

A Brief Review on Diabetes Mellitus and its Associated Severe Multi-Disorders

Pranjali Gadakari¹, Omkar Chougule²

Dr. Bapuji Salunkhe Institute of Pharmacy, Miraj-416410, Maharashtra, India

Abstract: *Hyperglycaemia is a hallmark of diabetes mellitus (DM), a chronic metabolic disease caused by deficiencies in either insulin action or secretion, or both. It has two primary forms: Type 1 diabetes (T1DM), an autoimmune disease that causes the pancreatic beta-cells to be destroyed, and Type 2 diabetes (T2DM), which is mostly associated with insulin resistance and ultimately beta-cell failure. The rising incidence of type 2 diabetes, which is frequently linked to sedentary lifestyles, obesity, and aging populations, presents a serious public health concern. Furthermore, if left untreated, gestational diabetes mellitus (GDM), a condition that develops during pregnancy, can cause problems for both the mother and the unborn child. In order to manage the condition and avoid consequences including cardiovascular disease, nephropathy, retinopathy, and neuropathy, early detection, lifestyle changes, and pharmaceutical therapies are essential. Blood glucose control, nutrition, exercise, and pharmaceuticals such as insulin, metformin, and more recent pharmacological classes like SGLT2 inhibitors are the main focuses of management efforts.*

Keywords: Diabetes Mellitus, Hyperglycaemia, Insulin Resistance, Blood Glucose Control, Diabetes Management

Diseases Associated with Diabetes

Diabetes is a chronic metabolic disorder that affects millions of people worldwide. It is characterized by high blood sugar levels, which can lead to a variety of complications and associated diseases.

Cardiovascular Diseases

- Cardiac Disease:** Diabetes increases the risk of heart disease, heart failure, and cardiac arrhythmias.
- Hypertension:** High blood pressure is a common comorbidity with diabetes, which can further increase the risk of cardiovascular disease.
- Hyperlipidaemia:** Diabetes can lead to abnormal lipid profiles, increasing the risk of atherosclerosis and cardiovascular disease.

Micro vascular Complications

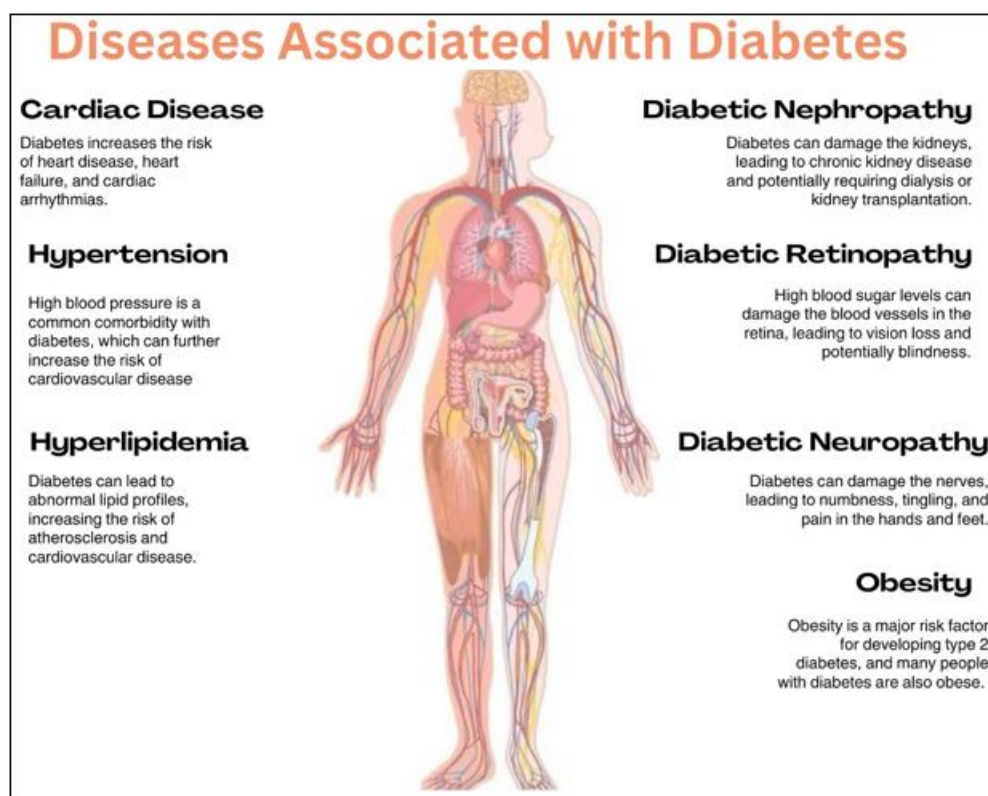
- Diabetic Nephropathy:** Diabetes can damage the kidneys, leading to chronic kidney disease and potentially requiring dialysis or kidney transplantation.
- Diabetic Retinopathy:** High blood sugar levels can damage the blood vessels in the retina, leading to vision loss and potentially blindness.

Neurological Complications

Diabetic Neuropathy: Diabetes can damage the nerves, leading to numbness, tingling, and pain in the hands and feet.

Other Associated Diseases

Obesity: Obesity is a major risk factor for developing type 2 diabetes, and many people with diabetes are also obese. ⁽¹⁾



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Abbreviations:

- 1) DM – Diabetes Mellitus
- 2) T1DM – Type 1 Diabetes Mellitus
- 3) T2DM – Type 2 Diabetes Mellitus
- 4) GDM – Gestational Diabetes Mellitus
- 5) FBG – Fasting Blood Glucose
- 6) OGTT – Oral Glucose Tolerance Test
- 7) HbA1c – Glycated Haemoglobin (a measure of long-term blood glucose control)
- 8) DPP-4 – Dipeptidyl Peptidase-4 (a class of diabetes medications)
- 9) SGLT2 – Sodium-Glucose Cotransporter-2 (a class of diabetes medications)
- 10) GLP-1 – Glucagon-like Peptide-1 (a type of diabetes medication)
- 11) PCOS – Polycystic Ovary Syndrome
- 12) NPH – Neutral Protamine Hagedorn (a type of insulin)
- 13) TZDs – Thiazolidinediones (a class of diabetes medications)
- 14) SGLT2 inhibitors – Sodium-glucose cotransporter 2 inhibitors (a type of diabetes medication)
- 15) DKA – Diabetic Ketoacidosis

1. Introduction

Diabetes Mellitus is a chronic condition characterized by high blood sugar (hyperglycaemia) due to insufficient insulin production or impaired insulin function. This leads to persistent high blood sugar and glucose intolerance, which can cause short-term issues requiring hospitalization and long-term complications such as eye problems (retinopathy), kidney damage (nephropathy), and nerve damage (neuropathy). Diabetes is diagnosed when fasting blood sugar is 7.0 mmol/L or higher, or if blood sugar is 11.1 mmol/L or more two hours after eating. Slightly higher sugar levels (impaired glucose tolerance) may not cause immediate damage but increase the risk of heart disease and developing full diabetes. Diabetes can be caused by Type 1, an autoimmune disease that destroys insulin-producing cells, or Type 2, where the body becomes resistant to insulin. ⁽²⁾

**Types of diabetes**

- 1) Type 1 diabetes
- 2) Type 2 diabetes

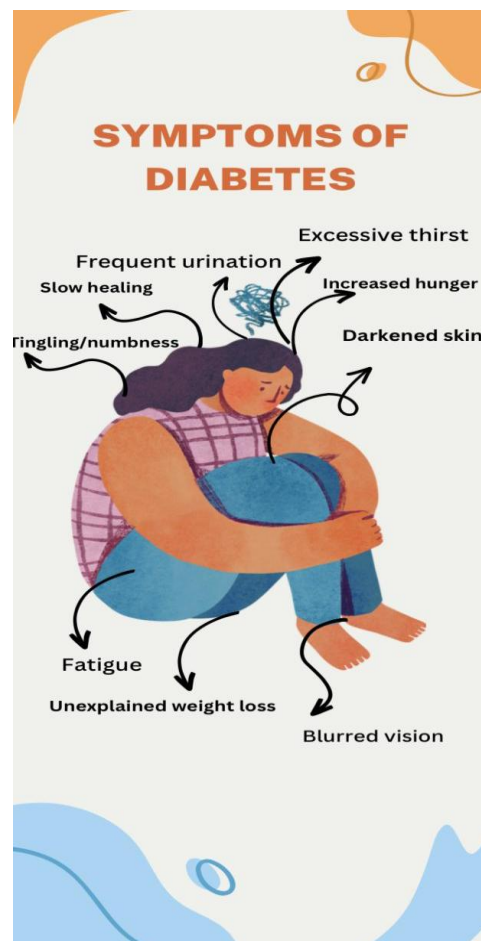
Type 1 Diabetes: Type 1 diabetes is an autoimmune disease where the body's immune system attacks and destroys the insulin-producing beta cells in the pancreas, leading to insulin deficiency. This results in elevated blood glucose levels (hyperglycaemia). It typically manifests in childhood or adolescence but can occur at any age. Symptoms include increased thirst, frequent urination, weight loss, and fatigue. Without insulin, the body cannot properly utilize glucose for energy. Management involves lifelong insulin therapy, either through injections or an insulin pump. Tight glucose control is necessary to prevent complications like diabetic retinopathy, nephropathy, and neuropathy. ⁽³⁾

Type 2 Diabetes: Type 2 diabetes is characterized by insulin resistance, where the body's cells do not respond effectively to insulin. Over time, the pancreas is unable to produce

enough insulin to overcome this resistance, resulting in elevated blood glucose levels. Risk factors include obesity, lack of physical activity, and family history. Symptoms may include fatigue, increased thirst, frequent urination, and slow healing wounds. Early management includes lifestyle changes such as diet and exercise, followed by oral medications like metformin. If blood sugar control worsens, insulin therapy may be required. Chronic hyperglycaemia can lead to complications such as cardiovascular disease, neuropathy, and diabetic retinopathy. ⁽⁴⁾



- Blurred vision – High blood sugar affects the eye's lens.
- Slow wound healing – High sugar levels impair circulation and immune function.
- Frequent infections – Especially skin, gum, and yeast infections.
- Numbness or tingling in hands/feet – Nerve damage (diabetic neuropathy).
- Dark skin patches (Acanthosis Nigricans) – A sign of insulin resistance, seen in the neck, armpits, or groin. ⁽⁶⁾



Symptoms and causes of Diabetes-

Symptoms of diabetes-

Type 1 diabetes: - symptoms develop suddenly and can be severe.

Main Symptoms (The "3 P's")

- Polyuria (Frequent urination) – High blood sugar leads to excess urine production.
- Polydipsia (Excessive thirst) – Dehydration caused by frequent urination.
- Polyphagia (Increased hunger) – Body lacks glucose for energy.

Other Common Symptoms

- Unexplained weight loss – The body burns fat and muscle for energy.
- Fatigue and weakness – Lack of insulin prevents glucose absorption.
- Blurred vision – High sugar affects eye fluid balance.
- Slow-healing wounds – Poor circulation and immune response.
- Frequent infections – Skin, gum, or yeast infections.
- Fruity-smelling breath – A warning sign of diabetic ketoacidosis (DKA).
- Nausea, vomiting, or stomach pain – Indicates DKA, requiring urgent medical attention. ⁽⁵⁾

Type 2 diabetes: - symptoms develop gradually and may go unnoticed for years.

Common Symptoms

- Frequent urination (Polyuria) – Excess glucose leads to more urine production.
- Increased thirst (Polydipsia) – Dehydration from frequent urination.
- Increased hunger (Polyphagia) – Cells don't get enough glucose for energy.
- Fatigue – Poor glucose utilization leads to low energy.

Causes of diabetes include-

- 1) **Causes of type 1 diabetes-**Type 1 diabetes is caused by the autoimmune destruction of pancreatic β -cells, leading to insulin deficiency.

Main Causes: -

- Autoimmune Response – The immune system mistakenly attacks insulin-producing cells.
- Genetics – Linked to HLA-DR3, HLA-DR4 genes; first-degree relatives have a 10x higher risk.
- Environmental Triggers – Viral infections (e.g., Coxsackievirus, rubella) and dietary factors (e.g., early cow's milk exposure).
- Vitamin D Deficiency – May increase susceptibility.
- Other Autoimmune Diseases – Associated with conditions like Hashimoto's thyroiditis. ⁽⁷⁾

- 2) **Causes of type 2 diabetes-** Type 2 diabetes occurs due to insulin resistance and impaired insulin secretion.

Main Causes: -

- Genetics – Strong family history; multiple genes linked.
- Obesity – Excess fat, especially abdominal fat, increases insulin resistance.
- Physical Inactivity – Reduces glucose uptake by muscles, worsening insulin resistance.
- Unhealthy Diet – High sugar and processed foods contribute to weight gain and insulin resistance.
- Aging – Risk increases with age >40 due to declining β -cell function.
- Metabolic Syndrome – Includes high blood pressure, cholesterol imbalance, and central obesity.
- Hormonal Imbalances – Conditions like polycystic ovary syndrome (PCOS) can increase risk. ⁽⁸⁾

Diagnostic tests for diabetes mellitus**1) Fasting Blood Glucose (FBG)**

- Normal: < 100 mg/dL
- Diabetes: ≥ 126 mg/dL after at least 8 hours of fasting
- Purpose: Initial screening test for diabetes.

2) Oral Glucose Tolerance Test (OGTT)

- Normal: < 140 mg/dL (2 hours after ingesting a glucose solution)

- Diabetes: ≥ 200 mg/dL
- Purpose: Used to diagnose prediabetes and diabetes, especially in pregnant women (gestational diabetes).

3) Glycated Haemoglobin (HbA1c)

- Normal: < 5.7%
- Pre-diabetes: 5.7% to 6.4%
- Diabetes: $\geq 6.5\%$
- Purpose: Reflects average blood glucose over 2–3 months and is used for both diagnosis and monitoring of diabetes.

4) Random Blood Glucose Test

- Diabetes: ≥ 200 mg/dL with associated symptoms of hyperglycaemia (polyuria, polydipsia, etc.)
- Purpose: Useful for rapid diagnosis, especially in an emergency or when symptoms are present.

5) Urine Tests (For Glucose and Ketones)

- Purpose: Detects glucose (indicating hyperglycaemia) or ketones (indicative of diabetic ketoacidosis, DKA).
- Significance: Mainly used for monitoring, particularly in Type 1 diabetes.

These tests are essential for the early diagnosis and management of diabetes mellitus.⁽⁹⁾

**Treatment for diabetes-****1) Type 1 Diabetes Treatment:**

- Insulin Therapy: Essential for Type 1 diabetes since the pancreas cannot produce insulin. Both long-acting (basal) and rapid-acting (bolus) insulin are used.
- Continuous Insulin Infusion (Insulin Pump): For more precise control, especially in children and adolescents.
- Monitoring and Lifestyle: Regular blood glucose checks, diet control, and physical activity.⁽¹⁰⁾

2) Type 2 Diabetes Treatment:

- Lifestyle Modifications: Diet, exercise, and weight loss are crucial for controlling blood glucose levels.
- Oral Medications:
 - Metformin: First-line medication, reduces glucose production by the liver and improves insulin sensitivity.
 - Sulfonylureas: Stimulate the pancreas to produce more insulin.
 - DPP-4 Inhibitors (e.g., Sitagliptin): Help increase insulin release and reduce glucose production.

- SGLT-2 Inhibitors (e.g., Canagliflozin): Increase glucose excretion via urine.
- GLP-1 Agonists: Enhance insulin secretion and inhibit glucagon release.
- Insulin Therapy: When oral medications are not sufficient, insulin injections or insulin pumps may be used.

3) Gestational Diabetes Treatment:

- Dietary Management: Control carbohydrate intake and focus on balanced meals.
- Insulin Therapy: Used when blood glucose is not controlled through diet alone.
- Monitoring: Frequent blood glucose checks throughout pregnancy to avoid complications.⁽¹¹⁾

4) Pharmacological treatments for diabetes**a) Type 1 Diabetes:**

- Insulin Therapy: Insulin is the cornerstone of treatment for Type 1 diabetes, as these patients lack insulin production.

- Insulin Types: Rapid-acting, short-acting (Regular), intermediate-acting (NPH), long-acting insulins (glargine, detemir), and insulin pumps are discussed.
 - Insulin Regimens: These include basal-bolus regimens or insulin pump therapy to provide continuous subcutaneous insulin infusion.
 - Insulin Analogues: Use of long-acting insulin analogues for basal insulin and rapid-acting insulin for meals.
- b) Type 2 Diabetes:**
- Metformin: First-line therapy for Type 2 diabetes, working by reducing hepatic glucose production and increasing insulin sensitivity.
 - Sulfonylureas: These drugs stimulate insulin release from the pancreas.
Examples: Glimepiride, Glipizide.
 - Thiazolidinediones (TZDs): Improve insulin sensitivity in peripheral tissues.
Example: Pioglitazone.
 - DPP-4 Inhibitors: Enhance the effect of incretin hormones to increase insulin release and reduce glucagon Example: Sitagliptin.
 - GLP-1 Agonists: Stimulate insulin secretion in response to meals, inhibit glucagon secretion, and slow gastric emptying Example: Exenatide, Liraglutide.
 - SGLT2 Inhibitors: Block glucose reabsorption in the kidneys, leading to glucose excretion in urine Example: Empagliflozin.
 - Insulin: In cases where oral medications are insufficient, insulin may be used for Type 2 diabetes as well, particularly with advanced disease. ⁽¹²⁾

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