



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

The Global Diabetes Challenge: Epidemiological Insights, Pathophysiological Mechanisms, and Emerging trends

1Ruchi Kamble, 2Nikhil Karade, 3Sayli Karle, 4Pradip Kokani, 5Nishant Koli, 6Satish Pandav

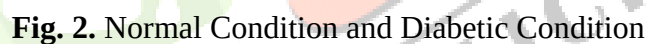
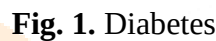
1. Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Maharashtra, India
2. Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Maharashtra, India
3. Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Maharashtra, India
4. Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Maharashtra, India
5. Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Maharashtra, India
6. Assistant Professor, Department of Pharmaceutics, Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Maharashtra, India

ABSTRACT:

Diabetes Mellitus (Diabetes Mellitus) also known as simply diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. It is resulting from a defect in insulin secretion, insulin action, or both. Insulin deficiency in turn leads to chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism. It is the most common endocrine disorder and by the year 2010, it is estimated that more than 200 million people worldwide will have Diabetes Mellitus and 300 million will subsequently have the disease by 2025. Diabetes Mellitus are categorised into two major types are type 1 and type 2. Type 1 Diabetes Mellitus or insulin-dependent Diabetes Mellitus in which body fails to produce insulin, and presently requires the person to inject insulin or wear an insulin pump. Type 2 Diabetes Mellitus or Non-insulin dependent diabetes mellitus, results from insulin resistance, condition in which cells fail to use insulin properly, with or without an absolute insulin deficiency. Clinical symptoms include polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger), Paraesthesia (numbness or tingling sensation on hands or feet). Recent trends in treating diabetes include using oral hypoglycaemic agents and novel drug delivery approach. Various herbal drugs have been also proved effective due to their beneficial contents in treatment of diabetes. Appropriate diet and healthy lifestyle strategies should be followed with drugs. This review article gives a detail on Historic approach, Epidemiology, Pathophysiology, and treatment Strategies with a brief about herbal strategies.

Keywords: Diabetes Mellitus, Insulin, Insulin Dependent Diabetes Mellitus, Non-Insulin Dependent Diabetes Mellitus, Hypoglycaemic, Polyuria, Polydipsia, Paraesthesia, Polyphagia, Diabetic Ketoacidosis.

Diabetic Mellitus, often termed as “Silent Pandemic”, or Hyperglycaemia, or Diabetes, is a chronic disorder characterised by decreased in the level of insulin or insulin action to regulate blood glucose level in the body. The pancreatic islet cells produce the hormone insulin. By transferring sugar into the cells, where the body can use it as fuel, insulin regulates the blood's sugar content. As an anabolic hormone, it has a significant impact on how proteins, lipids, carbohydrates, and fats are metabolized. The type and duration of diabetes can affect how severe the symptoms are. People who have high blood sugar levels, especially children who don't have any insulin at all, may have symptoms like weight loss, increased appetite, polydipsia, polyuria, and vision issues.



An estimated 366 million people were diagnosed with diabetes mellitus in 2011, and by 2030, that figure is expected to increase to 552 million. Type 2 diabetes mellitus is becoming more commonplace globally, with lower-middle-income nations accounting for 80% of cases. Diabetes mellitus was the cause of 4.6 million deaths in 2018. It is anticipated that 439 million people will have type 2 diabetes mellitus by 2030. Because of environmental and lifestyle factors, the prevalence of this condition varies by region. The prevalence of diabetes mellitus, especially type 2, is predicted to rise dramatically worldwide over the next 20 years, with developing nations seeing the largest increase. The condition primarily affects people between the ages of 45 and 64.

80% of diabetics receive a diagnosis, 60% percent of individuals with diabetes aged 40 and above take statins, and 80% percent of those with diabetes have good control over their blood pressure and glycaemia. and blood glucose self-monitoring and reasonably priced insulin are available to all individuals with type 1 diabetes.

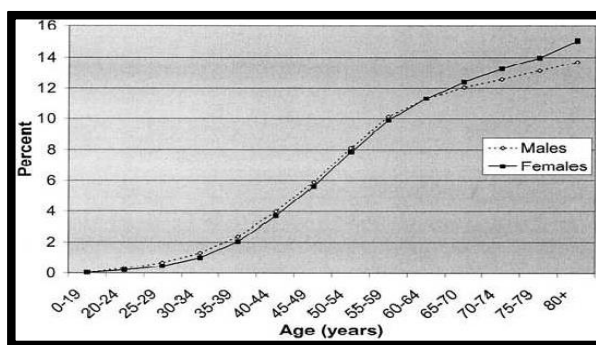


Fig. 3. Epidemiology of Diabetes: Global Review

EPIDEMIOLOGY OF DIABETES IN INDIA

Diabetes is a rapidly growing health concern worldwide, with a particularly alarming rise in developing countries. According to global estimates, approximately 285 million people (6.6%) in the 20–79 age group had diabetes in 2010. By 2030, this number is expected to rise to 438 million people (7.8%). A significant proportion of this increase will be concentrated in developing economies, with India and China contributing the largest share of this growth. It is estimated that India had around 50.8 million people living with diabetes in 2010, and this number is expected to increase to 87.0 million by 2030.[17]

Table. 1: “Top 10” countries in the world, in terms of number of people with diabetes, for 2010 and 2030, are shown in following

Rank	Country / Territory	2010 (millions)	Country / Territory	2030 (millions)
1	India	50.8	India	87.0
2	China	43.2	China	62.6
3	U.S.	26.8	U.S.	36.0
4	Russian Federation	9.6	Pakistan	13.8
5	Brazil	7.6	Brazil	12.7
6	Germany	7.5	Indonesia	12.0
7	Pakistan	7.1	Mexico	11.9
8	Japan	7.1	Bangladesh	10.4
9	Indonesia	7.0	Russian Federation	10.3
10	Mexico	6.8	Egypt	8.6

Recent data shows a substantial difference in the prevalence of diabetes between urban and rural populations in India. According to the World Health Organization (WHO) criteria, the prevalence of diagnosed diabetes was 5.6% in urban areas and 2.7% in rural areas. Research by Ramachandran et al. in 2000 found the age-standardized prevalence of diabetes and impaired glucose tolerance (IGT) in urban India to be 12.1% and 14.0%, respectively, with no significant gender differences. Key factors that are positively associated with diabetes in India include age, body mass index (BMI), waist-to-hip ratio, a family history of diabetes, higher monthly income, and sedentary lifestyle. Similarly, IGT was associated with age, BMI, and family history of diabetes.

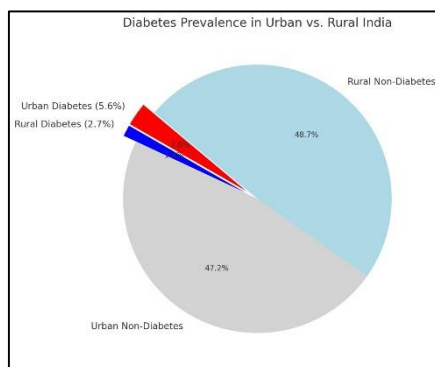


Fig. 4 Diabetes Prevalence in Urban VS Rural India

In recent years, the prevalence of diabetes has been rising across various regions of India, including both urban and rural areas. The increase in prevalence in rural areas is primarily driven by recent socioeconomic transitions, including urbanization, changing dietary habits, and decreased physical activity. Urbanization, poor dietary patterns, sedentary behaviour, and rising obesity levels are key drivers of this rising prevalence.

The global increase in diabetes cases is largely due to factors such as population growth, aging, urbanization, and lifestyle changes, including poor dietary habits and physical inactivity. In contrast to Western countries, where older adults are more commonly affected, diabetes in Asia disproportionately affects younger to middle-aged adults [18,19], posing significant challenges for the healthcare systems of developing countries. This trend is likely to have long-lasting impacts on national health outcomes and economies.

Diabetes is projected to account for 11.6% of global healthcare expenditures in 2010, with an estimated \$376 billion (USD) in global healthcare costs for the treatment and prevention of diabetes and its complications. By 2030, these expenditures are expected to rise to over \$490 billion. The leading countries in terms of diabetes prevalence, both in 2010 and 2030, include India, China, and the United States. The global landscape of diabetes is rapidly changing, and the growing diabetes burden in China, with 92.4 million adults living with the condition, is expected to further shift global epidemiological trends.

As diabetes prevalence continues to rise, it is crucial for public health efforts to focus on early detection, lifestyle interventions, and improved healthcare infrastructure to manage the escalating burden of diabetes in India and globally.

CLASSIFICATION OF DIABETES MELLITUS:

Diabetes is classified into many types, but above all majorly into two types; Type 1 Diabetes Mellitus and Type 2 Diabetes Mellitus. They are being classified on the basis of etiology into Insulin dependent Diabetes Mellitus and Non-Insulin Dependent Diabetes Mellitus.

Insulin Dependent Diabetes Mellitus (Type1 IDDM or T1DM)

This type of diabetes mellitus is also called autoimmune diabetes and previously known as juvenile-onset or keto prone diabetes. Type I diabetes is an autoimmune disease characterized by a local inflammatory reaction in and around islets that is followed by selective destruction of insulin secreting cells. This type is characterized by presence of Islet cell cytoplasmic antibodies, Anti-glutamic acid decarboxylase, islet antigen 2 or insulin antibodies which identifies autoimmune process associated with β -cell destruction. As a result, the body's pancreatic cells are unable to produce insulin. This occurs in patients who have little or no endogenous insulin secretory thus insulin therapy is required to survive.

Around 8.75 million people with diabetes were living with the condition, with 1.52 million under 20. The exact causes of type 1 are not yet be known. Genetic factors are one of the causes leading diabetes.

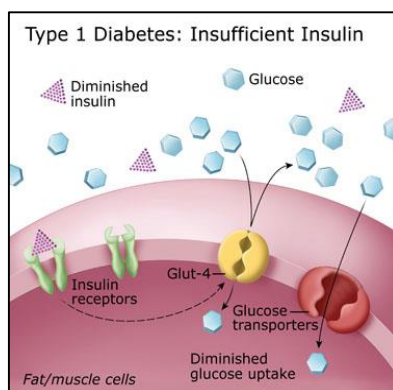


Fig. 5. Type 1 Diabetic condition

Non-Insulin Dependent Diabetes Mellitus (Type2 NIDDM or T2DM)

Type 2 Diabetes Mellitus is the commonest form of diabetes characterized by disorders of Insulin resistance and insulin secretion, either which of one may be predominant. Type II diabetes is characterized by peripheral insulin resistance and impaired insulin secretion². Insulin levels is within normal level at initial stage, as it progresses further the level of insulin become deficient for normal functioning. Insulin resistance in type 2 diabetes patients increases the demand for insulin in insulin-target tissues. In addition to insulin resistance, the increased demand for insulin could not be met by the pancreatic β cells due to defects in the function of these cells [18].

On the contrary, insulin secretion decreases with the increased demand for insulin by time due to the gradual destruction of β cells [57] that could transform some of type 2 diabetes patients from being independent to become dependent on insulin. Most type 2 diabetes patients are not dependent on insulin where insulin secretion continues and insulin depletion rarely occurs.

Type 2 diabetes is common in individuals over the age of 40. It is often associated with obesity, decreased physical activity and heredity. (Diabetes mellitus and its treatment saleem batski)

Ketoacidosis seldom occurs spontaneously in this type of diabetes; when seen, it usually arises in association with the stress of another illness such as infection.

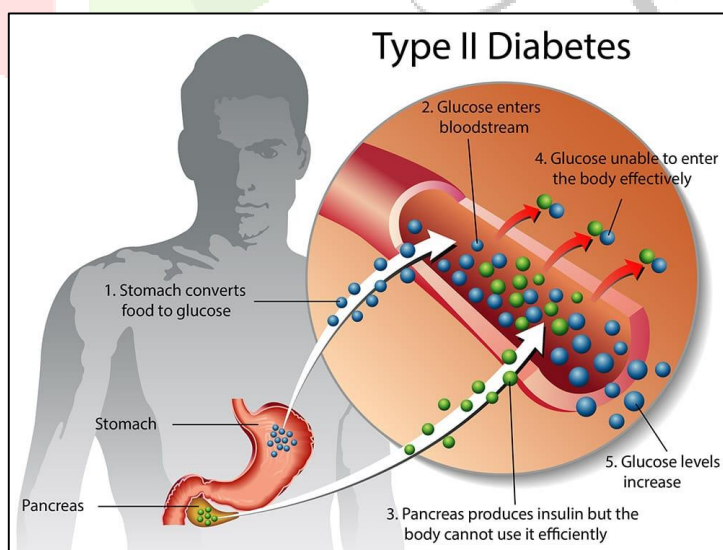


Fig. 6 Type 2 Diabetes

Gestational Diabetes Mellitus

Gestational diabetes mellitus is a metabolic condition of pregnancy that presents as newly developing Hyperglycaemia in pregnant women who did not have diabetes before getting pregnant, and it normally resolves after giving birth. The occurrence of GDM is typically seen between weeks 24 and 28 weeks of pregnancy. The incidence of Gestational diabetes mellitus is growing globally due to certain factors including increase in maternal weight gain, maternal age, and inactivity. It occurs in about 4% of all pregnancies. Patients with GD have a 30% to 50% chance of developing DM, usually type 2 DM.

The body, during gestation period, becomes less responsive to insulin, which leads to an increased production of insulin by pancreatic beta cells. If regular insulin levels fail to elicit the desired response from insulin resistance may develop. To compensate, beta cells must produce more insulin than usual to maintain maternal blood glucose levels.

GDM is essential to detect and treat during pregnancy due to the harmful impact it has on both the mother and the foetus. Gestational diabetes can cause short-term pregnancy complications such as high blood pressure, the necessity for a cesarean section (C-section), pre-eclampsia, and difficulty during childbirth.

Monogenic Type

Alternative Specific sort (Monogenic Types) The most common variety of heritable kinds of polygenic disease is developed with mutations on body twelve in a very internal organ transcription issue brought up as hepatocyte nuclear issue (HNF)-1a. They additionally brought up as genetic defects of beta cells. These varieties of polygenic disease are of times characterised by onset of symptom at associate early age.

Other types

Include genetic defects of the pancreatic β cell or in insulin action pathways (insulin receptor mutations or post-receptor defects)⁴⁴ as well as disease of the exocrine pancreas (e.g., Pancreatitis, pancreatic reaction, or cystic fibrosis) are less common causes of DM.⁴⁵ Endocrinopathies producing insulin counter regulatory hormones excess (e.g., Cushing's syndrome, acromegaly) may result in Diabetes Mellitus.⁴⁵ Certain drugs like glucocorticoids, Pentamidine, niacin, and α -interferon may also lead to DM ⁴⁶ (Diabetes mellitus and its treatment)

CLINICAL SYMPTOMS

Type 1 Symptoms

The most common symptoms of type 1 diabetes include:

- Abnormal thirst and dry mouth
- Sudden weight loss
- Frequent urination
- Lack of energy, tiredness
- Constant hunger
- Blurred vision

Type 2 Symptoms

The symptoms of type 2 diabetes are similar to those for type 1 diabetes and include:

- Excessive thirst and dry mouth
- Frequent urination
- Lack of energy, tiredness
- Slow healing wounds
- Recurrent infections in the skin

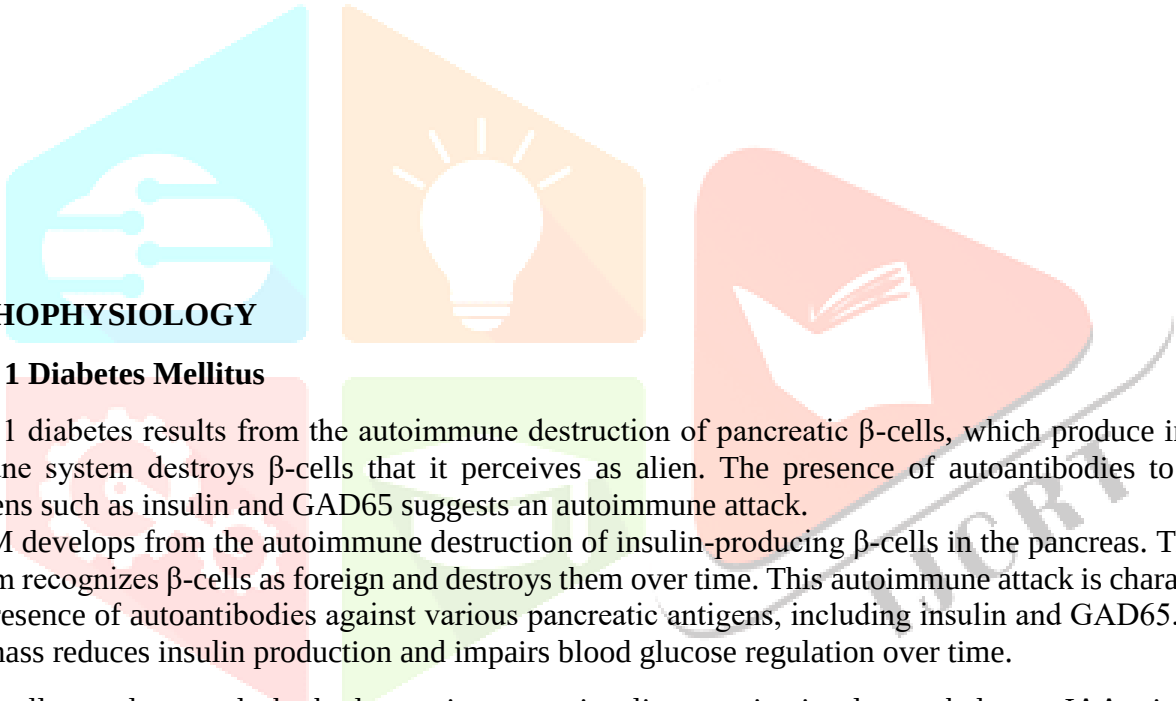
- Blurred vision
- Tingling or numbness in hands and feet.

These symptoms can be mild or absent, so people with type 2 diabetes can live several years with the condition before being diagnosed.

Gestational Diabetes Mellitus

Gestational diabetes often has no symptoms. However, some women may experience symptoms such as:

- Increased thirst and urination.
- Fatigue.
- Blurred vision.
- Nausea.
- Frequent infections, such as yeast infections.
- Polydipsia
- General Malaise
- High Blood Pressure



PATHOPHYSIOLOGY

Type 1 Diabetes Mellitus

Type 1 diabetes results from the autoimmune destruction of pancreatic β -cells, which produce insulin. The immune system destroys β -cells that it perceives as alien. The presence of autoantibodies to pancreatic antigens such as insulin and GAD65 suggests an autoimmune attack.

T1DM develops from the autoimmune destruction of insulin-producing β -cells in the pancreas. The immune system recognizes β -cells as foreign and destroys them over time. This autoimmune attack is characterized by the presence of autoantibodies against various pancreatic antigens, including insulin and GAD65. Loss of β -cell mass reduces insulin production and impairs blood glucose regulation over time.

As β -cells are destroyed, the body requires extra insulin to maintain glucose balance. IAAs, in particular, contribute to insulin resistance and glucose variability. At high levels, these antibodies bind to insulin and block its function

Hyperglycaemia leads to insulin resistance and delayed insulin action, resulting in hypoglycaemia after meals. Immune-mediated interference with insulin function complicates T1DM treatment and can cause blood sugar fluctuations, making clinical control difficult. T1DM is a complex autoimmune disease with β -cell destruction, autoantibody production, and altered insulin activity. It causes impaired glucose metabolism, necessitating lifelong insulin therapy [10].

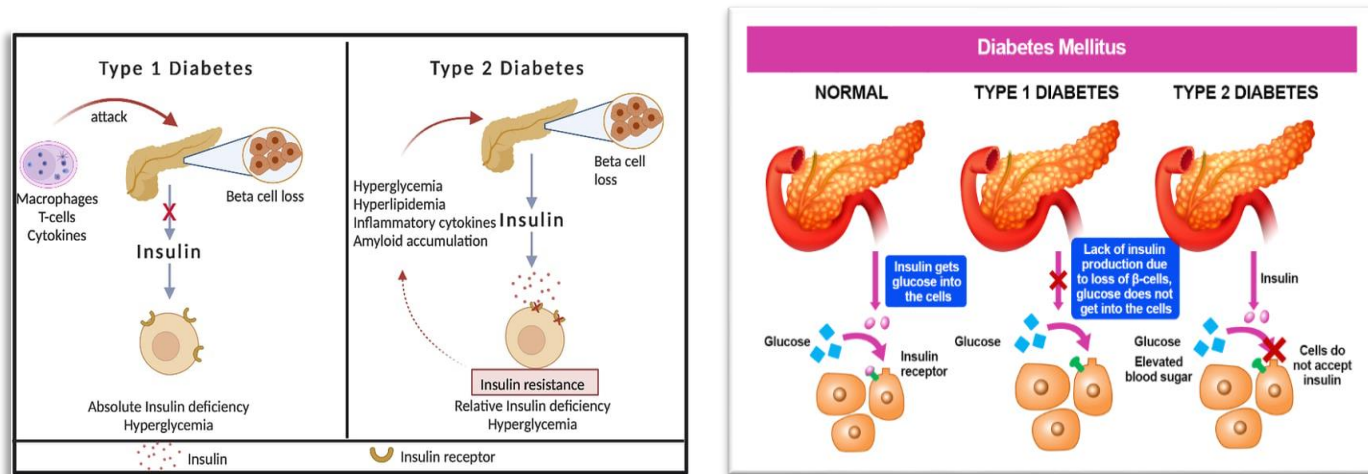


Fig. 7 Pathophysiology

Type 2 Diabetes Mellitus

T2DM, also known as non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes, accounts for 90-95 percent of all diabetes diagnoses. This type of diabetes involves insulin resistance and β -cell dysfunction. [11-13]

Insulin resistance is the primary pathological feature of type 2 diabetes mellitus (T2DM), which is caused by disruptions in various cellular signaling pathways, particularly in peripheral tissues like muscle, liver, and adipose tissue. This resistance reduces the tissues' sensitivity to insulin, impairing glucose uptake and utilization. Early in the disease, reduced insulin sensitivity causes compensatory hyperfunction of pancreatic β -cells, resulting in more insulin secretion to maintain normoglycemia.

As the disease progresses, β -cell function deteriorates due to chronic insulin overproduction. As insulin resistance worsens, β -cells' ability to secrete enough insulin becomes insufficient to balance it out. As β -cell dysfunction progresses, insulin deficiency occurs, making it impossible to maintain normoglycemia. Consequently, hyperglycaemia develops.

Despite the decline in insulin secretion, insulin levels are usually sufficient to prevent the development of diabetic ketoacidosis (DKA), a potentially fatal complication. DKA in T2DM is uncommon but can occur during times of high stress, such as infections, trauma, or other pathological conditions. Furthermore, certain medications, including sodium-glucose co-transporter-2 (SGLT2) inhibitors, corticosteroids, and atypical antipsychotics, can exacerbate DKA by impairing insulin function or glucose metabolism.

Most T2DM patients do not require insulin therapy at the time of diagnosis or as the disease progresses, provided there is no significant physiological stress. Lifestyle changes and oral medications are commonly used in management to improve insulin sensitivity and blood glucose regulation. [11-13]

Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is a condition characterized by elevated blood glucose levels that are first identified during pregnancy, typically developing in the second or third trimester, and is not previously diagnosed as diabetes before pregnancy.

Unlike preexisting diabetes, GDM usually resolves after childbirth or pregnancy termination.

Blood glucose levels are typically lower in early pregnancy, but they rise in the third trimester, causing GDM when they reach diabetic thresholds. GDM is responsible for more than 90% of diabetes cases during pregnancy, with incidence rates ranging from 1% to 14%, depending on the study population.

Age, obesity, previous pregnancies with large babies, and a history of impaired glucose tolerance or GDM all increase the risk of developing the condition. Women with GDM have a higher lifetime risk of developing type 2 diabetes (T2DM), so regular glucose testing is critical for early T2DM detection. [14-15]

In addition to T1DM, T2DM, and GDM, other types of diabetes are associated with specific conditions such as monogenic defects in β -cell function, genetic abnormalities affecting insulin action, endocrinopathies, exocrine pancreatic disorders, and other specific pathologies, although these are less common.

RISK FACTORS

Risk factors for type 1 diabetes

- Genetics (family history of T1DM)
- Autoimmune response (presence of autoantibodies)
- Age (commonly diagnosed in childhood or adolescence)
- Environmental triggers (e.g., viral infections)
- Geographical location (higher incidence in certain regions)
- Ethnicity (higher risk in people of European descent)
- Low birth weight
- Presence of other autoimmune diseases

Risk factors for type 2 diabetes

- Family history of diabetes
- Overweight
- Unhealthy diet
- Physical inactivity
- Increasing age
- High blood pressure
- Ethnicity
- Impaired glucose tolerance (IGT)*
- History of gestational diabetes
- Poor nutrition during pregnancy

Gestational Diabetes Mellitus

For The Mother

- High blood pressure
- Pre clampsia can affect mother and baby
- Type 2 diabetes
- Nephropathy
- Coronary artery disease
- Infection

For the Baby

- Congenital abnormalities
- Macrosomia
- Polycythemia
- Hypoglycemia
- Neonatal jaundice
- Fetal death

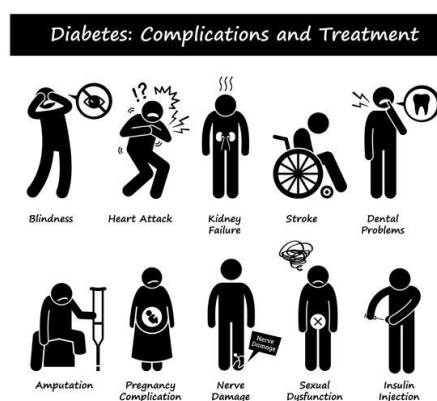


Fig.8 Diabetes Complication

COMPLICATIONS

The National Diabetes Committee has adopted T1DM diabetes, T2DM, and GTM. diabetes will contribute, if left untreated, to a multitude of serious health problems affecting on both smaller and large vessels, i.e. microvascular and macrovascular complications respectively, the microvascular risks affect the renal, the most expensive complication with diabetes, with persistent kidney failure (nephropathy) and nerve injury (neuropathy) raising the likelihood with diabetic foot ulcers and/or amputations while macrovascular disorders can lead to blindness

1. Retinopathy: Microvascular condition that may affect each of the peripheral retina, macula, or both is characterized by diabetic retinopathy is a serious cause of vision loss and blindness in diabetics. Vitreous haemorrhage or retinal objectivity may cause a total or partial loss of vision.

2.Neuropathy: In more than 15 percent of chronic diabetics, diabetic neuropathy tends to be the biggest and least known complication.

3.Peripheral Artery Disease: One of the most dangerous diabetes complications is peripheral artery disease its characterized as arterial obstructive excessive disease that lowers arterial blood fluid during rest and advanced exercise, by multiple studies success attained Peripheral artery disease has been found to be a very dangerous complication of diabetes naturally, but most frequently asymptotically. Hyperglycaemia has been identified as an independent risk factor for peripheral artery disease.

4. Cerebrovascular Disease: Macrovascular and microvascular conditions cause complex cerebrovascular conditions in patients with DM. Brain artery disorders can be categorized as ischemic cerebrovascular disease and haemorrhagic cerebrovascular disease, depending on pathogenesis and anatomy, in DM cases. Prolonged untreated DM results in Micrangium, hypoxic and ischaemic damage to the skin, which increases the likelihood of apoplexy and exacerbates cortical lesions.

5. Diabetic foot: Diabetic foot ulcers are lacerations that usually occur on the soles of the feet in patients with diabetes mellitus due to peripheral neuropathy or peripheral arterial disease on all skin layers, necrosis or inflammation, around 15% to 25% of diabetic patients will grow foot ulcers during their lives.

DIAGNOSTIC TEST FOR DIABETES MELLITUS

1.Urine Testing:

Urine tests are used to detect substances like ketones, glucose, and proteins, providing valuable insights into metabolic and health conditions. Tests such as Clinistix® and Diastix® use colour-changing strips to measure glucose levels, although urine glucose lags behind blood glucose. Ketones can be detected with dipstick tests like Acetest or Ketostix, helping to diagnose diabetic ketoacidosis in Type 1 diabetics ^[21,22]. Urine protein tests can indicate kidney problems, with more sensitive methods detecting microalbuminuria, early signs of kidney damage. While not as accurate as blood tests, urine tests are quick and useful for screening conditions like diabetes and kidney disease ^[23,24].

2.Blood Tests for Diabetes Diagnosis

Blood tests are commonly used to diagnose diabetes mellitus and assess its severity. The following are Key tests employed in the diagnosis and management of diabetes:

I. Fasting Glucose Test

The fasting glucose test is a key diagnostic tool for diabetes, as the plasma glucose level is directly related to the severity of the condition. This test is performed after an overnight fast of at least 8 hours, typically in the morning before breakfast. Blood is drawn from a vein, and the glucose level is measured in the plasma after

separating out the red blood cells. A plasma glucose level of 200 mg/dL or higher suggests diabetes, provided the patient is not on medications such as glucocorticoids, which can affect blood sugar levels. To confirm the diagnosis, the test is usually repeated on another day^[24]. Diabetic individuals with well-controlled blood sugar levels can experience wide fluctuations in their plasma glucose throughout the day, with levels ranging between 250 mg/dL to 3250 mg/dL, which is much

II. Postprandial Plasma Glucose Test

The postprandial plasma glucose test assesses how well the body handles carbohydrates by measuring the blood glucose level two hours after consuming a high-carbohydrate meal or a 75g glucose drink. This test is valuable in detecting impaired glucose metabolism. Glucose levels greater than 1400 mg/L are considered abnormal, while levels between 1200-1400 mg/L are inconclusive, and levels below 1200 mg/L are within the normal range. Although useful, this test can be inaccurate due to various factors that are difficult to control, such as age, weight, previous diet, physical activity, illness, medications, and the timing of the test. When a meal is used as the glucose load, the rate at which glucose is absorbed from the intestine depends on the digestion and absorption of different carbohydrates, further complicating the interpretation^[23,24].

While these tests are integral in diagnosing and monitoring diabetes, they are subject to variables that can influence the accuracy of the results[24].

Oral Glucose Tolerance Test (OGTT) and Other Diagnostic Tests

I. The Oral Glucose Tolerance Test (OGTT) is used to evaluate the body's ability to clear glucose from the bloodstream after a glucose load. The patient fasts for 8-14 hours before the test, during which a baseline blood sample is taken. Then, the patient drinks a glucose solution, and blood is drawn at specified intervals to measure glucose levels, and sometimes insulin. For diabetes screening, the critical measurement is taken two hours after ingestion. In non-diabetics, glucose levels rise and then gradually decrease as insulin works to metabolize the sugar. In diabetics, glucose levels remain high after drinking the solution. A plasma glucose level of 2000 mg/L or higher at the two-hour mark, along with elevated levels at another point during the test, confirms the diagnosis of diabetes. Various factors, such as illness, medications, and hormones, can influence the test's accuracy. The patient must remain ambulatory during the test, as inactivity can decrease glucose tolerance.

II. Intravenous Glucose Tolerance Test (IVGTT) For individuals with malabsorption issues or a history of gastrointestinal surgery, the **Intravenous Glucose Tolerance Test (IVGTT)** is an alternative. In this test, glucose is administered intravenously over 30 minutes. In non-diabetics, glucose levels rise and then gradually fall, returning to fasting levels within about 90 minutes. In diabetics, glucose levels remain elevated and only return to fasting levels more slowly [24].

III. The O'Sullivan Test is specifically used to detect gestational diabetes. The patient is given a 50g glucose load after fasting, and blood is drawn one hour later. A plasma glucose level above 1500 mg/L suggests gestational diabetes [26].

IV. The Glycated Haemoglobin (HbA1c) Test measures the percentage of haemoglobin that has bonded with glucose, reflecting the average blood glucose levels over the past 2-3 months. Elevated HbA1c levels are directly proportional to long-term hyperglycaemia. This test is crucial for monitoring diabetes but is not sensitive enough to detect early or borderline cases. Additionally, plasma albumin can also be measured for its degree of glycosylation, providing insight into short-term blood glucose levels due to its shorter half-life compared to haemoglobin^[27,28,29].

Emerging Trends and Future Directions

A .Conventional Treatment

The general approach to treating various types of diabetes includes regular exercise, weight management, a balanced diet, oral anti-diabetic medications, and insulin injections. Since the islets of Langerhans, liver, and skeletal muscles play a critical role in diabetes, therapies often target these organs. Additionally, maintaining a healthy diet and regularly monitoring blood glucose levels can significantly reduce the risk of complications associated with diabetes.

Diet Therapy

A healthy diet, combined with appropriate medication and regular physical activity, is critical for effectively controlling blood sugar levels. A well-planned and balanced diet is essential for achieving maximum benefits. A typical approach suggests that carbohydrates should account for 60-65% of the diet, fats for 25-35%, and proteins for 10-20%, with alcohol avoided entirely. Quitting smoking is also strongly recommended. Limit your intake of processed, preserved, high-density, and deep-fried foods, as these all contribute to visceral obesity. Onion, garlic, ginger, turmeric, bitter melon, okra, guava, radish, spinach, drumstick, black plum, tuls, chickpeas, and barley are all foods that can help you manage diabetes.

Exercise

Exercise plans should be tailored to each person's physical condition, capacity, motivation, and personal preferences. Regular exercise five to six days per week aids in weight loss and body fat reduction. However, healthcare providers should start patients at a lower intensity and gradually increase it to reduce the risk of adverse effects like hypoglycemia, injury, or cardiovascular complications.

Research and Innovation

From genetics to gut microbiota, cutting-edge research is revealing new pathways that will revolutionize diabetes management and treatment. These innovative advancements have far-reaching implications that go beyond clinical practice, propelling new research directions, influencing pharmaceutical development, and shaping healthcare policies.

Furthermore, precision medicine and the rise of technology-enabled solutions, such as constant glucose monitoring and insulin pumps, are improving diabetes care quality. These tools enable more personalized and immediate interventions, ultimately leading to improved disease management.

The potential role of lifestyle factors like diet, exercise, and stress management is receiving more attention. Researchers are investigating how these elements, along with genetic predispositions and the microbiome, influence diabetes development and progression.

To ensure that these advancements translate into real-world patient outcomes, researchers, clinicians, industry leaders, and policymakers must work together.

This collaboration will speed up the development, testing, and implementation of new treatments, transforming diabetes care into more effective, patient-centered solutions. With ongoing investments in research, technology, and policy reform, there is hope for a future in which diabetes is not only better managed, but possibly avoidable.

Oral Insulin Secretagogues (antidiabetic drugs)

Insulin secretion from pancreatic beta-cells is encouraged and blood glucose levels are lowered with oral hypoglycemic medications. Sulfonylureas, biguanides, thiazolidinediones (glitazones), alpha-glucosidase inhibitors, and meglitinides are the five primary groups into which these medications fall.

- **By inhibiting ATP-sensitive potassium channels** in pancreatic beta-cells, sulfonylureas (such as tolbutamide, chlorpropamide, glibenclamide, glibizide, gliclazide, and glimepiride) increase insulin secretion. Depolarization, calcium influx, and insulin release result from this action. Rather than directly promoting insulin secretion, biguanides (like metformin and phenformin) lower blood glucose through three mechanisms: decreasing hepatic gluconeogenesis, increasing peripheral glucose utilization, and preventing intestinal glucose absorption. Common side effects include hypoglycaemia and skin rashes.

- **Biguanides** also reduce LDL cholesterol and plasma triglycerides. The most common side effect of metformin, which is typically taken in doses of 1g twice daily, is gastrointestinal disturbance.

- **Thiazolidinediones** (glitazones), such as pioglitazone and rosiglitazone, increase insulin sensitivity by interacting with the liver, muscle, and adipose tissue's peroxisome proliferator-activated receptor gamma (PPAR- γ). Through calcium signaling, they also relax vascular smooth muscle and lower blood pressure. The usual dosage for pioglitazone is 15–45 mg once daily, whereas the usual dosage for rosiglitazone is 4–8 mg daily. Hepatotoxicity and weight gain are side effects.

- **Alpha-Glucosidase inhibitors**, such as Acarbose and Miglitol, inhibit enzymes in the small intestine that digest carbohydrates. This reduces postprandial carbohydrate absorption and aids in the management of postmeal hyperglycemia. These inhibitors are typically taken in doses of 50-100 mg three times per day, before meals. Gastrointestinal upset, such as bloating and diarrhea, is a frequent side effect.

- **Meglitinides**, like sulfonylureas, stimulate insulin secretion by blocking ATP-sensitive potassium channels in pancreatic beta-cells. Examples include Repaglinide and Nateglinide. They are especially effective at controlling post-prandial glucose levels in people with type 2 diabetes. Repaglinide is administered at doses of 0.25-4 mg before meals, while Nateglinide is dosed at 60-120 mg before each meal. The primary adverse effect is hypoglycemia, which occurs when meals are skipped or delayed.

In conclusion, oral antidiabetic medications differ in their mechanisms of action, dosage regimens, and side effect profiles, allowing for personalized treatment based on the patient's unique needs and health status.

Insulin Therapy

Insulin therapy is used when oral medications fail to keep blood sugar levels under control. Insulin is classified according to its onset and duration of action. • Ultrashort-acting insulin works in 10-20 minutes and lasts 3-5 hours. • Short-acting insulin has an onset time of 30-60 minutes and can last up to 5-8 hours. • Intermediate-acting insulin: onset in 1-2 hours; frequency 16-18 hours. • Long-Acting Insulin: onset in 1-6 hours; duration 20-36 hours.

Insulin resistance is a significant contributor to the development of diabetes. Increased waist circumference is a recognized indicator of high risk for cardiovascular disease and type 2 diabetes. Over the past two decades, there have been significant advancements in insulin delivery systems, which aim to provide more precise and targeted treatment for individuals with diabetes [27,28] .

Some of the more convenient methods for insulin administration include:

- **Insulin Syringes:** Featuring ultra-fine needles for subcutaneous injection, suitable for multiple uses.
- **Insulin Pens:** These portable devices contain insulin cartridges with replaceable needles, ideal for patients on the go.

- **Insulin Pumps:** Devices that automatically administer insulin based on the user's blood glucose readings, offering more flexibility in insulin delivery.
- **Biodegradable Microspheres:** Insulin is incorporated into biodegradable polymer microspheres, which release insulin in a controlled manner over time.
- **Inhaled Insulin:** Administered via a nebulizer (currently under clinical trials), providing an alternative to injections.

These innovations in insulin delivery systems and ongoing research are enhancing the quality of life for individuals with diabetes, providing more personalized and efficient treatment options.

B. Alternative treatment

Alternative diabetes treatments are often thought to have fewer side effects than conventional medications. There are several treatments available, including herbal remedies, mineral supplements, and Ayurvedic therapies, each with their own approach to disease management.

• Herbal treatment

Diabetes has been managed with medicinal plants since antiquity. Traditional herbal remedies contain phytochemicals that have shown promise in the treatment of diabetes, sparking interest in the creation of new therapeutic agents. Although over 400 traditional plants have been identified as potentially useful in diabetes management, only a small number have been scientifically tested for efficacy.

Modern research focuses on digitizing the broad understanding of medicinal plants and arranging it with the World Health Organization's botanical medicine standards, thus broadening the potential of herbal drugs in diabetes care.

While these supplements may have certain advantages, they should only be used under medical guidance to ensure their efficacy and safety.

• Mineral Supplements

Taking micronutrients like chromium, magnesium, and vanadium can improve glucose metabolism in diabetic patients. These supplements can help lower fasting blood glucose levels, reduce insulin resistance, and improve glucose tolerance. Additionally, they may boost high-density lipoprotein (HDL) cholesterol, which can improve cardiovascular health in individuals with diabetes. To ensure safety and effectiveness, these supplements should be used under medical supervision, even if they offer supportive benefits [29].

• Ayurvedic treatment.

Ayurveda, an ancient Indian medical system, offers a comprehensive approach to managing chronic diseases such as diabetes. Ayurveda embodies physical, mental, and spiritual wellness, with a strong emphasis on three core components: *ausadh* (medication), *anhar* (diet), and *vihar* (workout).

Conclusion of the Comprehensive Review of Diabetes Mellitus.

Diabetes Mellitus (DM) is a complex group of metabolic disorders characterized by long-term hyperglycaemia caused by impaired insulin secretion, insulin resistance, or both. The article looked at various aspects of diabetes, such as classification, epidemiology, pathophysiology, diagnosis, treatment strategies, and complications. The study highlighted the disease's diverse nature and growing global burden, emphasizing the importance of effective public health strategies to combat its rising prevalence.

Type 1 diabetes is primarily an autoimmune disease, whereas type 2 diabetes is primarily caused by insulin resistance and beta-cell dysfunction.

A precise diagnosis is necessary for developing effective treatment protocols and understanding how the disease progresses in individuals.

Diabetes is becoming a global epidemic, with a significant increase in Type 2 diabetes cases blamed on

urbanization, sedentary lifestyles, and poor diets.

Diabetes has been identified as one of the leading causes of morbidity and mortality worldwide, with an increase evident in both developed and developing countries.

Chronic hyperglycaemia, regardless of cause, results in a series of metabolic changes that contribute to complications such as cardiovascular disease, diabetic retinopathy, and nephropathy.

References:

1. Bastaki, S. (2005). Diabetes mellitus and its treatment. *International journal of Diabetes and Metabolism*, 13(3), 111-134.
2. Deshmukh, C. D., Jain, A., & Nahata, B. (2015). Diabetes mellitus: a review. *Int. J. Pure Appl. Biosci*, 3(3), 224-230.
3. Tegegne, B. A., Adugna, A., Yenet, A., Yihunie Belay, W., Yibeltal, Y., Dagne, A., ... & Zeleke, T. K. (2024). A critical review on diabetes mellitus type 1 and type 2 management approaches: from lifestyle modification to current and novel targets and therapeutic agents. *Frontiers in Endocrinology*, 15, 1440456.
4. Sicree, R. (2006). Diabetes and impaired glucose tolerance. *Diabetes Atlas*, 15–109.
5. Raffel, L. J., Scheuner, M. T., & Rotter, J. I. (1997). Genetics diabetes. In D. Porte & R. S. Sherwin (Eds.), *Ellenberg & Rifkin's Diabetes Mellitus* (pp. 401–454). Stamford, CT, Appleton & Lange.
6. Seshadri, R. J. D. C. (2002). American diabetes association gestational diabetes mellitus. *Diabetes Care*, 25, S94-S96.
7. Pandit, M. K., Burke, J., Gustafson, A. B., Minocha, A., & Peiris, A. N. (1993). Drug-induced disorders of glucose tolerance. *Annals of internal medicine*, 118(7), 529-539.
8. DeFronzo, R. A., Ferrannini, E., Zimmet, P., & Alberti, G. (Eds.). (2015). *International textbook of diabetes mellitus*. John Wiley & Sons.
9. Banday, M. Z., Sameer, A. S., & Nissar, S. (2020). Pathophysiology of diabetes: An overview. *Avicenna journal of medicine*, 10(04), 174-188.
10. Leahy, J. L. (2005). Pathogenesis of type 2 diabetes mellitus. *Archives of medical research*, 36(3), 197-209.
11. DeFronzo, R. A. (2004). Pathogenesis of type 2 diabetes mellitus. *Medical clinics*, 88(4), 787-835.
12. Muoio Muoio, D. M., & Newgard, C. B. (2008). Molecular and metabolic mechanisms of insulin resistance and β -cell failure in type 2 diabetes. *Nature reviews Molecular cell biology*, 9(3), 193-205.
13. Noctor, E., Crowe, C., Carmody, L. A., Saunders, J. A., Kirwan, B., O'Dea, A., ... & ATLANTIC-DIP investigators. (2016). Abnormal glucose tolerance post-gestational diabetes mellitus as defined by the International Association of Diabetes and Pregnancy Study Groups criteria. *European journal of endocrinology*, 175(4), 287-297.
14. Aroda, V. R., Christophi, C. A., Edelstein, S. L., Zhang, P., Herman, W. H., Barrett-Connor, E., ... & Diabetes Prevention Program Research Group. (2015). The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with and without gestational diabetes: the Diabetes Prevention Program outcomes study 10-year follow-up. *The Journal of Clinical Endocrinology & Metabolism*, 100(4), 1646-1653.
15. <https://www.idfdiabeteschool.org/type-2-diabetes>
16. Mishra, M. K., Panda, B. B., Ghosh, G., Mishra, S. K., & Barik, B. B. (2008). Emerging trends in the management of diabetes: an overview. *Indian drugs*, 45(6), 441-446.
17. IDF Diabetes Atlas, 4th edition. International Diabetes Federation, 2009.
18. Chan, J. C., Malik, V., Jia, W., Kadowaki, T., Yajnik, C. S., Yoon, K. H., & Hu, F. B. (2009). Diabetes in Asia: epidemiology, risk factors, and pathophysiology. *Jama*, 301(20), 2129-2140.
19. Yang, W., Lu, J., Weng, J., Jia, W., Ji, L., Xiao, J., ... & He, J. (2010). Prevalence of diabetes among men and women in China. *New England journal of medicine*, 362(12), 1090-1101.
20. Friedemann, T. E., Sheft, B. B., & Miller, V. C. (1946). An assessment of the value of the nitroprusside reaction for the determination of ketone bodies in urine. *Quarterly Bulletin of the Northwestern University Medical School*, 20(3), 301.
21. R. Belinda, Gale 2004. Encyclopaedia of Alternative Medicine :2603-2605.
22. Mauer, A. C. (1979). The therapy of diabetes. *Clinical Chemistry: Theory, Analysis and Correlation*, 67, 422–428.
23. Ngugi, M. P. (2006). *Hypoglycemic effects of some Kenyan plants used in management of diabetes mellitus in eastern province* (Doctoral dissertation, MSc. thesis, Kenyatta University, Kenya).

24. Larsen, S., Hilsted, J., Philipsen, E. K., Tronier, B., Christensen, N. J., Nielsen, M. D., & Worning, H. (1990). Glucose counter regulation in diabetes secondary to chronic pancreatitis. *Metabolism*, 39(2), 138-143..
25. Dods, R. F., & Bolmeyer, C. (1979). Glycosylated hemoglobin assay and oral glucose tolerance test compared for detection of diabetes mellitus. *Clinical chemistry*, 25(5), 764-768.
26. Guthrow, C. E., Morris, M. A., Day, J. F., Thorpe, S. R., & Baynes, J. W. (1979). Enhanced nonenzymatic glucosylation of human serum albumin in diabetes mellitus. *Proceedings of the National Academy of Sciences of the United States of America*, 76(9), 4258–4261. <https://doi.org/10.1073/pnas.76.9.4258>
27. Pitter, A. G., Joseph, N. A., & Greenberg, A. S. (2004). Adipocytokines and insulin resistance. *The Journal of Clinical Endocrinology & Metabolism*, 89(2), 447-452.
28. Moller, D. E., & Kaufman, K. D. (2005). Metabolic syndrome: a clinical and molecular perspective. *Annu. Rev. Med.*, 56(1), 45-62.
29. Mooradian, A. D., Failla, M., Hoogwerf, B., Maryniuk, M., & Wylie-Rosett, J. (1994). Selected vitamins and minerals in diabetes. *Diabetes care*, 17(5), 464-479.

