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Diabetes Mellitus: Classification, Symptoms, Diagnosis, Treatment, Prevention, and Implications

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Abstract

Diabetes mellitus (DM) is a chronic, progressive metabolic disorder marked by persistent hyperglycemia due to defects in insulin secretion, insulin action, or both. Insulin, a vital hormone produced by the pancreas, facilitates the uptake of glucose into cells and helps maintain blood glucose homeostasis. When insulin production is insufficient or its action is impaired, glucose accumulates in the bloodstream, leading to elevated blood sugar levels. Over time, this imbalance can result in serious and potentially irreversible complications affecting multiple organ systems, including the heart, kidneys, eyes, nerves, and blood vessels.

Diabetes is generally classified into two main types: Type 1, characterized by autoimmune destruction of pancreatic beta cells, and Type 2, which involves insulin resistance and relative insulin deficiency. Both types present with common symptoms such as excessive thirst, frequent urination, unexplained weight loss, fatigue, and blurred vision. If not diagnosed and managed early, diabetes can lead to long-term health issues such as cardiovascular diseases, nephropathy, retinopathy, and neuropathy. The global burden of diabetes is increasing at an alarming rate, with projections indicating a possible doubling of cases in the coming decades. Early diagnosis through blood glucose testing and glycosylated hemoglobin (HbA1c) measurement is crucial for timely intervention. Management strategies typically involve lifestyle modifications, dietary regulation, regular physical activity, and pharmacological therapies including insulin and oral hypoglycemics. This paper provides a detailed examination of the pathophysiology, symptoms, diagnostic methods, complications, and comprehensive management approaches associated with diabetes mellitus.

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GRAPHICAL ABSTRACT



INTRODUCTION

As per data provided by the WHO, diabetes ranks amongst the world's top 10 most common causes of death. One person per 5 seconds perishes due to its complexities. Its first reporting dates back to 3000 years ago in Egyptian manuscripts. The islets of Langerhans of the pancreas contain beta cells, which are designed to secrete this Polypeptide/anabolic hormone, called insulin. Diabetes leads to resistance in cells to this

hormone. This turns into an unresponsive insulin hormone. This action in turn enhances degrees of glucose in the bloodstream, causing type 2 D.M. Diabetes. Diabetes-affected patients show various traits of this ailment, which are polyuria, polyphagia, polydipsia, blurred vision, slow wound healing, weight loss, etc. Despite all these early signs affecting people, some can still be asymptomatic. Those affected by type 2 D.M are among the affected which come under the asymptomatic category.



Ramifications of this fatal disease, particularly in early stages if untreated are- trouble in blood vessels, head and kidney ailments, blindness glaucoma, nerve and foot complexities, Diabetes is common in patients with endocrine diseases like excess release of growth hormones, glucocorticoids, glucagon and epinephrine in disease like acromegaly, Cushing's syndrome, glucagonoma, and pheochromocytoma. Diabetes is common in patients with genetic disorders like Down syndrome, Klinefelter syndrome, Turner syndrome, and Wolfram syndrome.

Classification of Diabetes Mellitus: This fatal malady of diabetes has been categorized into varied sub-sections, which have been catalogued below for easy understanding:

Type 1 diabetes

Destruction of beta cells occurs in the pancreas due to autoimmune processes, leading to the absence of insulin or extremely low insulin levels. Abnormal insulin secretion started before 2 years of diagnosis. At the same time, the sensitivity of beta cells towards glucose also decreases. After the diagnosis has been done, the insensitivity of beta cells towards insulin increases. After diagnosis is done, a lesser amount of insulin may continue for years, which leads to a small amount of insulin or no insulin. Elevated glucose in our body is a sign of T1D. During the T1D, significant glucose variations also occur.



- I. **Idiopathic T1D:** It is a unique form of T1D without indication of autoimmune disorder, and it is less severe than T1D. Patients with idiopathic diabetes are at risk of ketoacidosis and insulin insufficiency.
- II. **Fulminant T1D:** It is another type of T1D and was discovered in 2000. It is similar to idiopathic; neither is autoimmune. Keto-acidosis occurs rapidly after the hyperglycaemia, and serum C-peptide levels are indiscernible, and blood glucose amount is also high, i.e., 288 mg/dL. Quick and complete β -cell death leads to no residual insulin. This condition is due to genetic and environmental factors. An increased immune response

without noticeable genesis of autoantibodies striking the pancreatic β cells.

Type 2 diabetes: This is the most common form of diabetes, and it occurs due to flawed insulin secretion. The body makes more or less Insulin based on what it needs to keep blood sugar levels normal. The disposition index shows how the sensitivity of insulin and the secretion of insulin work together to keep the blood sugar level normal. Type 2 diabetic patients have both flawed insulin secretion as well as inadequate insulin sensitivity therefore disposition index is low in these patients.

Gestational diabetes: This type of diabetes mostly occurs in pregnancy in the second or third trimester. The hyperglycemia in pregnancy increases the risk of adverse outcomes for the mother and child. The child is at high risk of developing diabetes in adolescence. The complications due to gestational diabetes include premature birth, weight variations in the baby, mostly elevated weight, caesarean delivery, and elevated blood pressure. Risk factors of gestational diabetes include hereditary

338 © 2025 Sefat Baidar, Anchal Dhawan, Diksha Sharma, Shivani Sharma. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY NC ND). https://creativecommons.org/licenses/by/4.0/ influence, obesity, PCOS, inactive lifestyle, and environmental factors.

Hybrid forms of diabetes

- a. Latent autoimmune diabetes in adults (LADA): Also known as Slowly evolving immune-mediated diabetes, it is similar to type 2 diabetes, but it involves the formation of pancreatic autoantibodies. Firstly, patients with LADA are treated with oral hypoglycaemic agents and lifestyle modifications. The patients require insulin treatment sooner as compared to patients with type 2 diabetes. The subtype of LADA includes LADY (latent autoimmune diabetes in youth), mostly present in children and adolescents, formation of autoantibodies also takes place.
- b. Ketosis-prone type 2 diabetes: It is a rare clinical disease mostly seen in young African Americans and people of sub-Saharan Africa. Firstly, patients develop episodes of ketosis and insulin deficiency. Patients with this condition usually get better, and insulin therapy may not be required. 90% of people may experience diabetic ketoacidosis within ten years. There is no information on genetic or autoimmune involvement. Experts believe that elevated blood sugar damages the beta cells (glucose toxicity). After insulin therapy function of beta cells is restored to normal functioning, and blood glucose levels also become normal.

Other Types of Diabetes Mellitus

Hereditary defects of the beta-cell: Maturity-onset diabetes of the young (MODY): This type of diabetes is mostly seen in younger people, usually before 25 years of age. It is due to deviant monogenetic beta cell function. It includes less insulin secretion and less or no insulin action. It is caused by to autosomal dominant factor, which means one of the copies gene from the parent causes this condition. It occurs due to mutations of various genes. MODY runs through generation to generation, patients can be treated with oral hypoglycaemics and lifestyle modifications.

Genetic defects in insulin action: Insulin receptors undergo gene mutations, which further causes abnormal insulin functioning which leading to increased insulin levels and elevated blood sugar, which further leads to severe diabetes. The pateints may also experience skin darkening, enlarged ovaries (PCOS), and development of male characters.

Diseases of the Pancreas: Diabetes also develops due the various disease conditions like Pancreatic cancer, trauma, pancreatectomy, and pancreatitis. In most cases, diabetes develops when the pancreas is badly affected; even small damage to the pancreas can also lead to diabetes. Diseases like cystic fibrosis (thick sticky mucus in various organs like lungs), hemochromatosis (iron accumulation in organs like the pancreas, liver, etc), adenocarcinoma (cancer of glandular cells), *fibrocalculous pancreatopathy* (damage and stones in the pancreas) also inhibit secretion and damage pancreatic beta cells.

Endocrinopathies: Some hormones are released in excess amounts, like the excess release of growth hormone causes acromegaly, excess glucagon causes glucagonoma, excess cortisol levels cause Cushing syndrome, which leads to increased insulin action. Certain hormones can antagonize insulin action and lead to diabetes. Diabetes is worsened in patients who have prior insulin secretion problems. Hypokalaemia (a lesser amount of potassium in the blood), which further leads to diabetes.

Chemical or Drug -induced diabetes: This type of diabetes is very rare. This type of diabetes occurs due to certain medications or chemicals, and toxins that alter the functioning of beta cells and insulin action, either they altering these functions or they promoting diabetes in patients who already have insulin resistance. Long-term use of steroids like glucocorticoids, antineoplastic medications (drugs used in the treatment of cancer), antipsychotics (medicines used in the treatment of mental health conditions) like clozapine, and excess intake of Nicotinic acid. Permanent damage to beta cells occurs due to toxins like vacor, pentamidine. Long-term exposure to environmental toxins, like arsenic (As) and heavy metals, can lead to the development of diabetes mellitus.

Infections: The viruses like coxsackievirus B, congenital rubella, mumps, adenovirus, and cytomegalovirus have been associated with the damage of beta-cells. These viruses promote diabetes in patients who have a genetic history of type 1 diabetes. Patients who are prone to diabetes, these viruses promote the autoimmune response, leading to beta cell destruction.

Prediabetes

A condition where glucose in your bloodstream is not at levels that could be considered diabetic. In prediabetes, glucose ratings range b/w 100-125 mg/dl. Healthy glucose parameters in a human bloodstream are in the range of 70-99 mg/dl. This condition is thus also referred to as a warning of type 2 DM. The American Diabetes Association (ADA) proclaims that there is are 9-14% probability of turning prediabetes into actual diabetes for the age group of 45 years and older. This precursor to diabetes can be reversed with necessary lifestyle adjustments like healthy eating habits and consistent physical activity.

Symptoms of Diabetes

Diabetes produces various signs and symptoms, which may vary from patient to patient depending on the type of diabetes and severity of the disease. The most common signs and symptoms are:

- Increased thirst and frequent urination: Elevated blood sugar levels overload the kidneys, pressuring them to eliminate excess sugar through urination. Excessive urination leads to dehydration, which results in increased thirst.
- Weight loss: When glucose does not arrive in the cells, the body starts to break down fat and muscles for energy.

- Fatigue: A lesser amount of insulin or ineffective action of insulin can leave you feeling tired. This is due to glucose fluctuations and dehydration.
- Blurred vision: Elevated blood sugar levels cause conditions like diabetic retinopathy, diabetic macular edema, and changes in the shape of the lens.
- Slow-healing or frequent infections: elevated blood sugar damages the blood vessels, leading to impaired blood flow. Diabetic neuropathy decreases the sensations, weakened immune system can alter the body's capacity to heal and fight infections.
- Dry skin and itching: Due to Dehydration, nerve damage, and alterations in circulation, dry and itchy skin.
- Presence of ketones in urine: When cells do not get glucose, the breakdown of muscles and fats takes place and produces ketone bodies.
- Numbness in feet: This is due to nerve damage (diabetic neuropathy).

Role of Glucose in Diabetes: Glucose is an ingredient in our food that we eat. Food and liver account for our glucose intake. Human cells encompass our muscles & body tissues, and use glucose as a source of energy. Sugar, when engrosses into our bloodstream, enters our cells with the assistance of insulin. The liver acts as a reservoir unit of insulin. At the time of low sugar levels, insulin assists in keeping this level in a desired range. Higher secretion of glucose in the human bloodstream leads to diabetes.

Role of Insulin in Diabetes: Insulin is an anabolic hormone. responsible for the metabolism of carbohydrates, lipids, and proteins. It works as a primary messenger by which glucose is moved into the cell, which is further utilized as energy. It also encourages the liver to store glycogen. At the juncture of higher glycogen in the liver, the pancreas has to secrete more the insulin to maintain the glucose at the optimum degree. As it helps the cells to open up for more intake of glucose, its secretion level needs to be at an optimum to keep glucose in our bloodstream at a desired range. People with diabetes, with a lack symptoms insulin, experience like increased of appetite, polydipsia, dysuria, weight loss, increased appetite, and vision problems. Some people do not experience any symptoms, as in type 2 diabetic patients.

Complications of D.M.

The aggravations involved with diabetes are summarized as:

- 1. Complications to the heart, blood vessels, eyes, kidneys, nerves & teeth and gums.
- 2. People living with this disease are up to three times more susceptible to developing cardiovascular disease.
- 3. Some sort of vision loss in around 30% of diabetic individuals develops in the later part of their lives.
- 4. Retinopathy is a common underlying ailment in affected people.
- 5. Kidney Nephropathy in the kidneys of diabetic people is 10 times more likely to occur.

- 6. It targets body functioning, attacks nerves. This leads to neuropathy, causing limbs and feet to be impaired. Every 30 seconds, a lower limb perishes in diabetic individuals.
- 7. Cardiovascular diseases are one of the prime underlying ailments associated with this malady.
- 8. It can cause oral health aggravations, affecting teeth, gums & mouth, primarily because higher glucose promotes deleterious bacteria in the human mouth.
- 9. One of its tenets is prolonged wound healing.

Diabetes Prevention: T1D is not yet preventable. T1D can be averted by the factors discussed below;

- As an unhealthy lifestyle is one of the primary attributes of diabetes, IDF advocates consistent physical activity at least b/w 3-5 days a week for a minimum of 30-45 minutes.
- b) Balanced diet, regular and consistent exercise, and elimination of sugary and processed foods.
- c) Maintaining optimum weight, as obesity enhances the probability of diabetes.
- d) Regular screening aids in detecting the malady at early stages.
- e) Healthier diet for the contrived patients.
- f) Water, coffee or tea over fruit juices, soda, or other sugarsweetened beverages is advocated.
- g) Fresh fruits thrice a day is endorsed. Green leafy vegetables on top of that is even more beneficial.
- h) For a snack, nuts or unsweetened yoghurt is recommended.
- i) Alcohol intake beyond 2 standard drinks needs to be avoided.
- j) Avoid processed meat and pick white meat in lean cuts, poultry, and seafood.
- k) Pick peanut butter over chocolate or jam.
- 1) Avoid rice intake and consume whole-grain bread instead.
- m) Substitute unsaturated fats (olive oil, corn oil, canola oil, or sunflower oil) over saturated fats (butter, ghee, animal fat, coconut oil, or palm oil).

Diagnosis of D.M.: Currently, various tests help in its diagnosis, which are;

a) Fasting Plasma Glucose (FPG).
Normal less than 100 mg/dl
Prediabetes: 100-125 mg/dl
Diabetes greater than or equal to 136 mg/dl
Test requirements: Avoid calorie intake for up to 8 hrs.

b) Oral Glucose Tolerance Test (OGTT):

Normal less than 140 mg/dl Prediabetes: 140-199 mg/dl Diabetes greater or equal to 200 mg/dl Procedure: Measure plasma glucose after the space of 1 hr after a glucose load of 75g is provided.

c) Random Plasma Glucose (RPG):

Diabetes is diagnosed if greater or equal to 200 mg/dl in case of a patient suffering from classic traits of hyperglycemia.

d) Hemoglobin A1C (HbA1C):

Normal less than 5.7% Prediabetics range b/w 5.7-6.4% Diabetes greater than or equal to 6.5% Mean glucose levels are reflected for a time gap of 2-3 months

e) Confirmatory Testing:

For asymptomatic individuals, abnormal results must be confirmed on a separate day using the same test on a different test. For patients showing no traits of the disease, a different test should be done on a separate day to check for any abnormality in the results.

Management of D.M.: Management of diabetes includes lifestyle modifications as well as medical treatment. Lifestyle modification is essential for individuals who are in a prediabetic condition as well as for confirmatory cases of diabetes. Individuals should have proper physical activity, and the proper dietary plan should be followed. Patients should increase the intake of fruits, vegetables, whole grains, nonfat dairy, and lean meats and should avoid foods that are rich in sugar and fats. Individuals should also guit smoking and drinking alcohol. Currently, Nanotechnology has also been used in diabetic patients, it delivers drugs as nanoparticles to lower the blood glucose level. It is a non-surgical approach used for insulin therapy and vaccination. Nowadays, Gene therapy is also used in the treatment of diabetes involves the establishment of a normal gene at the site of the defective gene. Its main benefit is that it's a single treatment that can cure the disease permanently. Stem cell therapy is also used in the treatment of diabetes, but the requirement of donors limits its confined. The medicinal treatment for the malady comprises both oral and injectable treatments. Type 1 of this ailment has a singular treatment, which is insulin therapy. The other type, which is type 2, has a dual remedy, one with oral antidiabetic drugs followed by insulin therapy. The latter is provided only if the glucose in the blood does not recede with oral antidiabetics.

The common medications at our disposal are:

Insulin Treatment: Rapid Acting: Insulin lispro, Insulin aspart, Insulin glulisine

Short Acting: Regular/Soluble Insulin

Intermediate Acting

- Lente insulin
- Isophane

Long Acting (Analogous)

- Insulin glargine
- Insulin detemir

Inhaled Insulin

- Exubera Afrezza
- Oral Antidiabetic

Medications

Enhance Insulin Secretion

a. KATP Channel Blockers

Sulfonylureas and glinides both work similar mechanism of action both provoke insulin release, KATP potassium channel also known as ATP sensitive potassium channel control the insulin release present on the membrane of beta cells but the binding site of both these drugs is distinct they prompt channel termination and cell depolarization resulting in elevated calcium in the cytoplasm of the cell which promotes insulin secretion. Common side effects are hypoglycemia and weight gain.

- (i) Sulfonylurea include tolbutamide, glibenclamide, glipizide, glimepiride.
- (ii) Megalitinide include Repaglinide, Nateglinide.

b. Dipeptidyl peptidase-4/DPP-4 Inhibitors

These drugs work by inhibiting the breakdown of GLP-1 and GIP (incretin hormones). These hormones are responsible for insulin secretion and they restrain glucagon secretion resulting in reduction of blood glucose level. Drugs like sitagliptin, vildagliptin, saxagliptin, alogliptin, teneligliptin, linagliptin are under this category.

2. **Overcome Insulin Resistance:**

a. **Biguanide/AMPK Activator:** Biguanides function via decreasing glucose production in the liver, enhancing insulin sensitivity, and lessening glucose absorption. Drugs that came under this category are Metformin (standard treatment for type 2 diabetes). Side effects include abdominal discomfort, bloating, anorexia, diarrhoea, etc.

b. Thiazolidinedione/ PPARy Activator/ glitazones

These drugs activate peroxisome proliferator-activated receptor gamma, which stimulates elevated glucose absorption and decreases glucose formation. Commonly seen side effects are: fluid retention, weight gain, etc. Drugs included in this category are Pioglitazone.

3. Retard Carbohydrate Absorption

a. **\alpha-Glucosidase inhibitors:** Alpha-glucosidases are an enzyme that breaks complex carbohydrates into simpler ones, i.e, it converts oligosaccharides into monosaccharides. These drugs inhibit carbohydrate absorption and digestion, which reduces the postprandial (after-meal) hyperglycaemia. Commonly used alpha-glucosidase inhibitors are Acarbose, Miglitol, and Voglibose.

4. Miscellaneous Drugs

a. **Sodium glucose co-transport 2 (SGLT 2) Inhibitor**: These drugs promote the excretion of glucose through urine by inhibiting the absorption of glucose. These drugs are mostly used in type 2 diabetes. Side effects induced by these drugs are weight loss, glucosuria. Drugs included in this malady are: Dapagliflozin, Canagliflozin. b. **Dopamine D2 agonist:** These agents work by acting on hypothalamic dopamine receptors, which decrease gluconeogenesis, promote insulin sensitivity, and decrease fasting and post-prandial plasma glucose levels. Commonly seen adverse effects are orthostatic hypotension, constipation, etc. Drugs which come under this category are Bromocriptine.

CONCLUSION

An epidemic of the highest proportion, diabetes, is this century's one of the highest killers. As it is mostly a lifestylerelated fatality, necessary tempering in lifestyle, moderate weight, consistent and systematic exercise helps in its prevention. Complexities associated with this giant killer are-Neuropathy, Glaucoma, Cardiovascular diseases, Retinopathy, Kidney ailments, and problems of the oral cavity. A malady, if not treated at the right stage, can turn fatal. A series of diagnostic measures/tests are at our disposal for its early detection, which are- OGTT, HGBAIC, FPG, RPG. Injectable, inhalation, and oral hypoglycemic agents are readily available for their treatment.

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