



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

A Comprehensive Review on Diabetes Mellitus: Etiology, Diagnosis, and Pharmacological Management

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ARTICLE INFO

Published: 20 Feb 2026

Keywords:

Diabetes mellitus, Type 1 diabetes; Type 2 diabetes; Gestational diabetes, Insulin resistance, Diagnosis, Lifestyle modification, Antidiabetic drugs, Insulin therapy, Glycaemic control.

DOI:

10.5281/zenodo.18709984

ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action or both. It represents a major global public health challenge, with rapidly increasing prevalence and significant morbidity and mortality. This review provides a comprehensive overview of diabetes mellitus, including its definition, epidemiology, pathophysiology, classification, causes, clinical manifestations, diagnostic criteria, and management strategies. The major types of diabetes type 1 diabetes, type 2 diabetes, and gestational diabetes are discussed with emphasis on their distinct etiologies and clinical features. Common signs and symptoms such as polyuria, polyphagia, weight loss, fatigue, blurred vision, neuropathy, and delayed wound healing are outlined, along with underlying mechanisms. Diagnostic approaches based on World Health Organization and American Diabetes Association guidelines, including fasting plasma glucose, random blood glucose, oral glucose tolerance test, and HbA1c measurement, are summarized. The review also highlights key risk factors, including genetic predisposition, obesity, physical inactivity, insulin resistance, hormonal changes, aging, and environmental influences. Management strategies focus on lifestyle modification, including dietary changes, physical activity, and weight management, as well as pharmacological interventions such as metformin, other oral antidiabetic agents, insulin therapy, and advanced options like pancreas and islet cell transplantation. Overall, this review emphasizes the importance of early diagnosis, individualized treatment, and integrated lifestyle and pharmacological approaches to improve glycaemic control and reduce diabetes-related complications.

INTRODUCTION

Diabetes is a group of common endocrine diseases characterized by sustained high blood sugar

levels.[1,2] Diabetes is due to either the pancreas not producing enough of the hormone insulin, or the cells of the body becoming unresponsive to

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



insulin's effects.[3] Diabetes accounts for approximately 4.2 million deaths every year.[4] The number of people diagnosed as living with diabetes has increased sharply in recent decades, from 200 million in 1990 to 830 million by 2022. It affects one in seven of the adult population, with type 2 diabetes accounting for more than 95% of cases. Type 1 accounts for 5 to 10% of diabetes cases and is the most common type of diabetes diagnosed in patients under 20 years.[5] Insulin is a peptide hormone produced by beta cells of the pancreatic islets encoded in humans by the insulin gene.[6] It regulates the metabolism of carbohydrates, fats, and protein by promoting the absorption of glucose from the blood into cells of the liver, fat, and skeletal muscles.[7]

Types

1. Type 1 diabetes:-

It is an autoimmune condition where the body's immune system attacks the beta cells in the pancreas, preventing the production of insulin. This condition is typically present from birth or develops early in life. 5 to 10% of diabetes cases and is the most common type of diabetes diagnosed in patients under 20 years [8].

This form of diabetes most commonly develops in children, adolescents, or young adults, but it can occur at any age. Unlike Type 2 diabetes, Type 1 is not caused by lifestyle factors such as diet or exercise and cannot be prevented [9].

The exact cause of Type 1 diabetes is not fully understood, but it is believed to involve a combination of genetic predisposition and environmental triggers, such as viral infections [10,11].

Because insulin is critical for allowing glucose to enter the body's cells for energy, people with Type

1 diabetes must rely on lifelong insulin therapy, delivered through injections or an insulin pump. Without insulin, blood sugar levels can rise to dangerously high levels, leading to acute complications like diabetic ketoacidosis (DKA) and long-term damage to organs and tissues [12].

2. Type 2 Diabetes:-

Type 2 Diabetes Mellitus is a chronic metabolic disorder characterized by insulin resistance and a relative deficiency in insulin secretion, resulting in persistent hyperglycaemia [13]. It is the most prevalent form of diabetes, accounting for more than 90% of all diabetes cases globally [14]. Unlike Type 1 diabetes, which is primarily autoimmune in nature, T2DM develops due to a combination of genetic, behaviour and environmental factors. Major risk factors include obesity, physical inactivity, poor dietary habits, family history of diabetes, and increasing age [15]. The rising incidence of T2DM is closely linked to global increases in obesity and sedentary lifestyles, making it a significant public health concern. T2DM often has a gradual onset and may remain undiagnosed for years due to its asymptomatic or mild early presentation. However, if not properly managed, it can lead to serious complications, including cardiovascular disease, nephropathy, retinopathy, and neuropathy [13]. Early diagnosis, lifestyle modification, and appropriate pharmacological interventions are essential for preventing disease progression and improving long-term outcomes.

The development of type 2 diabetes is caused by a combination of lifestyle and genetic factors. While some of these factors are under personal control, such as diet and obesity, other factors are not, such as increasing age, female sex, and genetics.

Lifestyle factors are important to the development of type 2 diabetes, including obesity and

being overweight (defined by a body mass index of greater than 25), lack of physical activity, poor diet, psychological stress, and urbanization [16].

Most cases of diabetes involve many genes, with each being a small contributor to an increased probability of becoming a type 2 diabetic. The proportion of diabetes that is inherited is estimated at 72%. More than 36 genes and 80 Single nucleotide polymorphism (SNPs) had been found that contribute to the risk of type 2 diabetes. All of these genes together still only account for 10% of the total heritable component of the disease [17].

The World health organization definition of diabetes (both type 1 and type 2) is for a single raised glucose reading with symptoms, or for raised glucose readings on two separate dates, of either.

- fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL)
- or
- Glucose tolerance test with two hours after the oral dose a plasma glucose ≥ 11.1 mmol/L (200 mg/dL).

WHO Diabetes Diagnostic Criteria

| Condition | 2-hour glucose | | Fasting glucose | | HbA1c | |
|----------------------------|----------------|------------|-----------------|------------|-----------|---|
| | mmol/l | mg/dl | mmol/l | mg/dl | mmol/l | DCCT (Diabetes Control and Complications Trial) % |
| Normal | < 7.8 | < 140 | < 6.1 | < 110 | < 42 | < 6 |
| Impaired fasting glycaemia | < 7.8 | < 140 | 6.1-7.0 | 110-125 | 42-46 | 6.0-6.4 |
| Impaired Glucose tolerance | ≥ 7.8 | ≥ 140 | < 7 | < 126 | 42-46 | 6.0-6.4 |
| Diabetes Mellitus | ≥ 11.1 | ≥ 200 | ≥ 7 | ≥ 126 | ≥ 48 | ≥ 6.5 |

There are several classes of diabetes medicines available. Metformin is generally recommended as a first line treatment as there is some evidence that it decreases mortality; however, this conclusion is questioned. Metformin should not be used in those with severe kidney or liver problems.

Glimepiride is an antidiabetic medication. It works by increasing the amount of insulin released by the pancreas in order to lower blood glucose. It may be used alone, or in combination with insulin or another oral medicine such as metformin.

3. Gestational Diabetes:-

Gestational diabetes resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2–10% of

all pregnancies and may improve or disappear after delivery [18].

Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy.

It is recommended that all pregnant women get tested starting around 24–28 weeks gestation. It is most often diagnosed in the second or third trimester because of the increase in insulin-antagonist hormone levels that occurs at this time [19].

Methodology: literature searching strategy

The search of works of literature was done utilizing search engines such as PubMed, Web of Science, Scopus, Science Direct, Wiley Online Library, Google Scholar, and Research get to

compile the findings of lifestyle modification and new and innovative medications used globally to manage diabetes mellitus. We have conducted an extensive search using keywords/phrases such as “diabetes definition,” “signs and symptoms of diabetes,” “diagnosis of diabetes,” “cause of diabetes,” “treatment of diabetes,” to find relevant papers addressing our goal. In addition, a thorough investigation is done on literature that is written in English and is sound scientifically.

Some Common Sign and Symptoms

In diabetes mellitus, cells fail to metabolized glucose in the normal manner, effectively become starved [20].

Diabetic ketoacidosis is a medical emergency that occurs most commonly in type 1, but may also occur in type 2 if it has been longstanding or if the individual has significant β -cell dysfunction [21].



1) Polyuria (frequent urination):-

Polyuria is defined as the production of excessive urine volume, commonly more than 3 lit. per day in adults. It is one of the hallmark symptoms of uncontrolled diabetes mellitus and results from the body's inability to reabsorb all filtered glucose in the kidneys [22].

2) Polyphagia (increased hunger) :-

Polyphagia is characterized by excessive hunger and increased food intake and is often a compensatory response to metabolic or endocrine dysregulation. It is a hallmark symptom in several systemic diseases, most notably uncontrolled diabetes mellitus, where despite hyperglycaemia, cells are unable to utilize glucose due to absolute or relative insulin deficiency [23].

3) Unintended weight loss :-

Unintended weight loss is a key clinical symptom commonly associated with uncontrolled diabetes, especially type 1 diabetes mellitus (T1DM) but also sometimes seen in type 2 diabetes mellitus (T2DM) in advanced stages or during poor glycaemic control [24].

4) Fatigue / weakness:-

Fatigue and weakness are among the most frequently reported symptoms in people with both type 1 and type 2 diabetes mellitus. These symptoms refer to a persistent feeling of tiredness, reduced energy, or diminished physical strength, and are often not proportional to activity level [24].

5) Blurred vision :-

Blurred vision in diabetes is often caused by high blood glucose levels, which lead to osmotic

changes in the lens of the eye, causing it to swell and alter its ability to focus. This results in temporary visual disturbances. Over time, uncontrolled diabetes can cause diabetic retinopathy, a condition involving damage to the retinal blood vessels, leading to progressive and possibly permanent vision loss if not treated [28].

6) Slow healing of wounds / cuts, frequent infections:-

In diabetes mellitus, delayed wound healing and frequent infections are common complications due to several factors. Persistent hyperglycaemia impairs immune cell function, particularly neutrophil chemotaxis and phagocytosis, weakening the body's defence against pathogens. Furthermore, diabetic microangiopathy reduces blood flow, limiting oxygen and nutrient delivery to injured tissues. Peripheral neuropathy contributes by diminishing protective sensations, allowing wounds to go unnoticed and untreated, often resulting in chronic ulcers prone to infection [25].

7) Mood changes :-

Mood changes are a common and significant concern for people living with diabetes mellitus. Both type 1 and type 2 diabetes are associated with an increased prevalence of depression, anxiety, irritability, and emotional distress.

Fluctuations in blood glucose levels significantly affect brain function. Episodes of hypoglycaemia (low blood sugar) can cause acute mood symptoms such as irritability, anxiety, confusion, and agitation. Conversely, chronic hyperglycaemia can impair neurotransmitter systems, contributing to mood disturbances.

Diabetes is linked to inflammatory processes and hormonal imbalances that may disrupt normal brain chemistry, affecting mood regulation [26].

8) Numbness or tingling :-

Numbness and tingling sensations—often described by patients as "pins and needles"—are common early symptoms of diabetic peripheral neuropathy (DPN), the most frequent form of diabetic neuropathy. This condition results from chronic hyperglycaemia, which leads to metabolic and vascular changes that damage the peripheral nerves, particularly in the lower limbs. These sensory abnormalities typically present in a bilateral and symmetrical "stocking-glove" distribution, affecting the feet and hands [27].

CAUSES OF DIABETES

Diabetes is caused by a combination of factors including genetics, lifestyle choices, and certain medical conditions. Some more common cause of diabetes.

a) Autoimmune reaction :-

An autoimmune reaction in Type 1 Diabetes Mellitus is a process in which the body's immune system destroys its own pancreatic β -cells, leading to absolute insulin deficiency. This reaction involves autoantibodies and autoreactive T cells that target and damage β -cells, resulting in hyperglycaemia and dependence on exogenous insulin [28].

b) Genetics :-

Genetics plays a key role in both Type 1 and Type 2 Diabetes, but the mechanisms are different.

Type 1 Diabetes: Genes mainly affect immune system and attack pancreatic β -cells.



Type 2 Diabetes: Genes mainly affect insulin resistance or insulin secretion, often worsened by lifestyle factors [28].

c) Insulin-Resistance :-

Insulin resistance is a condition in which the body's cells (especially in muscle, fat, and liver) do not respond properly to insulin. As a result, the body needs higher levels of insulin to move glucose from the blood into the cells. Over time, this leads to high blood sugar and may cause Type 2 Diabetes Mellitus [29].

d) Obesity :-

Its means having an excessive amount of body fat, usually defined as a Body Mass Index (BMI) of 30 kg/m² or higher. It is one of the most important risk factors for developing type 2 diabetes mellitus (T2DM). When a person is obese, especially with fat around the abdomen, the body becomes less sensitive to insulin a condition called insulin resistance. Because of this, glucose (sugar) builds up in the blood instead of being used by the body's cells for energy [30].

e) Lack of physical activity :-

Lack of physical activity is a major risk factor for developing type 2 diabetes mellitus. Physical inactivity reduces the body's ability to use insulin effectively, leading to insulin resistance. When muscles are not regularly used, they take up less glucose from the blood, causing blood sugar levels to rise. Over time, this can contribute to the development of diabetes, obesity, and other metabolic problems [30].

f) Hormonal change :-

Hormonal changes cause diabetes when they either reduce insulin action or secretion or increase glucose production. The most important hormonal

disturbance is insulin deficiency or resistance, but excesses of cortisol, GH, glucagon, and catecholamines can also lead to or worsen diabetes.

Hormonal changes are the main cause of gestational diabetes, as this condition develops due to hormonal alterations during pregnancy [31].

g) Age :-

As people get older, several natural changes in the body's metabolism make them more likely to develop diabetes particularly Type 2 diabetes mellitus.

These age-related factors affect insulin production, insulin action, and glucose metabolism [31].

h) Prediabetes :-

Prediabetes is a clinical condition in which blood glucose levels are elevated above normal but not high enough to meet the diagnostic criteria for diabetes mellitus.

It is considered an intermediate metabolic state between normal glucose regulation and Type 2 diabetes mellitus, characterized by impaired fasting glucose (IFG) or impaired glucose tolerance [31].

i) Environmental factor :-

Environmental factors play a significant role in the pathogenesis of both type 1 and type 2 diabetes. In type 2 diabetes, lifestyle behaviours such as consumption of diets high in processed foods, physical inactivity, smoking, and chronic psychological stress contribute to obesity, insulin resistance, and impaired glucose metabolism, thereby increasing disease risk [16]. Environmental exposures, including air pollution

and endocrine-disrupting chemicals, have also been implicated in disrupting insulin signalling and β -cell function [32]. In type 1 diabetes, environmental triggers such as viral infections, vitamin D deficiency, and exposure to certain chemicals may precipitate an autoimmune response against pancreatic β -cells in genetically susceptible individuals, leading to disease onset [33].

DIAGNOSIS OF DIABETES

Type 1 diabetes symptoms often develop suddenly and are frequently the reason for initial blood glucose testing. In contrast, symptoms of type 2 diabetes or prediabetes usually develop more gradually and may be subtle or absent. To identify individuals at risk, the American Diabetes Association (ADA) has established screening recommendations:

a) Adults with overweight or obesity:

Anyone with a body mass index (BMI) ≥ 25 kg/m² (≥ 23 kg/m² for Asian Americans) should be screened if they have additional risk factors such as hypertension, dyslipidemia, physical inactivity, a history of polycystic ovary syndrome, cardiovascular disease, or a first-degree relative with diabetes.

b) Age-based screening:

All adults aged ≥ 35 years should have an initial blood glucose screening. If normal, repeat screening should occur at least every three years.

c) History of gestational diabetes:

Women who previously had gestational diabetes should be screened every three years.

d) Prediabetes:

Individuals with a prior diagnosis of prediabetes should undergo annual testing.

e) HIV infection:

Persons living with HIV are advised to undergo diabetes screening due to increased risk [34].

Tests for type 1 and type 2 diabetes

I. Fasting blood sugar test:-

A blood sample is taken after an overnight fast in which you avoid eating or drinking anything except water. A fasting blood sugar level below 100 mg/dL (5.6 mmol/L) is considered normal, while a level between 100 and 125 mg/dL (5.6 to 6.9 mmol/L) indicates prediabetes. A value of 126 mg/dL (7 mmol/L) or higher, confirmed on two separate tests, is diagnostic of diabetes [35].

II. Random blood sugar test :-

A random blood sugar (RBS) test measures your blood glucose level at any time of the day, regardless of when you last ate. It is commonly used to screen for diabetes when symptoms are present, such as frequent urination, increased thirst, blurred vision, or unexplained weight loss. In this test, a blood sample is taken without requiring fasting. A random blood sugar level of 200 mg/dL (11.1 mmol/L) or higher, along with symptoms of high blood sugar, strongly suggests diabetes. Because it is quick and does not require preparation, the RBS test is especially useful in emergency or routine clinical settings to rapidly assess glucose status. These clinical principles are described in standard medical physiology texts such as Guyton and Hall Textbook of Medical Physiology [35].

III. Oral glucose test :-

The Oral Glucose Tolerance Test is a standardized diagnostic procedure used to assess glucose handling and identify disturbances in carbohydrate metabolism. The patient undergoes an overnight fast of 8–12 hours, after which a fasting plasma glucose level is obtained. The patient then ingests a 75-gram oral glucose solution, and plasma glucose concentrations are measured over the subsequent two hours to evaluate the glycemic response.

Diagnostic Interpretation (2-Hour Plasma Glucose)

- < 140 mg/dL (7.8 mmol/L): Normal glucose tolerance
- 140–199 mg/dL (7.8–11.0 mmol/L): Impaired glucose tolerance (prediabetes)
- \geq 200 mg/dL (11.1 mmol/L): Diagnostic for diabetes mellitus [36].



Treatment of Diabetes

Depending on the type of diabetes you have, your treatment may include checking your blood sugar, taking insulin, or taking medicine by mouth. Eating healthy foods, staying at a healthy weight, and being active every day are also important for managing diabetes. Keeping a healthy weight with

IV. HBA1C (A1c) TEST :-

The HbA1c test, also called the A1C or glycated hemoglobin test, is a blood test that shows your average blood sugar level over the past 2–3 months. It works by measuring the amount of sugar that is attached to hemoglobin, which is the protein in red blood cells that carries oxygen. The more sugar in your blood, the higher your HbA1c will be.

This test is used to diagnose diabetes and prediabetes. An HbA1c level of 6.5% or higher means diabetes, 5.7%–6.4% means prediabetes, and below 5.7% is normal. It is also used to check how well diabetes treatment is working, because it gives a long-term picture of blood sugar control. You do not need to fast before this test, which makes it very convenient [36].

good food choices and regular exercise helps you stay healthier and control your diabetes better [37].

1. Lifestyle modification:-

Lifestyle modification plays a crucial role in the management of diabetes mellitus, as it enhances insulin sensitivity, promotes better glycemic control, and helps prevent long-term

complications. Unlike many pharmacological treatments, lifestyle changes do not produce adverse side effects, making them a safe and effective first-line approach for diabetic care.

A. Diet :-

Diet modification is one of the most effective non-pharmacological strategies for managing diabetes because food intake directly affects blood glucose levels and overall metabolic control. A diabetes-friendly diet emphasizes low-glycemic index carbohydrates, such as whole grains, legumes, vegetables, and most fruits, to prevent rapid post-meal spikes in blood sugar. Increasing dietary fiber through foods like vegetables, oats, and whole grains helps slow glucose absorption and improves satiety, which supports better glycemic stability. At the same time, reducing refined sugars and processed carbohydrates, including sweets, sugary drinks, and white flour products, is essential for minimizing hyperglycemia [31].

B. Physical activity :-

Physical activity is a key component in the management of diabetes mellitus as it improves insulin sensitivity, enhances glucose utilization by muscles, and helps maintain better glycemic control. Doing moderate activities like brisk walking, cycling, or swimming for at least 150 minutes each week is recommended because it helps the body use insulin better and lowers blood sugar levels [38].

C. Weight management :-

Physical activity plays an important role in treating diabetes because exercise helps the body use insulin more effectively and lowers blood sugar levels. Doing moderate activities such as brisk walking, cycling, or swimming for about 150

minutes each week helps reduce insulin resistance and improve overall glucose control [38].

2. Glycemic (medication/ insulin) control :-

Pharmacological therapy is indicated in patients with diabetes mellitus when lifestyle modification alone is insufficient to achieve glycemic targets. The choice of medication depends on the type of diabetes, patient age, comorbidities, risk of hypoglycemia, and individualized glycemic goals. In type 1 diabetes, insulin therapy is essential due to absolute insulin deficiency, while in type 2 diabetes, treatment usually begins with metformin and may be escalated with additional oral or injectable agents to achieve optimal glycemic control [31].

A. Self-monitoring :-

Self-Monitoring of Blood Glucose (SMBG) is an essential element of diabetes management that allows individuals with diabetes to regularly measure their blood glucose levels using a portable glucometer. Self-Monitoring of Blood Glucose is especially important for patients treated with insulin or insulin secretagogues, as it aids in detecting hypoglycaemia and hyperglycaemia and supports appropriate adjustment of insulin doses and other antidiabetic medications. The procedure involves proper hand hygiene, obtaining a capillary blood sample via a finger prick using a lancing device, applying the blood to a test strip, and reading the result on the glucometer. Systematic recording of blood glucose values assists healthcare professionals in assessing treatment outcomes and preventing diabetes-related complications [31].

B. Insulin therapy :-

Insulin therapy is essential in the management of type 1 diabetes mellitus due to absolute insulin



deficiency and is also indicated in type 2 diabetes mellitus when oral or non-insulin injectable agents fail to achieve glycemic control or when there is significant hyperglycemia, acute illness, or contraindications to other therapies. Insulin

preparations vary by onset and duration of action and are commonly administered using basal–bolus regimens or multiple daily injections to mimic physiological insulin secretion and maintain optimal glycemic control [40].



C. Pancreas and islet cell transplantation :-

Pancreas and islet cell transplantation are treatment options for selected patients with type 1 diabetes mellitus, particularly those with severe metabolic instability, recurrent hypoglycemia unawareness, or advanced diabetic complications such as end-stage renal disease. Pancreas transplantation can restore endogenous insulin secretion and achieve long-term normoglycemia but requires major surgery and lifelong immunosuppression. Islet cell transplantation involves the infusion of isolated pancreatic islet cells into the portal vein and offers a less invasive alternative; however, insulin independence is often partial or temporary, and ongoing immunosuppression is required [40].

D. First-line therapy :-

Lifestyle modification, including a balanced diet, regular physical activity, and weight control, is the cornerstone of initial management for all patients with diabetes mellitus. These measures help regulate blood glucose levels and reduce the risk of long-term complications.

In type 1 diabetes mellitus, insulin therapy is mandatory and serves as the first-line treatment due to absolute insulin deficiency. Without insulin, patients with type 1 diabetes cannot maintain normal blood glucose levels, making it essential for survival and overall metabolic control.

For type 2 diabetes mellitus, lifestyle interventions are the initial step, but when these measures alone are insufficient to achieve glycemic targets, pharmacological therapy is indicated. Metformin (metformin hydrochloride, metformin HCl) is the recommended first-line drug in such cases. It is available in immediate-release and extended-release tablets, as well as a liquid formulation. Metformin lowers blood glucose through multiple mechanisms: it decreases hepatic glucose production, reduces intestinal glucose absorption, and enhances insulin sensitivity in peripheral tissues [39].

E. Second line therapy :-

In type 2 diabetes mellitus, when adequate glycemic control is not achieved with lifestyle modification and first-line therapy (metformin),

second-line pharmacological agents are added. The choice of second-line therapy depends on patient-specific factors such as cardiovascular disease, chronic kidney disease, risk of hypoglycemia, body weight, cost, and tolerability.

Second-Line Agents Include:

- Sulfonylureas (e.g., glimepiride, gliclazide) – increase insulin secretion
- DPP-4 inhibitors (e.g., sitagliptin, linagliptin) – enhance incretin action
- GLP-1 receptor agonists (e.g., liraglutide, semaglutide) – increase insulin secretion, promote weight loss
- SGLT-2 inhibitors (e.g., empagliflozin, dapagliflozin) – increase urinary glucose excretion
- Thiazolidinediones (e.g., pioglitazone) – improve insulin sensitivity
- Basal insulin – considered when oral agents fail or in marked hyperglycemia [40].

CONCLUSION

Diabetes mellitus is a complex, chronic metabolic disorder that continues to pose a significant global health burden due to its increasing prevalence, long-term complications, and impact on quality of life. This review has comprehensively discussed the definition, epidemiology, pathophysiology, classification, causes, clinical manifestations, diagnostic criteria, and management strategies of diabetes mellitus, with particular emphasis on type 1 diabetes, type 2 diabetes, and gestational diabetes. Each type exhibits distinct etiological mechanisms and clinical features, yet all share the common consequence of chronic hyperglycaemia and its associated complications.

Early recognition of signs and symptoms, combined with accurate diagnosis using standardized criteria recommended by the World

Health Organization and the American Diabetes Association, is essential for timely intervention. Identification of key risk factors such as genetic predisposition, obesity, physical inactivity, insulin resistance, hormonal alterations, aging, and environmental influences allows for targeted preventive strategies, particularly in individuals at high risk.

Management of diabetes mellitus requires a comprehensive and individualized approach. Lifestyle modification, including dietary regulation, regular physical activity, and weight management, remains the foundation of diabetes care and plays a critical role in improving insulin sensitivity and glycaemic control. Pharmacological therapy, including oral antidiabetic agents, insulin therapy, and newer drug classes, is necessary when lifestyle measures alone are insufficient. Advanced therapeutic options such as pancreas and islet cell transplantation offer potential benefits in selected patients with type 1 diabetes, although their use is limited by cost, availability, and the need for lifelong immunosuppression.

Overall, effective diabetes management depends on early diagnosis, patient education, regular monitoring, and a multidisciplinary approach that integrates lifestyle interventions with appropriate pharmacological treatment. Continued research, improved access to healthcare, and awareness programs are essential to reduce the burden of diabetes mellitus and prevent its acute and chronic complications.

REFERENCES

1. "Diabetes world Health organization". . Archived from the original on 29 January 2023. Retrieved 29 January 2023.
2. "Diabetes mellitus – hormonal and metabolic Disorders". . MSD Manual Consumer



- Version. Archived from the original on 1 October 2022. Retrieved 1 October 2022
- Shoback DG, Gardner D, eds. (2011). "Chapter 17". *Greenspan's basic & clinical endocrinology* (9th ed.). New York: McGraw-Hill Medical.
 - "IDF DIABETES ATLAS NIHTH EDITION 2019" (PDF). www.diabetesatlas.org. Archived (PDF) from the original on 1 May 2020. Retrieved 18 May 2020
 - World Health Organization. Diabetes: Fact sheet. 14 November 2024. Available at:
 - Voet D, Voet JG (2011). *Biochemistry* (4th ed.). New York: Wiley.
 - Stryer L (1995). *Biochemistry* (Fourth ed.). New York: W.H. Freeman and Company. pp. 773–74.
 - Diabetes Fact sheet N0312. WHO. November 2016. Archived from the original on 26 August 2013. Retrieved 29 May 2017.
 - Kliegman, R. M., St. Geme, J. W., Blum, N. J., Shah, S. S., Tasker, R. C., & Wilson, K. M. (Eds.). (2020).
 - Erlich H, Valdes AM, Noble J, Carlson JA, Varney M, Concannon P, et al. (2008).
 - NIDDK. August 2014. Archived from the original on 10 August 2016. Retrieved 31 July 2016.
 - Pathak, R., Dhungana, S., Banerjee, S. K., & Yousuf, M. S. (2019). Therapies for Type 1 Diabetes: Current Scenario and Future Perspectives. *Current Drug Targets*, 20(5), 497–510.
 - American Diabetes Association. (2024). Standards of Medical Care in Diabetes—2024. *Diabetes Care*, 47(Supplement_1), S1–S292.
 - World Health Organization. (2023). Diabetes.
 - Centers for Disease Control and Prevention. (2023). National Diabetes Statistics Report. U.S. Department of Health and Human Services.
 - Hu, F. B. (2011). Globalization of diabetes: The role of diet, lifestyle, and genes. *Diabetes Care*, 34(6), 1249–1257.
 - Mahajan, A., Taliun, D., Thurner, M., Robertson, N. R., Torres, J. M., Rayner, N. W., ... & McCarthy, M. I. (2018).
 - National Diabetes Clearinghouse (NDIC) : National Diabetes Statistics 2011. U.S. Department of Health and Human Services. Archived from the original on 17 April 2014. Retrieved 22 April 2014.
 - Soldavini J (November 2019). "Krause's Food & The Nutrition Care Process". *Journal of Nutrition Education and Behaviour*. 51 (10): 1225.
 - Ross and Wilson. *Anatomy and Pathophysiology in Health and Illness*, Churchill Livingstone Elsevier, 11th edition, 2010, 227-229.
 - Penman I, Ralston S, Strachan M, Hobson R (2023). *Davidson's Principles and Practice of Medicine* (24th ed.). Elsevier. pp. 703–753.
 - Fathollahi, A., Daneshgari, F., & Hanna-Mitchell, A. T. (2015). Effect of Polyuria on Bladder Function in Diabetics versus Non-Diabetics: An Article Review. *Current Urology*, 8(3), 119–125.
 - Jameson, J. L., Fauci, A. S., Kasper, D. L., Hauser, S. L., Longo, D. L., & Loscalzo, J. (2018). *Harrison's Principles of Internal Medicine* (20th ed., Vol. 1, pp. 2851–2853).
 - Melmed, S., Polonsky, K. S., Larsen, P. R., & Kronenberg, H. M. (2020). *Williams Textbook of Endocrinology* (14th ed.). Elsevier. In Chapter 31,
 - Fitzpatrick, J. E., Johnson, B. E., & Ferringer, T. C. (2013). *Robbins Basic Pathology* (9th ed., pp. 678–680).
 - Golden, S. H., Lazo, M., Carnethon, M., Bertoni, A. G., Schreiner, P. J., Diez Roux, A. V., & Lyketsos, C. (2008). Mood disorders and diabetes mellitus. In J. L. Jameson, A. S.



- Fauci, D. L., Kasper, S. L., Hauser, D. L., Longo, & J. Loscalzo (Eds.), *Harrison's Principles of Internal Medicine* (17th ed., Vol. 2, pp. 2205–2211).
27. Edwards, J. L., Vincent, A. M., Cheng, H. T., & Feldman, E. L. (2008). Diabetic neuropathy: Mechanisms to management. In D. LeRoith, S. I. Taylor, & J. M. Olefsky (Eds.), *Diabetes Mellitus: A Fundamental and Clinical Text* (3rd ed., pp. 749–767).
28. Kumar, V., Abbas, A. K., & Aster, J. C. (2021). *Robbins & Cotran Pathologic Basis of Disease* (10th ed.). Philadelphia, PA: Elsevier. — Chapter 24, “The Endocrine System,”
29. Guyton, A. C., & Hall, J. E. (2021). *Textbook of Medical Physiology* (14th ed.). Philadelphia: Elsevier. (Chapter: “Insulin, Glucagon, and Diabetes Mellitus”)
30. Kumar, P., & Clark, M. (2021). *Kumar and Clark's Clinical Medicine* (10th ed.). Elsevier.
31. Kasper, D. L., Fauci, A. S., Hauser, S. L., Longo, D. L., Jameson, J. L., & Loscalzo, J. (2022). *Harrison's Principles of Internal Medicine* (21st ed.). New York: McGraw-Hill Education.
32. Rajagopalan, S., et al. (2018). Environmental factors and diabetes: The role of pollution and endocrine disruptors. *Current Diabetes Reports*, 18, 86.
33. Knip, M., Veijola, R., Virtanen, S. M., Hyöty, H., Vaarala, O., & Akerblom, H. K. (2005). Environmental triggers of type 1 diabetes. *Cold Spring Harbor Perspectives in Medicine*, 2(7), a007690.
34. American Diabetes Association. Standards of Care in Diabetes—2025. *Diabetes Care*. 2025;48(Suppl. 1):S1–S211.
35. Hall, J. E. (2021). *Guyton and Hall Textbook of Medical Physiology* (14th ed.). Elsevier.
36. Melmed, S., Auchus, R., Koenig, R., Rosen, C., & Grossman, A. (Eds.). *Williams Textbook of Endocrinology* (14th ed.). Elsevier.
37. Smeltzer, S. C., Bare, B. G., Hinkle, J. L., & Cheever, K. H. (2010). *Brunner & Suddarth's Textbook of Medical-Surgical Nursing* (12th ed.). Philadelphia: Lippincott Williams & Wilkins.
38. Joslin Diabetes Center. *Joslin's Diabetes Mellitus*, 15th Edition. Lippincott Williams & Wilkins.
39. *Davidson's Principles and Practice of Medicine*, 24th Edition. Elsevier. Chapter: Diabetes Mellitus.
40. Powers AC, Stafford JM, Rickels MR. Diabetes Mellitus: Management and Therapies. In: *Harrison's Principles of Internal Medicine*, 21st ed. New York: McGraw-Hill Education; 2022.

HOW TO CITE: Ajay Singh, Dr. Rishi Kumar, A Comprehensive Review on Diabetes Mellitus: Etiology, Diagnosis, and Pharmacological Management, *Int. J. of Pharm. Sci.*, 2026, Vol 4, Issue 2, 3221-3233. <https://doi.org/10.5281/zenodo.18709984>

