International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Diabetes Mellitus: A Review on Introduction of Diabetes Mellitus and Effect of Oral Hypoglycemic Drugs on Diabetes Mellitus

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Abstract: ***Diabetes is a heterogeneous metabolic disease that includes different diseases. It is characterized by high blood sugar, or hyp erglycaemia, caused by abnormalities in insulin secretion or insulin action, or both. Hyperglycaemia takes many forms and manifests its elf differently; resulting in dysfunction of carbohydrate, fat and protein metabolism. Chronic hyperglycaemia often leads to various mic rovascular and macrovascular complications of diabetes and is one of the leading causes of diabetes and death. Hyperglycaemia is also an important biomarker for the diagnosis of diabetes. This review will focus on the classification of diabetes and its pathophysiology, inc luding its various types. This report focuses specifically on diabetes (1). Diabetes is described in old books and is considered a serious dis ease, but it does not seem to be encountered very often by doctors or physicians. People's health and development have been increasingl y affected by the number of people suffering from this disease over the past few years. At the 2011 United Nations High Level Political C onference, it became the focus of political advocacy for the prevention and control of non-communicable diseases (NCDs), including dia betes, cardiovascular diseases, cancer and chronic respiratory diseases. Noncommunicable disease care framework with 9 targets to be a chieved by 2025. Diabetes and its main problems are related to goals and indicators such as reducing malnutrition and physical inactivit y, influencing the increase in blood sugar levels, improving access to healthcare and reducing premature deaths. Under the 2030 Agend a for Sustainable Development, Parties aim to reduce premature deaths from non-communicable diseases, including diabetes, by one-th ird and achieve universal health.***

Keywords: diabetes, hyperglycaemia, insulin abnormalities, non-communicable diseases, sustainable health development

1. Etiology

Diabetes mellitus comprises a group of intricate, enduring metabolic disorders characterized by elevated blood glucose levels. Insulin, a pancreatic hormone, regulates glucose levels by managing its storage and metabolism. In diabetes, there may be diminished insulin responsiveness to glucose metabolism or reduced insulin production by the pancreas, leading to disturbances in carbohydrate, protein, and fat metabolism. Consequently, hyperglycaemia ensues, potentially resulting in acute metabolic complications such as ketoacidosis and contributing to chronic microvascular complications over time. Clinically, diabetes mellitus is typified by elevated blood glucose levels due to either complete or relative insulin deficiency.

The classification of diabetes mellitus has undergone significant discussion in recent years. The traditional classification system, based solely on insulin dependency, was deemed inadequate. Previously, patients were categorized as either Insulin Dependent Diabetes Mellitus (IDDM) or Non-Insulin Dependent Diabetes Mellitus (NIDDM). However, in 1998, the World Health Organization (WHO) proposed a new classification system based on the underlying etiological factors of diabetes. This updated system, outlined below, has since become the accepted standard for classifying diabetes mellitus.

Type 1 DM: Characterized by immune-mediated or idiopathic B-cell dysfunction, resulting in absolute insulin deficiency. This autoimmune disorder necessitates complete reliance on insulin for survival.

Type 2 DM: Typically develops in adulthood and may stem from insulin resistance, relative insulin deficiency, or secretory defects. This condition, strongly influenced by genetics, involves insufficient insulin secretion and tissue insensitivity to insulin, resulting in a relative insulin deficiency.

Type 3 DM: Encompasses various specific types of diabetes, including genetic defects in insulin action and disorders of the exocrine pancreas.

Type 4: Gestational diabetes

2. Pathogenesis

Pathogenesis of Type 1 Diabetes Mellitus
Type 1 diabetes typically manifests in children and young adults, characterized by the immune system's targeting and destruction of pancreatic beta cells—the sole producers of insulin, essential for blood glucose regulation.

While only 5% of diabetes cases fall under this category, its global prevalence is on the rise, increasing at approximately 3% annually. Notably, though diagnosis often occurs during childhood, a significant proportion—84%—of individuals living with type 1 diabetes are adults.

The pathogenesis involves the destruction of beta cells within pancreatic islets. The majority of cases are autoimmune (Type 1A), where detectable antibodies targeting beta cells are present in the bloodstream. However, some cases are idiopathic (Type 1B), lacking such antibodies. In both subtypes, circulating insulin levels are markedly reduced,

rendering patients more susceptible to ketosis. Type 1 diabetes is relatively less common and exhibits a lower degree of genetic predisposition.

Pathogenesis of type 2 Diabetes Mellitus Unlike Type 1 diabetes, Type 2 diabetes typically does not involve significant loss of beta cell mass or detectable anti-beta-cell antibodies. Instead, it arises due to inadequate insulin production or cellular resistance to insulin. Genetic predisposition plays a prominent role in the onset of Type 2 diabetes, which manifests as a diverse condition characterized by varying degrees of reduced insulin secretion and increased insulin requirement across individuals.

The primary driver of hyperglycaemia in Type 2 diabetes is the liver's excessive glucose production coupled with diminished glucose uptake in peripheral tissues owing to insulin resistance. Although insulin secretion may initially rise during the early stages of diabetes, it gradually declines over time due to progressive beta cell dysfunction. Additional mechanisms contributing to Type 2 diabetes and insulin resistance include heightened circulating glucagon levels, abnormalities in lipid metabolism such as increased intracellular deposition, and central nervous system-mediated effects.

3. Symptoms

General symptoms
Common symptoms of diabetes include:

- Increased appetite
- Excessive thirst
- Unexplained weight loss

Causes of diabetes
While the precise origins of diabetes remain unclear, various environmental, genetic, and lifestyle factors are thought to exert influence. Below are potential causes associated with each type of diabetes:

Type 1 diabetes The exact cause of Type 1 diabetes is not definitively known. However, it is believed that the immune system erroneously targets and destroys insulin-producing beta cells in the pancreas. Genetic predisposition may contribute to some cases, and viral infections could potentially trigger the immune system's attack.

Type 2 diabetes Type 2 diabetes arises from a blend of genetic predisposition and lifestyle elements. Factors such as obesity or being overweight increase the risk by rendering cells less responsive to insulin, leading to elevated blood sugar levels. This condition often runs in families, with shared genes influencing susceptibility to both Type 2 diabetes and obesity.

Gestational diabetes Gestational diabetes results from hormonal changes during pregnancy. Hormones produced by the placenta can diminish a pregnant woman's cells' sensitivity to insulin, leading to elevated blood sugar levels. Overweight women at the onset of pregnancy face a higher risk of developing gestational diabetes.

Type 1 diabetes You're more likely to get type-1 diabetes if you're a child or teenager and you have a parent and sibling with the condition, or if you carry certain genes that are linked to the disorder.

Type 2 diabetes Your risk for type 2 diabetes increases if you:

- are overweight
- are age 45 or older
- have a parent or sibling with the condition

Diagnosis
Individuals exhibiting symptoms of diabetes or those at risk should undergo testing. Pregnant women should receive routine screening for gestational diabetes during their second or third trimesters. To diagnose pre-diabetes and diabetes, doctors employ the following blood tests.

Fasting Plasma Glucose (FPG) The Fasting Plasma Glucose (FPG) test evaluates blood sugar levels after an 8-hour fast. Typically conducted in the morning prior to breakfast, this test provides valuable diagnostic information.

Result	Fasting plasma glucose (FPG) test
Normal	Less than 100 mg/dl
Pre-diabetes	100 mg/dl to 125 mg/dl
Diabetes	126 mg/dl or higher

A1C Test
The A1C test offers insight into your blood sugar levels averaged over the past three months.

Result	A1C test
Normal	Less than 5.7%
Pre-diabetes	5.7% to 6.4%
Diabetes	6.5% or higher

Oral Glucose Tolerance Test (OGTT): The OGTT is a two- to three-hour examination assessing blood glucose levels before and after consuming a specific sweet beverage. This test provides insights into how your body metabolizes sugar.

Lifestyle Modification for Diabetic Patient: To effectively manage diabetes, consider incorporating the following lifestyle changes into your daily routine:

1) Consistent Meal Timing: Consume meals at the same time each day to minimize fluctuations in blood sugar levels.
2) Balanced Diet: Aim for a well-rounded diet comprising complex carbohydrates, proteins, fruits, and vegetables.
3) Portion Control: Monitor portion sizes to prevent overeating and maintain blood sugar levels.
4) Timely Medication and Meals: Adhere to a consistent schedule for medications and meals to avoid fluctuations in blood sugar levels.
5) Hydration: Stay hydrated by drinking plenty of water throughout the day to prevent dehydration.
6) Healthy Snacking: Keep light and nutritious snacks readily available for convenient consumption.
7) Avoidance of Harmful Substances: Refrain from smoking, consuming alcohol, fizzy drinks, and diet sodas, as they can negatively impact blood sugar control.

Lifestyle Modifications for Type 2 Diabetes Patients
Patients with Type 2 diabetes can benefit from the following lifestyle adjustments:

1) Dietary Changes: Prioritize a diet low in sugar, refined grains, and starchy vegetables to prevent spikes in blood glucose levels.
2) Physical Activity: Regular exercise enhances the body's glucose utilization, reducing excess sugar in the bloodstream.
3) Weight Management: Shedding excess weight, even a modest 5 to 7 percent, can ameliorate diabetes symptoms by regulating blood sugar levels and improving insulin resistance.

4. Oral Hypoglycemic drugs

A. Enhance insulin secretion

1. Sulfonylureas (K_{ATP} Channel blockers)
Sulfonylureas are a class of medications used to manage type 2 diabetes mellitus, with a history dating back to the 1950s. They all contain a phenyl-sulfonyl-urea structure, which contributes to their hypoglycemic effects. Patients with type 2 diabetes often use sulfonylureas either alone or in combination with other oral or injectable medications. Second-generation sulfonylureas, particularly, are widely prescribed due to their effectiveness and cost-effectiveness, reducing glycated hemoglobin A1C (HbA1c) levels by 1% to 1.25%. However, they are not recommended for elderly individuals or those with renal or hepatic impairment.

***Combinations*:** Sulfonylureas can be combined with various other oral antidiabetic medications except for meglitinides (nateglinide & repaglinide).

First Generation Drugs:
Generic name: Tolbutamide

- **Brand name-1: Rastinon**

Dose type: Tablet
Dose: 500mg
Company: Aventis Pharma Ltd.
2: Rastinone
: Tablet

Dose: 500mg
Company: Alcare David Ltd.

- **Brand name-3: Tolbutamide**

Dose type: Tablet
Dose: 500mg
Company: Unicure India Pvt. Ltd.

Second Generation Drugs:
Generic name: Glibenclamide

- **Brand name-1: Afdiex Dose type: Tablet**

Dose: 2.5mg/5mg
Company: Cadila Pharmaceuticals Ltd.

- **Brand name-2: Ardiex**

Dose type: Tablet
Dose: 2.5mg
Company: Cadila Pharmaceuticals Ltd.

- **Brand name-3: Aviglen Dose type: Tablet**

Dose: 2.5mg/5mg
Company: Avinash Health Products Pvt. Ltd.

- **Brand name-4: Betanase**

Dose type: Tablet
Dose: 5mg
Company: Zydus Cadila Healthcare Ltd.

Generic name: Glipizide
Brand name-1: Bimode SR

Dose type: Tablet
Dose: 5mg/10mg
Company: Emcure Pharmaceuticals Ltd.

- **Brand name-2: D Glip Dose type: Tablet**

Dose: 2.5mg/5mg
Company: Grandix Pharmacuticals

- **Brand name-3: Dibizide Dose type: Tablet**

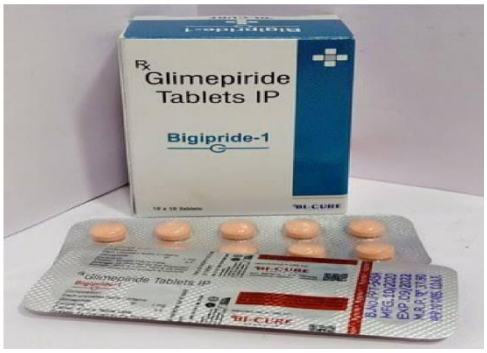
Dose: 2.5mg/5mg/10mg Company: Micro Labs Ltd.

- **Brand name-4: Glez**

Dose type: Tablet
Dose: 2.5mg/5mg/7.5mg/10mg
Company: Aristo Pharmaceuticals Pvt. Ltd.

Generic name: Glimepiride

- **Brand name-1: Abepride**



Dose type: Tablet
Dose: 1mg/2mg
Company: Abs Remedies Pvt. Ltd.

- **Brand name-2: Accuglim**

Dose type: Tablet
Dose: 1mg/2mg
Company: Cadell Healthcare Pvt. Ltd.

B. Overcome Insulin resistance

Biguanide (AMP_k activator): Biguanide refers to a group of oral diabetes medications that work by preventing the production of glucose in the liver, improving the body's sensitivity toward insulin and reducing the amount of sugar absorbed by the intestines. The only available biguanide medication is metformin, which is commonly used as a first-line treatment for type 2 diabetes.

Generic name: Metformin: It is usually prescribed as a single treatment (monotherpay), but it can also be combined with other medication in a single tablet – for example, metformin + pioglitazone (Competact), metformin + vildagliptin (Eucreas) and metformin + sitagliptin.

- **Brand name-1: Glumate**

Dose type: Tablet
Dose: 500mg/850mg/ Glumate EXT-500mg/ Glumet XR-500mg
Company: Cipla Limited

- **Brand name-2: Glycomet**

Dose type: Sustained release Tablet
Dose: 500mg/850mg/1000mg
Dose type: Tablet
Dose: 250mg/500mg/850mg/1000mg
Company: US Vitamins Limited

2. Thiazolidinediones:

Generic Name: Pioglitazone: Combination of Generics: Glimepiride 1mg+Pioglitazone 15mg+Mettypein (ER) 500mg)

- **Brand name-1: Diavista Dose type: Tablet**

Dose: 15mg/30mg
Company: Dr. Reddy's Laboratories

- **Brand name-2: Piodart Dose type: Tablet**

Dose: 15mg/30mg
Company: Biocon Limited

- **Brand name-3: Pioneer**

Dose type: Capsule/Tablet
Dose: 15mg/30mg/45mg
Company: Olcare Laboratories

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