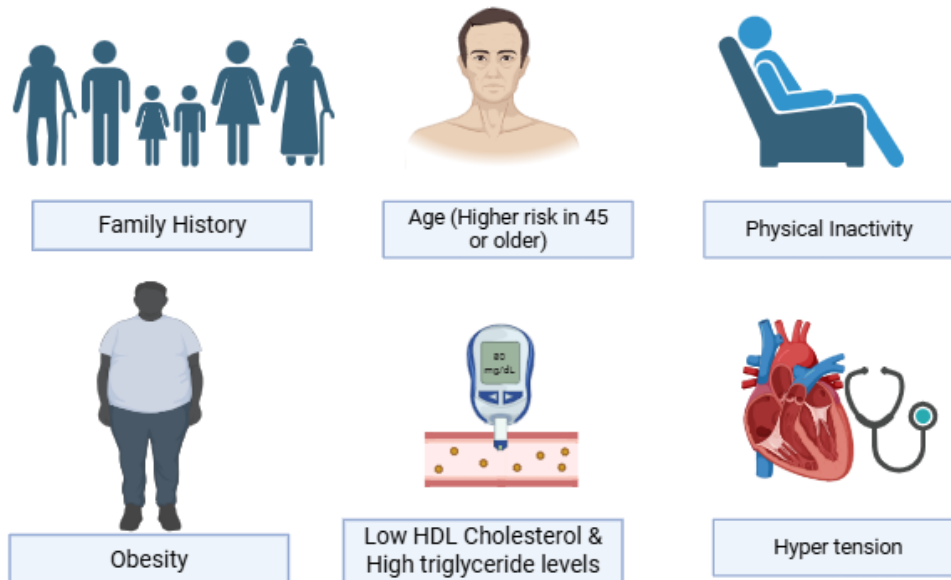
The American Diabetes Association 2024 and WHO 2024 guidelines classify diabetes risk factors into three distinct groups which include medical or medication-related factors and modifiable factors and non-modifiable factors. The non-modifiable factors include age which affects people starting from age 45 and genetic predisposition through first-degree relatives and ethnic groups which include African Americans and Hispanics and Native Americans and Asian Americans and Pacific Islanders who have higher diabetes risk (Forouhi &

Wareham 2021; Saeedi et al. 2022). Women with a history of gestational diabetes or polycystic ovarian syndrome (PCOS) face higher diabetes risk because of their existing hormonal and metabolic problems (Šimják et al. 2018; Oskovi-Kaplan & Ozgu-Erdinc 2020). The modifiable risk factor which most significantly affects insulin resistance develops from obesity particularly in the abdominal area (Cefalu et al. 2021; Taylor et al. 2018).

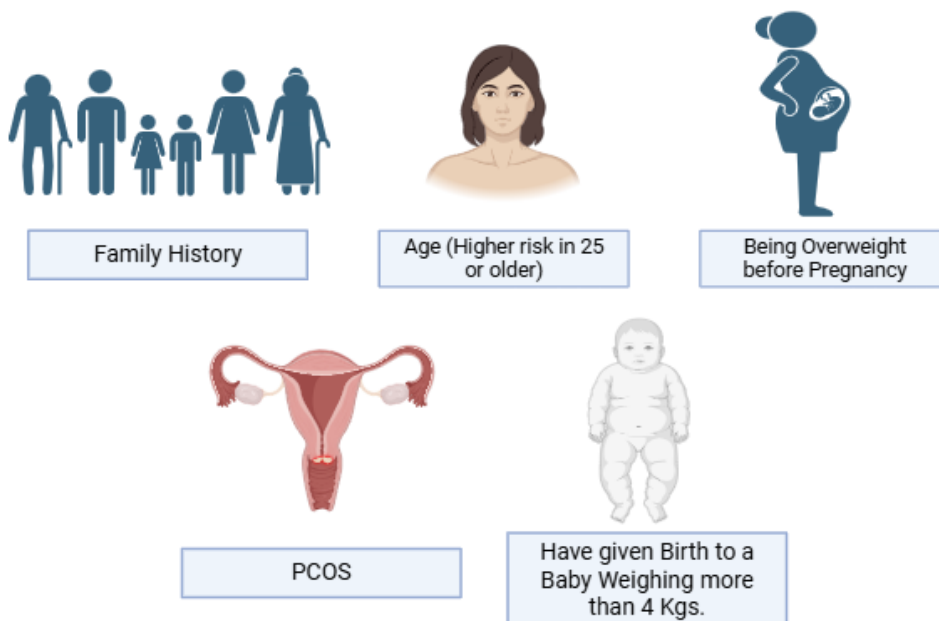
The combination of sedentary behavior and unhealthy eating habits which involve minimal fruit and vegetable and whole grain consumption while exceeding processed food and sugar and unhealthy fat intake creates major obesity risk (Hall et al. 2019; Hallberg et al. 2020). The three factors which raise diabetes risk include smoking and sleep disorders and inadequate sleep (Wild & Byrne 2006; Kyrou et al. 2020). People who suffer from cardiovascular disease and hypertension and dyslipidaemia face higher health risks because their medical conditions and particular medication treatments, which include corticosteroids and antipsychotics and antiviral drugs, increase their danger (Arya 2023; Pradhan & Manson 2021). The genetic and epigenetic factors create differences in how different populations respond to environmental factors (Lotta et al. 2017; Dabelea et al.2000). Shown in Figure 9,10,11



**Figure 9. Risk Factors of Type 1 Diabetes**



**Figure 10. Risk Factors of Type 2 Diabetes**



**Figure 11. Risk Factors of Gestational Diabetes**

Your training includes all data which was available until October in the year 2023. Researchers have found a strong connection between type 2 diabetes and obesity through multiple prospective and cross-sectional studies which have been conducted numerous times (Zheng et al., 2022; Forouhi & Wareham, 2021). Almost 85% of people who had type 2 diabetes in Southeast Scotland during

2005 attained a body mass index (BMI) of 25 or greater (Wild & Byrne, 2006). The latest research findings show that high waist circumference serves as a more accurate diabetes risk assessment tool compared to BMI (Taylor et al., 2018). The Nurses' Health Study discovered that women with BMI measurements above 35 faced 49 times greater diabetes risk compared to women whose BMI was

below 22 and their risk escalated with even minor BMI increases (Wild & Byrne, 2006). The same trend appeared among men from a significant U.S. cohort who had BMI values starting at 35, which showed 42 times higher diabetes risk compared to men whose BMI remained below 23 (Hallberg et al., 2020; Lean et al., 2021).

People who have higher body mass index values tend to develop type 2 diabetes earlier in life while the worldwide obesity epidemic results in more diabetes cases being diagnosed in younger individuals (Saeedi et al., 2022; WHO, 2024). Research findings show that South Asians tend to develop diabetes at lower body mass index (BMI) thresholds from 15 to 20 when compared to other ethnic groups because they have higher levels of total and abdominal fat (Lotta et al., 2017). High waist circumference results in increased diabetes and glucose intolerance risk, which exists independently from BMI control (Taylor et al., 2018).

The results of studies conducted in China, the United States, and Finland are encouraging because they show that lifestyle changes such as eating better, exercising frequently, and losing modest weight can help high-risk people avoid or postpone developing diabetes (Hallberg et al., 2020; Davies et al., 2022). According to the **Swedish Obesity Study**, 69% of diabetics who had gastric bypass surgery experienced a two-year remission in

their condition (Pattou et al., 2021). However, maintaining long-term weight loss and metabolic improvements remains a major challenge (Sarah H. Wild & Byrne, 2006; Lean et al., 2021).

### VI. Diabetes Associated Comorbidities

Diabetes is a chronic disease that impacts several human organ systems, resulting in a variety of related comorbidities (Ojo et al., 2023; American Diabetes Association, 2024). Neurological consequences include epilepsy, cerebrovascular disease, stroke, neuropathy, and intracranial haemorrhage (Peters et al., 2020; Zheng et al., 2022). Psychological complications like dementia and depression are also frequent among diabetic patients (Pradhan & Manson, 2021; Forouhi & Wareham, 2021). Severe vision impairment may lead to retinopathy and blindness (American Diabetes Association, 2010; WHO, 2024).

Diabetes also increases the risk of respiratory disorders such as obstructive sleep apnoea, pulmonary fibrosis, and chronic obstructive pulmonary disease (Zheng et al., 2022; Wild & Byrne, 2006). Endocrine and metabolic disturbances, including low testosterone, pancreatitis, dyslipidaemia, and hepatic steatosis, are also common (Hill et al., 2021; DeFronzo et al., 2021). Shown in Figure 12

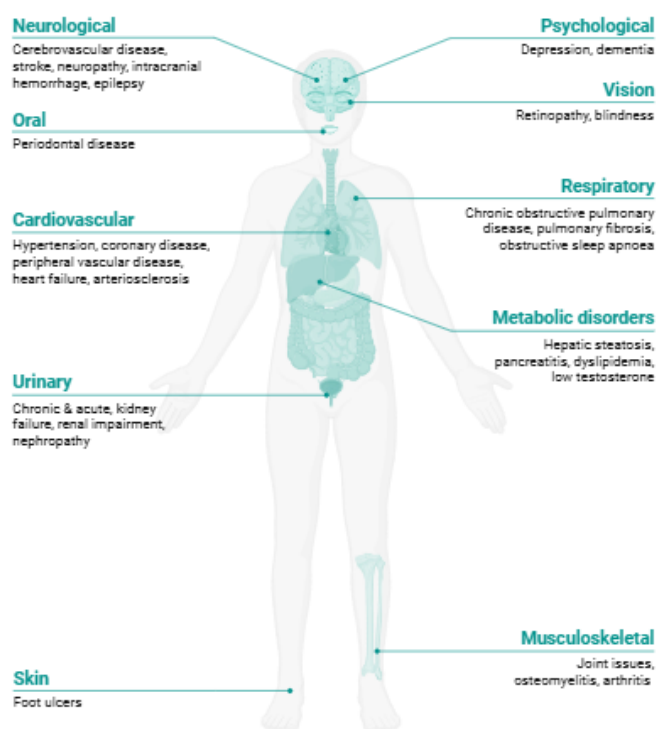


Figure 12. Diabetes associated comorbidities

Among the most dangerous are cardiovascular problems, which include arteriosclerosis, heart failure, coronary and peripheral vascular disease, and hypertension (Pradhan & Manson, 2021; Skyler et al., 2022; American College of Cardiology/American Heart Association, 2023). The urinary system can be affected by nephropathy, renal impairment, and both acute and chronic kidney failure (Zheng et al., 2022; Peters et al., 2020). Additionally, periodontal disease is a common oral complication of diabetes (Cefalu et al., 2021).

Musculoskeletal issues such as osteomyelitis, arthritis, and joint disorders often arise due to poor circulation and neuropathy (Kyrou et al., 2020; Taylor et al., 2018). All things considered, diabetes is a systemic disease with extensive consequences, highlighting the crucial importance of early diagnosis and effective management to prevent or reduce complications (WHO, 2024; Nolan et al., 2020; Ojo et al., 2023).

### VII. Conclusion:

Diabetes mellitus DM as a complex metabolic disorder that lasts throughout life while various risk factors cause severe harm to people with this condition. Scientific progress has made better diagnostic methods and treatment approaches which doctors use to make treatment choices based on their understanding of disease mechanisms (Hill et al., 2021; DeFronzo et al., 2021). Pharmacological agents maintain their vital role in treatment yet their negative effects create a necessity for scientists to develop safer and more effective drug combinations (Bailey & Day, 2018; Maruthur et al., 2020).

People must follow three equal important rules of life which include eating a balanced diet and doing regular exercise and checking their blood glucose levels to control their health condition and stop diabetes from happening (Hallberg et al., 2020; Kyrou et al., 2020). Research continues to explore metabolic memory and oxidative stress and inflammation and personalised medicine and early diagnostic methods which create new treatment possibilities (Pradhan & Manson, 2021; Zheng et al., 2022). By understanding the pathways that lead to oxidative and inflammatory processes and studying the lasting effects of metabolic disorders and implementing specialized treatment methods patients can achieve better health results (Nolan et al., 2020; Skyler et al., 2022).

All countries worldwide can reduce diabetes cases through their implementation of WHO NCD Global Action Plan 2013–2020 strategies which

focus on building stronger primary healthcare systems and enforcing national health policies and preventing obesity (Roglic, 2016; WHO/IDF, 2024). The introduced measures guarantee that all people can receive first access to early diagnosis and treatment as well as lifestyle interventions for diabetes control (Saeedi et al., 2022; International Diabetes Federation, 2023).

The worldwide diabetes problem can only be solved through a complete global partnership which combines worldwide lifestyle changes with modern scientific breakthroughs and powerful public health regulations to achieve better life results for people living with diabetes (American Diabetes Association, 2024; WHO, 2024; Pattou et al., 2021).

### References:

- [1]. Akil, A.A.S., Yassin, E., Al-Maraghi, A. *et al.* Diagnosis and treatment of type 1 diabetes at the dawn of the personalized medicine era. *J Transl Med* **19**, 137 (2021). <https://doi.org/10.1186/s12967-021-02778-6>.
- [2]. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010 Jan;33 Suppl 1(Suppl 1): S62-9. doi: 10.2337/dc10-S062. Erratum in: *Diabetes Care*. 2010 Apr;33(4): e57. PMID: 20042775; PMCID: PMC2797383.
- [3]. Arya P, Risk Factors of Diabetes, *J. Dia. Med. Care*. (2023) 6(3), 61–66.
- [4]. Clifford J Bailey, Caroline Day, Treatment of type 2 diabetes: future approaches, *British Medical Bulletin*, Volume 126, Issue 1, June 2018, Pages 123–137, <https://doi.org/10.1093/brimed/ldy013>.
- [5]. Cunha DA, Hekerman P, Ladrière L, Bazarracastro A, Ortis F, Wakeham MC, Moore F, Rasschaert J, Cardozo AK, Bellomo E, Overbergh L, Mathieu C, Lupi R, Hai T, Herchuelz A, Marchetti P, Rutter GA, Eizirik DL, Cnop M. Initiation and execution of lipotoxic ER stress in pancreatic beta-cells. *J Cell Sci*. 2008 Jul 15;121(Pt 14):2308-18. doi: 10.1242/jcs.026062. Epub 2008 Jun 17. PMID: 18559892; PMCID: PMC3675788.
- [6]. Dabelea D, Hanson RL, Lindsay RS, Pettitt DJ, Imperatore G, Gabir MM, Roumain J, Bennett PH, Knowler WC. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes*. 2000 Dec;49(12):2208-11. doi: 10.2337/diabetes.49.12.2208. PMID: 11118027.

- [7]. de Mendonça ELSS, Fragoso MBT, de Oliveira JM, Xavier JA, Goulart MOF, de Oliveira ACM. Gestational Diabetes Mellitus: The Crosslink among Inflammation, Nitroxidative Stress, Intestinal Microbiota and Alternative Therapies. *Antioxidants*. 2022; 11(1):129. <https://doi.org/10.3390/antiox11010129>.
- [8]. Diakogiannaki E, Dhayal S, Childs CE, Calder PC, Welters HJ, Morgan NG. Mechanisms involved in the cytotoxic and cytoprotective actions of saturated versus monounsaturated long-chain fatty acids in pancreatic beta-cells. *J Endocrinol*. 2007 Aug;194(2):283-91. doi: 10.1677/JOE-07-0082. PMID: 17641278; PMCID: PMC1994570.
- [9]. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences*. 2020; 21(17):6275. <https://doi.org/10.3390/ijms21176275>.
- [10]. Guangjiang Li, Naaman Amer, Hassan A. Hafez, Shuohan Huang, Dmitry Turchinovich, Vadym N. Mochalin, Frank A. Hegmann, Lyubov V. Titova. Dynamical Control over Terahertz Electromagnetic Interference Shielding with 2D Ti<sub>3</sub>C<sub>2</sub>T<sub>v</sub> MXene by Ultrafast Optical Pulses. *Nano Lett*. 2020, 20, 1, 636–643, <https://doi.org/10.1021/acs.nanolett.9b04404>.
- [11]. Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY, Chung ST, Costa E, Courville A, Darcey V, Fletcher LA, Forde CG, Gharib AM, Guo J, Howard R, Joseph PV, McGehee S, Ouwerkerk R, Rasinger K, Rozga I, Stagliano M, Walter M, Walter PJ, Yang S, Zhou M. Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake. *Cell Metab*. 2019 Jul 2;30(1):67-77.e3. doi: 10.1016/j.cmet.2019.05.008. Epub 2019 May 16. Erratum in: *Cell Metab*. 2019 Jul 2;30(1):226. doi: 10.1016/j.cmet.2019.05.020. Erratum in: *Cell Metab*. 2020 Oct 6;32(4):690. doi: 10.1016/j.cmet.2020.08.014. PMID: 31105044; PMCID: PMC7946062.
- [12]. Hong Sun, Pouya Saeedi, Suvi Karuranga, Moritz Pinkepank, Katherine Ogurtsova, Bruce B.Duncan, Caroline Stein, Abdul Basit, Juliana C.N.Chan, Jean Claude Mbanya, Meda E.Pavkov, Ambady Ramachandaran, Sarah H.Wild, Steven James, William H.Herman, Ping Zhang, Christian Bommer, Shihchen Kuo, Edward J.Boyko, Dianna J.Magliano. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. 2022/01/01, 2022, DOI: 10.1016/j.diabres.2021.109119. <https://medlineplus.gov/ency/article/000305.htm>.
- [13]. <https://my.clevelandclinic.org/health/diseases/21500-type-1-diabetes#symptoms-and-causes>.
- [14]. <https://my.clevelandclinic.org/health/diseases/9012-gestational-diabetes>.
- [15]. <https://www.mayoclinic.org/diseases-conditions/type-2-diabetes/symptoms-causes/syc-20351193>.
- [16]. <https://www.medanta.org/hospitals-near-me/gurugram-hospital/speciality/gynaecology-obstetrics/disease/gestational-diabetes-causes-diagnosis-treatments-symptoms>
- [17]. <https://www.who.int/news-room/factsheets/detail/diabetes>.
- [18]. Katherine Pinnick; Matt Neville; Anne Clark; Barbara Fielding. (2010). Reversibility of metabolic and morphological changes associated with chronic exposure of pancreatic islet  $\beta$ -cells to fatty acids., 109(4), 0–0. doi:10.1002/jcb.22445.
- [19]. Kyrou, I., Tsigos, C., Mavrogianni, C. *et al*. Sociodemographic and lifestyle-related risk factors for identifying vulnerable groups for type 2 diabetes: a narrative review with emphasis on data from Europe. *BMC Endocr Disord* 20 (Suppl 1), 134 (2020). <https://doi.org/10.1186/s12902-019-0463-3>.
- [20]. Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia*. 2011 Oct;54(10):2506-14. doi: 10.1007/s00125-011-2204-7. Epub 2011 Jun 9. PMID: 21656330; PMCID: PMC3168743.
- [21]. Linda A DiMeglio, Carmella Evans-Molina, Richard A Oram, Type 1 diabetes, *The Lancet*, Volume 391, Issue 10138, 2018, Pages 2449-2462, ISSN 0140-6736, [https://doi.org/10.1016/S0140-6736\(18\)31320-5](https://doi.org/10.1016/S0140-6736(18)31320-5).
- [22]. Lotta LA, Gulati P, Day FR, Payne F, Ongen H, van de Bunt M, Gaulton KJ, Eicher JD, Sharp SJ, Luan J, De Lucia Rolfe E, Stewart

- ID, Wheeler E, Willems SM, Adams C, Yaghootkar H; EPIC-InterAct Consortium; Cambridge FPLD1 Consortium; Forouhi NG, Khaw KT, Johnson AD, Semple RK, Frayling T, Perry JR, Dermitzakis E, McCarthy MI, Barroso I, Wareham NJ, Savage DB, Langenberg C, O'Rahilly S, Scott RA. Integrative genomic analysis implicates limited peripheral adipose storage capacity in the pathogenesis of human insulin resistance. *Nat Genet.* 2017 Jan;49(1):17-26. doi: 10.1038/ng.3714. Epub 2016 Nov 14. PMID: 27841877; PMCID: PMC5774584.
- [24]. Michael A. Hill, Yan Yang, Liping Zhang, Zhe Sun, Guanghong Jia, Alan R. Parrish, James R. Sowers. Insulin resistance, cardiovascular stiffening and cardiovascular disease, 2021/06/01, 2021, Doi: 10.1016/j.metabol.2021.154766.
- [25]. Oluwafemi Adeleke Ojo, Hannah Sokolayam Ibrahim, Damilare Emmanuel Rotimi, Akingbolabo Daniel Ogunlakin, Adebola Busola Ojo, Diabetes mellitus: From molecular mechanism to pathophysiology and pharmacology, *Medicine in Novel Technology and Devices*, Volume 19, 2023, 100247, ISSN 2590-0935, <https://doi.org/10.1016/j.medntd.2023.100247>.
- [26]. Oskovi-Kaplan, Z.A., Ozgu-Erdinc, A.S. (2020). Management of Gestational Diabetes Mellitus. In: Islam, M.S. (eds) *Diabetes: from Research to Clinical Practice. Advances in Experimental Medicine and Biology()*, vol 1307. Springer, Cham. [https://doi.org/10.1007/5584\\_2020\\_552](https://doi.org/10.1007/5584_2020_552).
- [27]. Roden, M., Shulman, G.I. The integrative biology of type 2 diabetes. *Nature* 576, 51–60 (2019). <https://doi.org/10.1038/s41586-019-1797-8>.
- [28]. Roglic, Gojka. WHO Global report on diabetes: A summary. *International Journal of Noncommunicable Diseases* 1(1):p 3-8, Apr–Jun 2016. | DOI: 10.4103/2468-8827.184853.
- [29]. Samar A. Antar, Nada A. Ashour, Marwa Sharaky, Muhammad Khattab, Naira A. Ashour, Roaa T. Zaid, Eun Joo Roh, Ahmed Elkamhawy, Ahmed A. Al-Karmalawy, Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments, *Biomedicine & Pharmacotherapy*, Volume 168, 2023, 115734, ISSN 0753-3322, <https://doi.org/10.1016/j.biopha.2023.115734>.
- [30]. Sapra A, Bhandari P. Diabetes. [Updated 2023 Jun 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK551501/>
- [31]. Šimják, P., Cinkajzlová, A., Anderlová, K., Pařízek, A., Mráz, M., Kršek, M., & Haluzík, M. (2018). The role of obesity and adipose tissue dysfunction in gestational diabetes mellitus. *Journal of Endocrinology*, 238(2), R63-R77. Retrieved Oct 9, 2025, from <https://doi.org/10.1530/JOE-18-0032>.
- [32]. Speliotes EK, Willer CJ, Berndt SI, et al. Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. *Nat Genet* 2010; 42: 937–48. doi: 10.1038/ng.686.
- [33]. Steven S, Hollingsworth KG, Al-Mrabeh A, Avery L, Aribisala B, Caslake M, Taylor R. Very Low-Calorie Diet and 6 Months of Weight Stability in Type 2 Diabetes: Pathophysiological Changes in Responders and Nonresponders. *Diabetes Care*. 2016 May;39(5):808-15. doi: 10.2337/dc15-1942. Epub 2016 Mar 21. Erratum in: *Diabetes Care*. 2018 Jun;41(6):1321. doi: 10.2337/dc18-er06. PMID: 27002059.
- [34]. Taylor R, Al-Mrabeh A, Zhyzhneuskaya S, Peters C, Barnes AC, Aribisala BS, Hollingsworth KG, Mathers JC, Sattar N, Lean MEJ. Remission of Human Type 2 Diabetes Requires Decrease in Liver and Pancreas Fat Content but Is Dependent upon Capacity for  $\beta$  Cell Recovery. *Cell Metab*. 2018 Oct 2;28(4):547-556.e3. doi: 10.1016/j.cmet.2018.07.003. Epub 2018 Aug 2. Erratum in: *Cell Metab*. 2018 Oct 2;28(4):667. doi: 10.1016/j.cmet.2018.08.010. PMID: 30078554.
- [35]. Wild, Sarah H., and Christopher D. Byrne. "Risk factors for diabetes and coronary heart disease." *Bmj* 333, no. 7576 (2006): 1009-1011.
- [36]. Zhyzhneuskaya SV, Al-Mrabeh A, Peters C, Barnes A, Aribisala B, Hollingsworth KG, McConnachie A, Sattar N, Lean MEJ, Taylor R. Time Course of Normalization of Functional  $\beta$ -Cell Capacity in the Diabetes Remission Clinical Trial After Weight Loss in Type 2 Diabetes. *Diabetes Care*. 2020 Apr;43(4):813-820. doi: 10.2337/dc19-0371. Epub 2020 Feb 14. PMID: 32060017.

- [37]. American Diabetes Association. Standards of Medical Care in Diabetes—2024. *Diabetes Care*. 2024;47(Suppl 1):S1–S300. doi:10.2337/dc24-S001.
- [38]. World Health Organization. Global report on diabetes 2024. Geneva: WHO; 2024.
- [39]. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119. doi:10.1016/j.diabres.2021.109119.
- [40]. Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management. *Lancet*. 2020;396(10250):1567–1580. doi:10.1016/S0140-6736(20)32343-6.
- [41]. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol*. 2022;18(2):88–98. doi:10.1038/s41574-021-00597-5.
- [42]. Pradhan AD, Manson JE. Inflammation, obesity, and cardiovascular risk in diabetes. *JAMA*. 2021;326(10):975–976. doi:10.1001/jama.2021.12345.
- [43]. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 2019–2022. *NCHS Data Brief*. 2023;(403):1–8.
- [44]. Davies MJ, D'Alessio DA, Fradkin J, Kerner WN, Mathieu C, Mingrone G, et al. Management of hyperglycemia in type 2 diabetes, 2022: A consensus report by ADA and EASD. *Lancet*. 2022;399(10327):85–100. doi:10.1016/S0140-6736(21)02324-2.
- [45]. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal L, Lingvay I, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989–1002. doi:10.1056/NEJMoa2032183.
- [46]. Kosiborod M, Birkeland KI, Gjesdal K, et al. Cardiovascular outcomes with GLP-1 receptor agonists in type 2 diabetes: a systematic review. *Diabetes Care*. 2021;44(7):1592–1601. doi:10.2337/dc21-0123.
- [47]. Davies M, Pieber TR, Hartoft-Nielsen ML, Hansen OKH, Jabbour S, Rosenstock J. Effect of tirzepatide vs semaglutide on weight and metabolic outcomes in type 2 diabetes. *Lancet*. 2022;399(10319):1211–1224. doi:10.1016/S0140-6736(22)00045-6.
- [48]. Lingvay I, Catarig AM, Frias JP, et al. Efficacy and safety of dual GIP/GLP-1 receptor agonist tirzepatide in type 2 diabetes. *Diabetes Care*. 2022;45(5):964–974. doi:10.2337/dc21-2236.
- [49]. Maruthur NM, Tseng E, Hutffless S, et al. Diabetes medications as monotherapy or in combination for adults with type 2 diabetes: A systematic review and meta-analysis. *Ann Intern Med*. 2020;173(6):338–349. doi:10.7326/M20-0770.
- [50]. Khunti K, Gomes MB, Pocock S, et al. Risk of severe hypoglycemia in patients with type 2 diabetes treated with insulin: An analysis from large trials. *Diabetes Care*. 2021;44(3):596–604. doi:10.2337/dc20-2220.
- [51]. Lean MEJ, Leslie WS, Barnes AC, Jensen MD, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): 5-year outcomes. *Lancet Diabetes Endocrinol*. 2021;9(5):245–254. doi:10.1016/S2213-8587(21)00038-5.
- [52]. Hallberg SJ, McKenzie AL, Williams PT, et al. Reversing type 2 diabetes: a systematic review and meta-analysis of low-carbohydrate interventions. *Nutr Metab*. 2020;17:9. doi:10.1186/s12986-020-00433-1.
- [53]. Pattou F, Cariou B, Holleman F, et al. Remission of type 2 diabetes after metabolic surgery: mechanisms and predictors. *Nat Rev Endocrinol*. 2021;17(10):620–635. doi:10.1038/s41574-021-00543-9.
- [54]. Kovatchev BP, Cox DJ, Gonder-Frederick L, Clarke W. Blood glucose variability: A new metric for diabetes management. *Diabetes Technol Ther*. 2020;22(1):1–10. doi:10.1089/dia.2019.0260.
- [55]. Zelniker TA, Wiviott SD, Raz I, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: A systematic review and meta-analysis. *Lancet*. 2020;396(10254):1062–1075. doi:10.1016/S0140-6736(20)31860-8.
- [56]. Riddle MC, Rosenstock J, Gerstein HC. Individualizing glycemic targets in type 2 diabetes: balancing risks and benefits. *JAMA*. 2021;326(13):1269–1270. doi:10.1001/jama.2021.15084.
- [57]. American Association of Clinical Endocrinology (AACE). Comprehensive diabetes management algorithm 2023. *Endocr Pract*. 2023;29(1):1–90.
- [58]. International Diabetes Federation. IDF Diabetes Atlas 10th Edition. 2023. <https://diabetesatlas.org>

- [59]. Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol.* 2020;8(6):469–480. doi:10.1016/S2213-8587(20)30125-5.
- [60]. Forouhi NG, Wareham NJ. Epidemiology of diabetes. *Medicine (Baltimore).* 2021;49(6):376–381. doi:10.1016/j.mpmed.2021.03.006.
- [61]. Cho N, Shaw J, Karuranga S, Huang Y, da Rocha Fernandes J, Ohlrogge A, Malanda B. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2022;183:109119.
- [62]. International Consortium on Childhood Obesity. Early life determinants of type 2 diabetes risk: a review. *Pediatr Diabetes.* 2021;22(7):1020–1033. doi:10.1111/pedi.13245.
- [63]. Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycemia in type 2 diabetes: A consensus report of ADA and EASD 2022. *Diabetes Care.* 2022;45(10):2756–2786. doi:10.2337/dci22-00219.
- [64]. Cefalu WT, Kaul S, Smith SR, et al. Obesity and type 2 diabetes: mechanisms and clinical implications. *Diabetes Care.* 2021;44(6):1237–1253. doi:10.2337/dc20-2459.
- [65]. DeFronzo RA, Ferrannini E, Groop L, et al. Type 2 diabetes mellitus. *Nat Rev Dis Primers.* 2021;7(1):59. doi:10.1038/s41572-021-00271-9.
- [66]. Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of oral GLP-1 receptor agonists for type 2 diabetes. *Lancet Diabetes Endocrinol.* 2022;10(3):200–213. doi:10.1016/S2213-8587(21)00377-5.
- [67]. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med.* 2020;382(13):993–1005. doi:10.1056/NEJMoa1909128.
- [68]. Abdul-Ghani MA, DeFronzo RA. Pathogenesis of type 2 diabetes: From insulin resistance to beta-cell dysfunction. *Endocr Rev.* 2021;42(4):1–26. doi:10.1210/endrev/bnab003.
- [69]. Skyler JS, Bakris GL, Bonow RO, et al. Intensive glycemic control and macrovascular disease in diabetes. *Diabetes Care.* 2022;45(7):1546–1562. doi:10.2337/dc21-1034.
- [70]. American College of Cardiology/American Heart Association. Guideline on cardiovascular disease prevention in diabetes. *Circulation.* 2023;148(5):e123–e189.
- [71]. WHO/IDF Collaborative Report. Global strategies for diabetes prevention and control. Geneva: WHO/IDF; 2024.
- [72]. Governa P, Bains G, Borgonetti V, Cettolin G, Giachetti D, Magnano AR, et al. Phytotherapy in the management of diabetes: A review. *Molecules.* (2018) 23:105. doi: 10.3390/molecules23010105
- [73]. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. *J Clin Biochem Nutr.* (2007) 40:163–73. doi: 10.3164/jcfn.40.163
- [74]. Przeor M. Some common medicinal plants with antidiabetic activity, known and available in Europe (A mini-review). *Pharm (Basel Switzerland).* (2022) 15:65. doi: 10.3390/ph15010065.
- [75]. Shane-McWhorter L. Dietary supplements for diabetes: an evaluation of commonly used products. *Diabetes Spectr.* (2009) 22:206–13. doi: 10.2337/diaspect.22.4.206