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Diabetes Mellitus

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Abstract

In the following studies, we are discussed about the different types of Diabetes mellitus. These studies also include the Anatomy and Physiology of the production of the insulin. It consists of what are mode or ways of appearing Diabetes Mellitus. This article composed of reason of diabetes and what are preventive measures must be taken to control the Diabetes. In the we explain about what are the complications occurs due to the chronic Diabetes and how it turned as a chronic disorder. Following consists of the symptoms of prediabetes and Diabetic condition.

Keywords: Diabetes mellitus; Cystic fibrosis; Hyperglycemia; Gestational diabetes

1. Introduction

Diabetes is a condition that happens when your blood sugar levels are high. It develops when your pancreas doesn't make enough insulin, or when your body is not responding to the effects of insulin properly. Diabetes mellitus is a chronic disease and can be manageable with medications and by life style changes. Insulin is a hormone released by the pancreas that works as the primary messenger for moving glucose from consumed meals to flow from the blood stream into the body cells where it is used as energy.

Insulin is secreted by β-cells and glucagon is secreted by α-cells; both are in islets of Langerhans's. Insulin decreases the blood glucose levels, whereas glucagon increases the blood glucose levels. Diabetes is classified into Type-1 (insulin dependent) and Type-2(non-insulin dependent). Diabetes causes serious health problems globally, primarily increasing the risk of heart diseases, obesity and other complications.

As per Indian Council of Medical Research -India Diabetes (ICMR INDIAB) study published in 2023, the prevalence of diabetes is 10.1 crores. The International Diabetes Federation (IDF) estimates the total number of diabetes subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025.

2. Types of diabetes

- Prediabetes
- Type-1 diabetes
- Type-2 diabetes
- Gestational diabetes
- Maturity onset diabetes of the young (MODY)

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- Neonatal diabetes
- Steroid induced diabetes
- Cystic fibrosis diabetes
- Latent auto immune diabetes in adults (LADA)
- Type 3c diabetes
- Alstrom syndrome
- Wolfram syndrome

2.1. Prediabetes

When your blood sugar level is higher than normal but not high enough for a doctor to diagnose diabetes, it is called prediabetes. Even though most Americans are not aware of it, about one-third of them have it. Heart disease and type 2 diabetes can both be more likely to strike someone with prediabetes. Increasing your physical activity and dropping excess weight—even if it is only 5% to 7% of your body weight—can reduce those risks.

2.2. Type-1 diabetes

Diabetes that is insulin-dependent is another name for type 1 diabetes. Because it commonly starts in young age, it was formerly known as juvenile-onset diabetes. Diabetes type 1 is an autoimmune disease. It occurs when antibodies produced by our human body target your pancreas. Due to that injury, the β-cells are unable to produce insulin.

This kind of diabetes may be inherited. It may also occur because of issues with the insulin-producing cells in human pancreas. Damage to the small blood vessels in your eyes (diabetic retinopathy), nerves (diabetic neuropathy), and kidneys (diabetic nephropathy) is the primary cause of many health issues associated with type 1. An increased risk of heart disease and stroke is also present in individuals with type 1.

2.3. Type-2 diabetes

Diabetes with an adult onset or non-insulin-dependent was the previous term for type 2 diabetes. But during the last 20 years, it has become more common among children and teens, primarily as the proportion of overweight or obese young people has increased. Type 2 diabetes affects about 90% of those with diabetes. Insulin is typically produced by the pancreas in people with type 2 diabetes.

However, it may not be sufficient or your body may not be using it properly. Insulin resistance, or the inability of your cells to respond to insulin, is primarily found in muscle, fat, and liver cells. Diabetes type 2 is frequently less severe than type 1. However, it can still lead to serious health issues, particularly in the small blood vessels found in your eyes, kidneys, and nerves. Additionally, type 2 increases the risk of heart disease. [1]

2.4. Gestational diabetes

One of the most prevalent medical issues during pregnancy is gestational diabetes mellitus (GDM), and if left untreated, it can have major negative implications on both the mother's and the child's health. [2,3] The International Diabetes Federation (IDF) has released updated statistics showing that GDM affects about 14.0% of pregnancies globally, or about 20 million babies yearly. [4] Maternal diabetes mellitus (GDM) carriers bear the potential risk of maternal hypertension, pre-eclampsia, and caesarean delivery. [5]

Furthermore, gestational diabetes mellitus raises the likelihood of problems such as heart disease, obesity, and impaired glucose metabolism, which can result in the development of type 2 diabetes in both the mother and the child. [6] The etiology of GDM is yet unknown, but the data that have been collected thus far point to a complicated mechanism involving the interaction of numerous genetic, metabolic, and environmental variables.[7]

2.5. Maturity onset of diabetes of the young (MODY)

Maturity-onset diabetes of the young (MODY) is a kind of monogenic diabetes that was initially identified in children, adolescents, and young adults who were not fat as a mild and asymptomatic form of the disease. Treatment with sulfonylureas has been shown to improve blood glucose levels. As genetic technology has advanced, more genes associated with MODY have been characterized and sequenced. [8]

2.6. Neonatal diabetes

A mutation in a single gene that impacts pancreatic beta cell activity is often the cause of neonatal diabetes mellitus (DM), which is characterized by the emergence of persistent hyperglycemia within the first six months of life because of reduced insulin function.

2.7. Steroid induced diabetes

The steroidal drugs have been widely utilized to treat a wide range of acute and chronic conditions.[9] The primary cause of drug-induced hyperglycemia is steroid.[10] In addition to aggravating like hyperglycemia in individuals with diagnosed diabetes mellitus (DM), they can also induce DM in individuals without a history of hyperglycemia prior to starting glucocorticoid therapy.[11]

This phenomenon has been observed in as many as 46% of patients, and they can result in increases in glucose levels of up to 68% relative to baseline.[12] Additionally, they may cause nonketotic hyperosmolar condition, diabetic ketoacidosis, and in rare cases, death in certain populations, particularly in those with pre-existing DM.[13]

2.8. Cystic fibrosis diabetes

The terms type 1 and type 2 diabetes might be familiar to you. Though it has similarities with both type 1 and type 2 diabetes, CFRD is specific to individuals with cystic fibrosis. Like type 1 diabetes, the pancreas produces insufficient insulin in CFRD. Insulin resistance, which is seen in type 2 diabetics, can also develop in patients with CFRD.

Pancreatic scarring can result from cystic fibrosis (CF) due to thick, sticky mucus. Because of this, persons with CF may experience insulin insufficiency or possibly become totally deficient in the hormone insulin due to the pancreas' inability to produce adequate amounts of the hormone. Insulin resistance can occur in people with CFRD, particularly when they are sick, using steroids, or in specific situations like pregnancy.

2.9. Type-3c diabetes

Diabetes type 3c is a condition when pancreatic damage results from another illness. Pancreatitis, cystic fibrosis, hemochromatosis, and pancreatic cancer are the disorders associated with type 3c. If you suffer additional injury that requires the removal of all or part of your pancreas, you may potentially acquire type 3c.

Comparison of type 1 and 2 diabetes		
Feature	**Type 1 diabetes**	**Type 2 diabetes**
Onset	Sudden	Gradual
Age at onset	Any age (mostly young)	Mostly in adults
Body habitus	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased
Concordance in identical twins	50%	90%
Prevalence	Less prevalent	More prevalent - 90 to 95% of U.S. diabetics

Figure 1 Comparison between type-1 and type-2 diabetes

3. Pathophysiology

3.1. Normal pathology in human body

In healthy individuals, the pancreas, an organ situated behind the stomach and liver, secretes digestive enzymes into the bloodstream along with the hormones glucagon and insulin to regulate blood glucose levels. Because glucose can enter body cells and undergo metabolism there, the release of insulin into the circulation lowers blood glucose levels, which are simply sugars from diet.

The pancreas secretes glucagon to accelerate the release of glucose from the liver when blood glucose levels fall too low. Blood glucose levels rise quickly after a meal because glucose and amino acids are immediately absorbed into the bloodstream. Increased blood glucose causes the pancreatic beta cells, which are key cells, to release large amounts of insulin into the bloodstream. After a meal, insulin reaches its highest level 20 minutes later.

Insulin permits glucose to enter the body's cells, especially the liver and muscles. Here, glucose storage for later use or burning for energy is determined by insulin and other hormones. High insulin levels cause the liver to cease generating glucose and store it in different forms until the body requires it once more. Approximately two to four hours after a meal, both blood glucose and insulin are at low levels. The pancreas decreases insulin production as blood glucose levels peak.

3.2. Type-1 diabetes

Children and young people are typically diagnosed with type 1 diabetes. It arises when pancreatic beta cells—the only cells in the body that produce the hormone insulin, which controls blood sugar—are destroyed by the immune system. This type of diabetes affects just 5% of those who have it. People with type 1 diabetes need insulin injected or administered via a pump to survive.

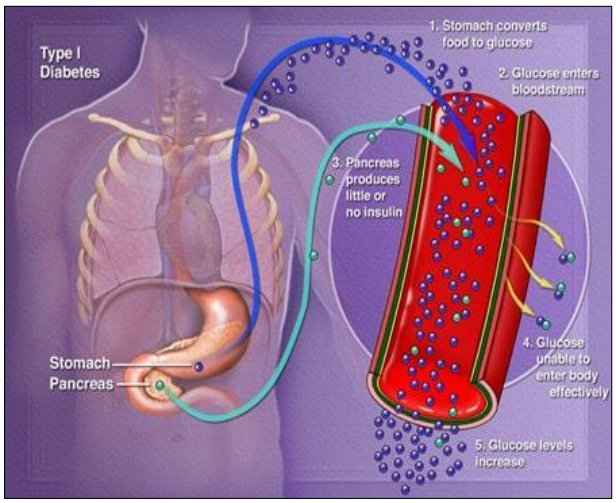

Figure 2 Raise in blood glucose level in type-1 diabetes

3.3. Type-2 diabetes

Type 2 diabetes is the most common form of the disease. The multifactorial causes of type 2 diabetes involve both hereditary and environmental factors that impact insulin sensitivity in the pancreas, muscle, liver, and adipose tissue, as well as beta-cell function. When a person has type 2 diabetes, their cells either reject insulin or the body does not make enough of it. Usually, it starts with insulin resistance, a condition where cells misuse insulin. The pancreas' capacity to make insulin progressively declines as demand for it increases.

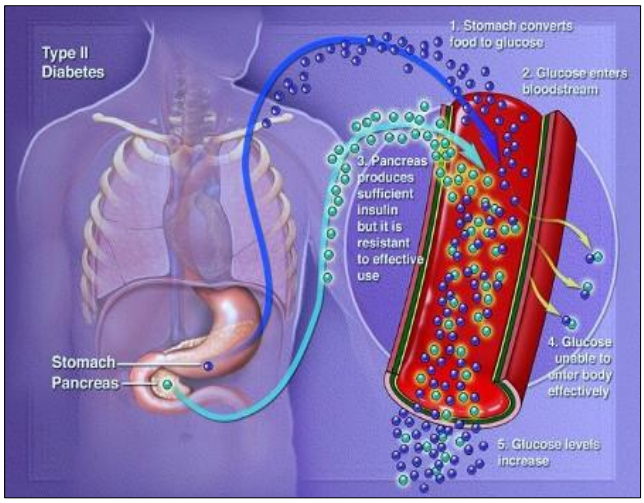

Figure 3 Raise in blood glucose level in type-2 diabetes

Heart disease, neurological damage, and kidney damage are just a few of the serious health effects that can result from glucose accumulation in the blood rather than cells. Kidney failure, non-traumatic lower limb amputations, and new cases of adult blindness in the US are all mostly caused by diabetes.

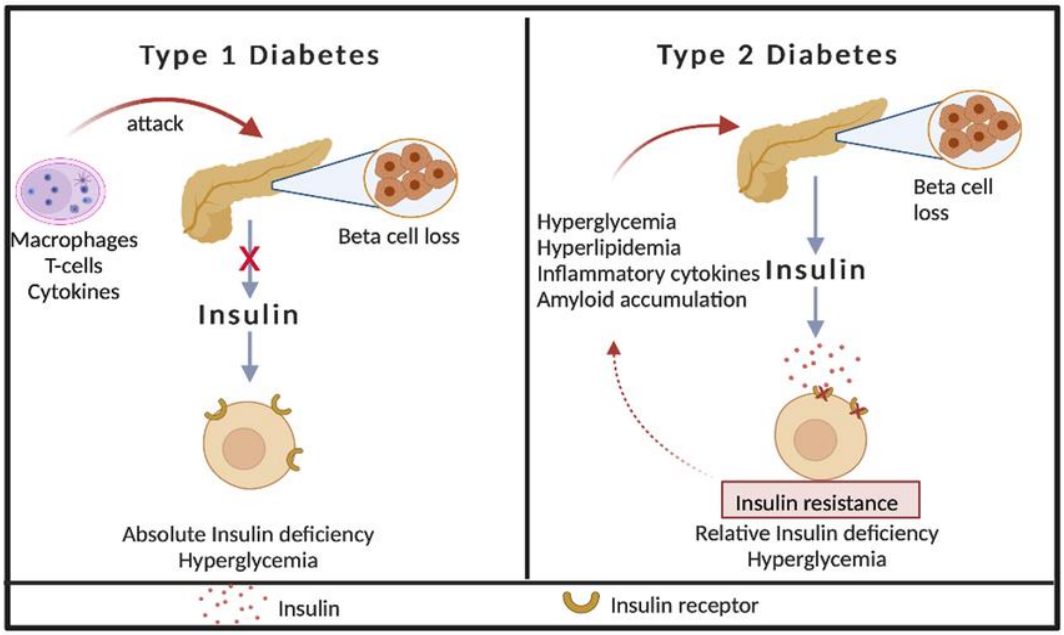

Figure 4 Comparision between type-1 and type-2 diabetes

Type 1 and type 2 diabetes pathogenesis. In individuals with type 1 diabetes, immune cells including macrophages and T cells kill pancreatic β-cells and create cytokines. This leads to a complete lack of insulin and hyperglycemia.

Amyloids, cytokines, hyperglycemia, and hyperlipidemia all harm pancreatic β-cells in type 2 diabetes. Despite the production of insulin by pancreatic β-cells, the amount of insulin produced is insufficient to counteract insulin resistance, resulting in a relative insulin shortage that ultimately causes hyperglycemia.

3.4. General symptoms

- Increased hunger
- Increased thirst
- Frequent urination
- Weight loss

- Blurred vision
- Extreme fatigue
- Sores that not heal

3.5. Symptoms in men

- Erectile dysfunction
- Decreased muscle strength.

3.6. Symptoms in women

- Urinary tract infections
- Dry and itchy skin.

3.7. Diagnosis

Using a blood test, medical professionals can diagnose diabetes by looking at your glucose level. There are three ways to determine your blood glucose level:

- Fasting blood glucose test
- Random blood glucose test
- A1C test

3.7.1. Fasting blood glucose test

- You must fast for at least eight hours prior to the test in order to avoid eating or drinking anything other than water. This test gives your healthcare professional access to your initial blood sugar levels, which can be significantly impacted by diet.

3.7.2. Random blood glucose levels

- The term "random" indicates that you can take this test whenever you want, even if you haven't fasted.

3.7.3. A1c test

- This test, commonly known as the HbA1C or glycated haemoglobin test, gives your average blood glucose level during the previous two to three months. An oral glucose tolerance test is ordered by healthcare practitioners to screen for and diagnose gestational diabetes.

3.8. Diabetes diagnosis test

Table 1 Blood glucose tests for diabetes

	DIABETES	**PREDIABETES**	**NORMAL**
A1C LEVEL (%)	6.5 or above	57-64	Below
FASTING BLOOD GLUCOSE TEST (mg/dl)	126 or above	100-125	99 or below
GLUCOSE TOLERANCE TEST (mg/dl)	200 or above	140-199	140 or below

4. Treatment of diabetes

4.1. Lifestyle changes

The cornerstone of managing diabetes is making lifestyle adjustments, which include:

- Dietary Changes: A balanced diet high in fruits, vegetables, whole grains, lean meats, and healthy fats is the main focus. It's vital to watch how many carbohydrates you eat.
- Exercise: Maintaining a regular exercise regimen can enhance insulin sensitivity and blood glucose regulation. A minimum of 150 minutes a week of moderate-intensity exercise is frequently recommended.

- Weight management: For certain patients, achieving and maintaining a healthy weight can lower their blood glucose levels and eliminate the need for medication. [14]

4.2. Oral hypoglycemic agents

Oral hypoglycemics are the medications used to manage blood glucose levels in patients with TYPE-2 diabetes. They are classified based on their MOA:

4.2.1. Biguanides

- Example: metformin
- MOA: reduces intestinal glucose absorption, increases insulin sensitivity in peripheral tissues, and reduces hepatic glucose synthesis. [15]

4.2.2. Sulfonyl urea's

- Examples: Glipizide, Glyburide, Glimepiride
- MOA: It is possible to trigger the release of insulin from pancreatic beta cells by binding to the sulfonylurea receptor, which blocks ATP-sensitive potassium channels, results in cell depolarization, and releases insulin. [16]

4.2.3. Meglitinides

- Examples: Repaglinide, Nateglinide
- MOA: You may trigger the release of insulin from pancreatic beta cells by connecting to the sulfonylurea receptor, which blocks ATP-sensitive potassium channels and results in cell depolarization and insulin release. [17]

4.2.4. Thiazolidinediones

- Examples: pioglitazone, rosiglitazone
- MOA: Increase insulin sensitivity with improving glucose absorption and reducing hepatic glucose synthesis in adipose tissue, muscle, and the liver by activating peroxisome proliferator-activated receptor-gamma (PPAR-γ) [18]

4.2.5. Dipeptidyl peptidase-4 inhibitors

- Examples: sitagliptin, Linagliptin
- MOA: Inhibit the enzyme DPP-4, which degrades incretins (GLP-1 and GIP). This inhibition increases incretin levels, leading to increased insulin secretion and decreased glucagon release. [19]

4.2.6. Sodium- Glucose Co- Transporter 2 Inhibitors

- Examples: canagliflozin, dapagliflozin, empagliflozin
- MOA: Inhibit SGLT2 in the proximal renal tubules to increase urine glucose excretion and decrease reabsorption of glucose. [20]
- Alpha- Glucosidase Inhibitors:
- Examples: Acarbose, Miglitol
- MOA: By preventing the enzyme alpha-glucosidase from breaking down complex carbs into simple sugars, you can postpone the absorption of carbohydrates from the intestine. [21]

4.3. Injectables

There are various kinds of insulin available. Each type's "onset"—the rate at which it begins to act—and "duration," or the length of time that its effects last, are distinct. The majority of insulin types peak, at which point their effects are at their highest. The effects of the insulin subside over the course of the following several hours or so after the peak. The various forms of insulin are listed in Table 1, together with information on when they peak, how quickly they act, and how long they last.

4.4. Ways to take insulin

The majority of diabetics use an insulin pump, insulin pen, or needle and syringe to take their medication. Less often used insulin delivery methods include insulin jet injectors and inhalers.

4.5. Needles and syringe

Insulin shots can be administered to oneself with a syringe and needle. Using the needle to draw up your dose of insulin into the syringe, you take it out of the vial or bottle. Insulin is most effective when injected into the abdomen, although your doctor might advise switching up where you inject it.

Insulin injections into the same location over time may cause the surrounding tissue to stiffen, making subsequent injections there more difficult. You can also inject insulin into your upper arm, buttocks, or thigh, however the effects of those injections may take longer to manifest. For some diabetics on insulin, two to four shots a day are necessary to meet their blood glucose goals.

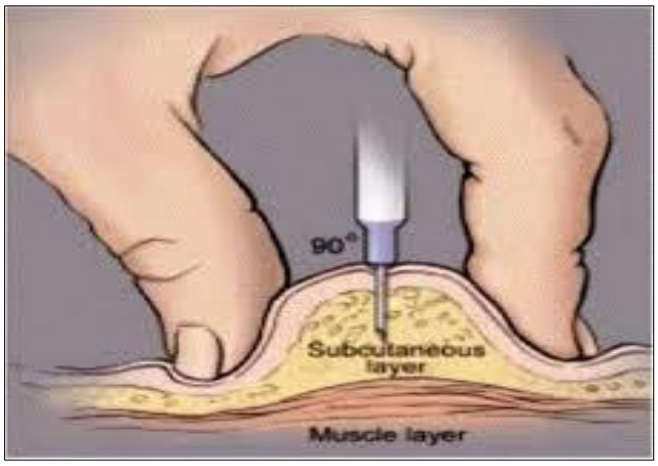

Figure 5 Insulin injection

4.5.1. Pen

An insulin pen resembles a writing pen, but instead of a tip, it has a needle. Certain disposable insulin pens already have insulin inside of them. Some contain a space for an insulin cartridge, which you use, then take out. Although insulin pens are more expensive than needles and syringes, many people find them to be easier to use.

If filling the syringe while holding the vial is difficult for you or you have trouble reading the markings on the syringe, you might want to think about using an insulin pen. Certain reusable pens have a memory feature that allows them to remember timing and dosage quantities. You can modify your insulin dosages by using other kinds of "connected" insulin pens that are designed to compute insulin doses and offer downloadable data reports.

Figure 6 Insulin pen

4.5.2. Pump

An insulin pump is a compact device that delivers consistent insulin doses to you all day long. One kind of pump is worn externally on a belt, in a pocket, or in a pouch. An extremely tiny needle and a tiny plastic tube are connected to the insulin pump. You put the needle-containing plastic tube under your skin and remove it. The plastic tubing connected to the insulin pump will remain placed for a few days.

The device may be set to provide more or less insulin according on your needs, and it continuously distributes insulin into your body through the tube. During mealtimes, you can also administer insulin dosages to yourself via the pump. Another kind of pump is tubeless. This pump is operated by a hand-held device that adheres directly to your skin using a self-adhesive pad. Every few days, the pump mechanism and plastic tube are replaced.

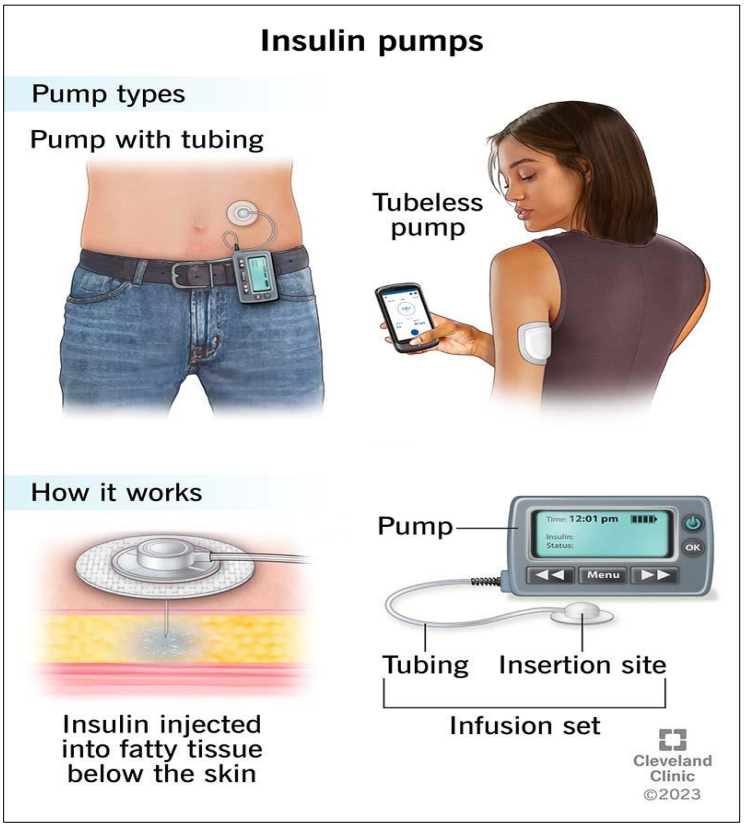

Figure 7 Insulin pump

4.5.3. Inhaler

Using an inhaler device to breathe powdered insulin into your mouth is an additional method of taking insulin. Insulin enters your lungs and enters your bloodstream rapidly. To avoid using needles, you might choose to use an insulin inhaler (NIH external link). Only persons with type 1 or type 2 diabetes can use inhaled insulin. It is less frequent to use an insulin. [22]

Figure 8 Inhaler insulin

5. Complications

Diabetes affects the body gradually and frequently progresses unnoticed. An excess of glucose, or sugar, in the blood over time can harm several organs. These are frequently referred to as diabetic "complications."

5.1. Kidney failure

Every minute, the kidneys filter around a half cup of blood, eliminating waste products and surplus fluid from your body. Diabetes can cause kidney damage over time to the point where dialysis or a kidney transplant are necessary. Dialysis is a process used to rid the blood of waste materials and extra fluid.

5.2. Heart and blood vessel damage

Your risk of complications such peripheral artery disease, chronic renal disease, atherosclerosis, stroke, and cardiovascular disease may increase if you have type 2 diabetes.

5.3. Nerve damage

Diabetic neuropathy is a disorder where nerve damage occurs because of high blood sugar levels over time. This may result in tingling, burning, or shooting pains that usually start at the fingers or toes and move upward, as well as numbness in the hands, fingers, toes, and feet. In addition to these symptoms, vomiting, diarrhoea, constipation, issues with sexual function, and dizziness can also be signs of this nerve injury.

5.4. Foot damage

Long-term excessive blood sugar can also harm feet's nerves and blood vessels. The feet experience discomfort, tingling, numbness, or lack of feeling because of this damage. In severe circumstances, minor wounds and blisters can result in ulcers, infections, and amputations.

5.5. Eye damage

Because of their elevated blood sugar levels, people with diabetes may have damage to their blood vessels and lenses. This can result in blindness and disorders like glaucoma and cataracts. [23]

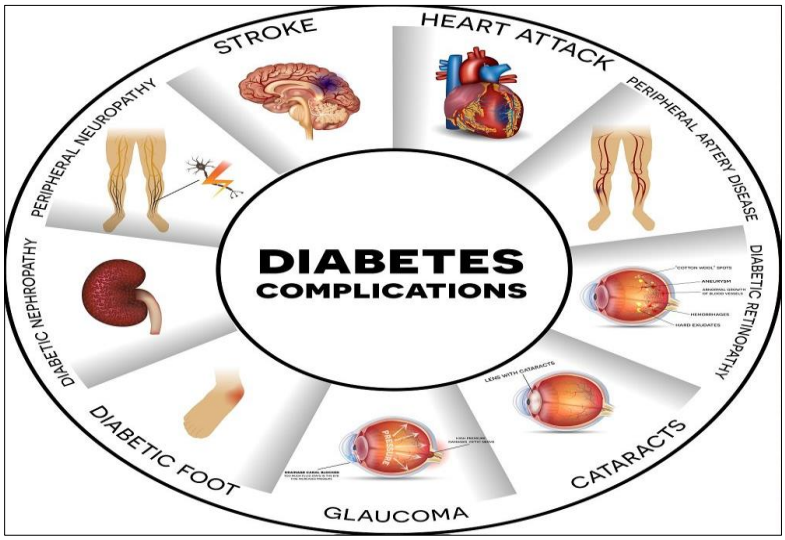

Figure 9 Diabetic complications

6. Conclusion

Diabetes mellitus is a complex and multifaceted condition that significantly impacts global health, with its prevalence continually rising. This chronic disease arises when the body's ability to regulate blood glucose levels is impaired due to inadequate insulin production or insulin resistance. The primary types of diabetes—Type 1, Type 2, and gestational diabetes—each have unique pathophysiological mechanisms and implications for treatment and management.

Type 1 Diabetes is an autoimmune disorder that necessitates lifelong insulin therapy due to the destruction of insulin-producing beta cells in the pancreas .Type 2 Diabetes, the most common form, often develops due to a combination of genetic and environmental factors leading to insulin resistance and a gradual decline in insulin production .Gestational Diabetes occurs during pregnancy and can pose risks to both the mother and child, with potential long-term implications for developing Type 2 diabetes later in life.

Effective management of diabetes involves a multifaceted approach including lifestyle modifications such as dietary changes, regular physical activity, and weight management, alongside pharmacological treatments tailored to the type and severity of diabetes. Oral hypoglycemic agents and injectable insulin therapies are essential for controlling blood glucose levels and preventing complications.

Diabetes can lead to severe complications affecting various organs, including the kidneys, heart, nerves, and eyes. Thus, rigorous management and regular monitoring are critical to mitigate these risks and improve quality of life. Given the global and escalating prevalence of diabetes, public health strategies focusing on early detection, prevention, and education are crucial. Continued research and advancements in diabetes care are essential to better understand the disease, develop more effective treatments, and ultimately reduce the burden of this chronic condition on individuals and healthcare systems worldwide.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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