

# Mechanism of pathogenesis, diabetic events, control and common risk factor in diabetic mellitus

Ume Salma<sup>1</sup>, Fariha Naz<sup>2</sup>, Mahnoor Yamin<sup>1</sup>, Amina Sagheer<sup>1</sup>, Sidra Altaf<sup>5</sup>, Tasawar Iqbal<sup>6\*</sup>

1. Department of Zoology, Wildlife and Fisheries, University of Agriculture Faisalabad, Pakistan
2. Department of Biochemistry, University of Agriculture Faisalabad, Pakistan
3. Department of Pharmacy, University of Agriculture Faisalabad, Pakistan
4. Institute of Physiology and Pharmacology, University of Agriculture Faisalabad, Pakistan

\*Corresponding Author: [tasawariqbal177@gmail.com](mailto:tasawariqbal177@gmail.com)

## ABSTRACT

A person with diabetes mellitus (DM) has excessive blood sugar due to a combination of metabolic illnesses. DM is caused by insufficient insulin production by the body or by a failure of cells that respond to the insulin that is produced. Insulin-dependent diabetes mellitus (IDDM) type 1 diabetes is a condition in which the body is unable to manufacture insulin and necessitates the use of an insulin pump. Non-insulin-dependent diabetic mellitus (NIDDM) type 2 diabetes is caused by insulin resistance, a disorder in which cells improperly utilize insulin, either completely or partially. Gestational diabetes, the third form, which elevated blood glucose levels in pregnant women. This article describes the pathogenicity in the three different types of diabetes, common risk factor and management of Diabetes

### Introduction

A metabolic condition called diabetes mellitus (DM) is defined by sustained hyperglycemia as well as abnormalities in protein, fat, and carbohydrate metabolism. Diabetes is a widely recognized medical condition with a history that dates back to ancient times. Differentiation comparing diabetes type 1 with type 2 was first described in the 20th century, and later, type 2 diabetes became a recognized component of the metabolic syndrome. The causes of diabetes are quite varied, but they generally include problems with insulin production or action. The majority of diabetic individuals have type 1. that commonly associated with an immune response or idiopathic causes. Diabetes Type 2, also called non-insulin dependent DM is the most typical form and classically includes elevated blood sugar, resistance of insulin, and a relative lack of insulin. Genetic factors, environmental factors, and a lifestyle that is not healthy are some of the multiple elements that have a hand in the occurrence of type 2 diabetes. In addition to this, prenatal factors, genetic syndromes, infections, and some pharmaceuticals can also lead to the expression of diabetes (1).

### Classification of Diabetes Mellitus

Efforts to advance the classification of DM have focused on integrating etiological perspectives. The very outdated terms, such as IDDM or NIDDM, were replaced by a new classification system introduced by the World Health Organization in 1980 and 1985. This new system categorizes diabetes into four types 1, 2, and "other particular types," and gestational diabetes.

### Diabetes Type 1

Type 1 diabetes mellitus, known as juvenile diabetes, occurs because of an autoimmune condition and leads to a lack of beta cells in insulin production. It is usually diagnosed by the presence of certain specific antibodies against antigens such as anti-glutamic acid decarboxylase, islet cell, or insulin. It infers that an autoimmune response against beta cells has started. The best therapeutic approach in treatment is insulin therapy for better management of the level of blood sugar (2).

### Type 2 diabetes

A current debate about the relative importance between insulin secretion and peripheral hormones in the pathogenesis of diabetes type 2. Eighty to ninety percent of cases of diabetes are type 2 diabetes (DM2). Insulin resistance is closely associated with intra-abdominal (visceral) obesity, which affects most people with Type 2 diabetes. Additionally, this demographic frequently experiences postprandial hyperlipidemia, which is defined as raised triglyceride and low HDL cholesterol levels, together with hypertension. The most common kind of diabetes, type 2, is frequently linked to older age, obesity, sedentary lifestyles, and a family history of the disease. It is more common in Black and Hispanic communities as well as in women, especially those with a history of gestational diabetes (3).

### Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus is a clinical condition that occurs in pregnant women with diabetes. It is typified by the emergence of Type 1 diabetes or the identification of asymptomatic Type 2 diabetes mellitus that had not previously been recognized. The majority of women affected by GDM will develop the condition during the 3<sup>rd</sup> pregnancy. trimester

### Pathogenesis and Pathophysiology of Diabetes Mellitus

The etiology of diabetes mellitus is intricate, encompassing genetic, environmental, and lifestyle factors that impact insulin production, insulin sensitivity, and glucose metabolism. Diabetes comes in two main Type 1 and Type 2

### Pathogenicity in Type 1 Diabetes

Type 1 diabetes arises from an autoimmune attack on the insulin-producing beta cells in the pancreas, triggered by the body's immune system. Genetic susceptibility, specifically certain HLA genotypes, shows a significant role in the increase of this condition. Additionally, environmental factors such as viral infections may also contribute to the onset of the autoimmune response in genetically inclined people (4).

### Pathogenicity in Type 2 Diabetes

Type 2 diabetes is commonly attributed to the disease known as insulin resistance, which causes cells to become less sensitive to the hormone, resulting in higher blood glucose levels. Beta Cell Dysfunction can occur over time, causing the pancreas to produce inadequate insulin to counter insulin resistance, leading to elevated concentrations of blood sugar. Obesity is one of the possible causes associated with type 2 diabetes, especially excess abdominal fat which increases insulin resistance, less physical activity reducing insulin sensitivity, genetic predisposition with a family history of diabetes, advancing age, particularly beyond 45 years, and certain ethnic backgrounds being more prone to the condition.

### Common Mechanisms in Diabetes Pathogenesis

High blood sugar levels, caused by inadequate insulin action or secretion, can lead to complications over time. Chronic high blood sugar can result in harm to blood vessels, nerves, or organs. Inflammation plays a role in both types of diabetes by affecting insulin sensitivity and beta cell activity. Lifestyle factors, such as diet, stress, and sleep patterns, can also impact glucose sensitivity (5).

### Type 1 diabetes mellitus mechanism

Insulin-producing cells in the pancreas are destroyed by immune cells in an autoimmune disease known as type 1 diabetes, as well as other immune cells infiltrating the islets. There are several factors that distinguish an autoimmune disease type 1 diabetes mellitus, including the occurrence of immune cells within the pancreatic islets, genetic vulnerability linked to specific genes in the main complex of histocompatibility, the production of autoantibodies targeting islets, and changes in immune cell regulation. Additionally, during the onset of the disease, certain immune cells produce interleukins that contribute to inflammation.

### Mechanism in Type 2 diabetes mellitus

Affected people are frequently seen to have other organ-specific autoimmune disorders. Around 85% of all patients exhibit flowing islet cell antibodies, with a common showing measurable anti-insulin antibodies prior to beginning insulin therapy. The primary target of islet cell antibodies is glutamic acid decarboxylase (GAD) in pancreatic B cells. The autoimmune death of pancreatic  $\beta$ -cells, which leads to insulin insufficiency and metabolic dysfunction, is the hallmark of type 1 diabetes mellitus (T1DM). While hyperglycemia typically reduces glucagon secretion, individuals with T1DM often have elevated glucagon levels due to insufficient suppression of glucagon secretion. Type 2 diabetes mellitus (DM2) is considered by two main pathophysiological defects reduced insulin production from

<https://biologicaltimes.com/>

Published on: 31 August, 2024

To cite this article: Salma U, F Naz, M Yamin, A Sagheer, S Altaf & T Iqbal. Mechanism of pathogenesis, diabetic events, control and common risk factor in diabetic mellitus. *Biological Times*. 2024 August 3(8): 24-25.

malfunctioning pancreatic  $\beta$ -cells and insulin resistance. In cases of severe insulin resistance,  $\beta$ -cells increase insulin making to compensate for the higher demand. Although plasma insulin levels are frequently elevated in absolute terms, they are insufficient relative to the level of insulin resistance to maintain normal glucose levels. The intricate relationship between insulin secretion and sensitivity in the regulation of glucose homeostasis makes it challenging to separate their roles in the development of DM2. Eventually, insulin resistance and hyperinsulinemia lead (6).

#### Insulin resistance

The primary factors causative to the increase of diabetes includes an initial decline in insulin discharge and a mixture of insulin shortage and peripheral insulin resistance in many individuals. Insulin resistance results in reduced uptake of glucose by the muscles and fat, inadequate control of glucose production through the liver, and decreased fat cells' absorption of triglycerides. The pancreas produces more insulin in an attempt to make up for insulin resistance. Individuals with type 2 diabetes typically experience elevated endogenous glucose production. In the early and intermediate stages of the disease, hepatic insulin resistance is the main source of high plasma sugar levels in type 2 diabetes.

#### Problems of diabetes mellitus

Short-term problems such as Diabetes ketoacidosis (DKA), hypoglycemia, and hyperglycemic hyperosmolar state (HHS) are examples of hyperglycemic crises. Chronic issues such as diabetic retinopathy, diabetic nephropathy, and microvascular problems, and diabetic neuropathy. Stress can impact a diabetes patient in the following ways. There is generally a rise in blood sugar concentration when stressed, the body releases hormones like cortisol and adrenaline which trigger the liver to manufacture additional sugar. This would be hard for a patient with diabetes to get blood glucose levels well controlled. Behavioral Stress can lead an individual to experience changes in behavior such as making poor choices of food, reduction of physical activity, sleep patterns' disruption, and the inability to adhere to medication schedules, thus making it hard to manage diabetes. It has been said that chronic stress will contribute to the development of diabetes-related complications like cardiovascular diseases, high blood pressure, and a weakened immune system. One of the most important parts of maintaining good health in a patient with diabetes is managing stress. Management Strategies such as mindfulness, regular physical activity, good sleep, healthy relationships, and consultation with health professionals, might mitigate the impact of stress on management. It is necessary for individuals with diabetes to use these strategies because they support their overall well-being (7).

#### Fasting plasma glucose examination

Employees are required to fast for eight hours prior to undergoing this test. A diabetes diagnosis is confirmed when blood glucose concentrations exceed 126 mg/dL on two separate examinations conducted on altered days. The fasting glucose level is determined, followed by the administration of 75 g of glucose (100 g for pregnant women). Blood samples are then taken every 30 minutes to an hour over a period of two to three hours. A normal test result is indicated by a blood glucose level under 140mg/dL after two hours.

#### Standards of Care for People with Diabetes

The Diabetes Control and Problems Trial (DCCT) had a significant impact on diabetes management standards, leading to the American Diabetes Association (ADA) recommending an A1C target of less than 7% (53 mmol/mol). DCCT, initiated in the year 1983, randomly assigned 1441 type 1 diabetes patients (with age of 27) to either severe or routine care. The target A1C level was set at less than 6.05% (43 mmol/mol) respectively, two standard deviations higher than the mean for people without diabetes. One or two daily insulin injections and one daily urine test or blood glucose test were part of the standard treatment regimen. aimed at reducing hyperglycemic and hypoglycemic symptoms. It is crucial to simultaneously manage other risk factors such as blood pressure and cholesterol, as supported by suggestions

from clinical trials and meta-analyses. The concept of the ABCs highlights the overarching treatment goals of A1C, blood pressure, and cholesterol/lipids, with specific targets defined for each. These goals have evolved over time to be more individualized (8).

#### Causes and Risk Factors

##### The origins of diabetes range relying on type

The precise factors contributing to although the exact cause of type 1 diabetes is unknown; it is thought to be the result of a genetic predisposition along with environmental factors such viral infections that can cause autoimmune reactions. Type 2 diabetes, on the other hand, is influenced by a variation of factors including genetics, obesity, deficiency of physical movement, and unhealthy eating habits. Gestational diabetes can also occur due to hormonal changes during pregnancy, leading to insulin resistance in some women.

#### Symptoms and Diagnosis

Increased hunger, urination, weight loss, blurred eyesight, and slow wound healing are common signs of diabetes. These problems include Cardiovascular complications. Neuropathy causes nerve damage and can result in pain, tingling, and numbness in the limbs. Nephropathy, or kidney disease which can cause kidney damage to the point of kidney failure. Retinopathy, which causes damage to the eyes and can cause blindness if not treated early (9).

#### Management and Treatment

Effective treatment of diabetes includes a mixture of lifestyle changes, medication, and consistent monitoring. Lifestyle modifications involve the adoption of a healthy diet, physical movement, weight management, and prevention from tobacco. Medications are prescribed on the basis of the type of diabetes for instance, insulin is the furthestmost important medication in the case of type 1 diabetes; oral medicines and injectable drugs are indicated in type 2 diabetes to improve blood sugar levels. Monitoring includes regular checks of blood sugar and HbA1c testing for long-term glucose control (10).

#### Conclusion

Untreated metabolic diseases fall under the diabetes mellitus and cause the blood to contain excessively high levels of glucose. DM Type 1 is characterized by the pancreas's inability to produce appreciably high levels of the hormone insulin. Contrarily, diabetes mellitus type 2 is believed to be caused by insulin resistance. A person with type 2 diabetes has high insulin production from the pancreas. Restoring normal glucose metabolism is the primary objective of managing diabetes to the greatest feasible level. Preventing or treating the numerous problems that can arise from both the disease and its treatment are additional objectives of diabetes care.

#### References

- [1] Balaji R, Duraisamy R, Kumar MP. Complications of diabetes mellitus: A review. *Drug Invention Today*. 2019 Jan 15;12(1).
- [2] Buchanan TA, Xiang AH. Gestational diabetes mellitus. *The Journal of clinical investigation*. 2005 Mar 1;115(3):485-91.
- [3] D'Addio F, Nasr MB, Lunati ME, Fiorina P. Autoimmune (Type 1) diabetes. In *The Rose and Mackay Textbook of Autoimmune Diseases 2024* Jan 1 (pp. 585-601). Academic Press.
- [4] Dwivedi M, Pandey AR. Diabetes mellitus and its treatment: an overview. *J Adv Pharmacol*. 2020;1(1):48-58.
- [5] Gubitosi-Klug RA, Braffett BH, Bebu I, Johnson ML, Farrell K, Kenny D, Trapani VR, Meadema-Mayer L, Soliman EZ, Pop-Busui R, Lachin JM. Continuous glucose monitoring in adults with type 1 diabetes with 35 years duration from the DCCT/EDIC study. *Diabetes Care*. 2022 Mar 1;45(3):659-65.
- [6] Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes care*. 2009 Jul;32(7):1335.
- [7] Magliano DJ, Zimmet P, Shaw JE. Classification of diabetes mellitus and other categories of glucose intolerance. *International textbook of diabetes mellitus*. 2015 Apr 17:1-6.
- [8] Sam S. Differential effect of subcutaneous abdominal and visceral adipose tissue on cardiometabolic risk. *Hormone molecular biology and clinical investigation*. 2018 Jan 26;33(1):20180014.
- [9] Sen S, Chakraborty R, De B. *Diabetes mellitus in 21st century*. Singapore: Springer; 2016 Jul 25.
- [10] Szablewski L. Role of immune system in type 1 diabetes mellitus pathogenesis. *International immunopharmacology*. 2014 Sep 1;22(1):182-91.
- [11] White NH. The DCCT and its implications for management of diabetes in children and adolescents. In *Pediatric Diabetes 2003* (pp. 337-368). Boston, MA: Springer US.