



FACULTY OF  
MEDICINE | كلية الطب

# Diabetes Mellitus

- **Written by:**

- 394: Aya Ashraf Sharaf El-Deen
- 396: Aya Abd-Almonem Fathallah
- 399: Aya Mohamed Khalifa
- 400: Aya Mohamed shetya
- 403: Ehab Nabil Aly
- 415: Baraa Tarek Yahia Shaker
- 416: Baraa Ahmed Abd-Alhameed
- 423: Basmala Ahmed Alhoseny
- 424: Basmala Ahmed Yahia
- 425: Basmala Osama Abu-Bakr
- 426: Basmalla Ashraf Mostafa

- **Introduction**

Diabetes Mellitus (DM) is included in the list of top ten fatal diseases globally. Recently, its prevalence and incidence are rising leading to an economic and health burden. “[1]” According to World Health Organization (WHO) 1.5 million people die every year because of diabetes. “[2]”

In Egypt prevalence of Diabetes is the ninth highest worldwide according to International Diabetes Federation (IDF) as Egypt has recorded a number of 8,850,400 adult diabetic patients in early 2020 with prevalence 15.2%. “[3]”

Historically (DM) has been known since long time ago. Symptoms like polyuria and excessive thirst have been described in ancient Egyptian papyri, Chinese literature and by ancient Indians. “[4]” it has widely been researched and still researched till now as it is considered one of the major health problems nowadays.

### **What is Diabetes Mellitus?**

DM is a disease of malfunction in controlling blood sugar (glucose) levels in blood. Subtypes of Diabetes include mainly Type1, Type2 in addition to Gestational Diabetes, Maturity Onset Diabetes of the Young (MODY), Neonatal (congenital) Diabetes Mellitus, Steroid induced Diabetes. “[5]”

- **Definition**

Diabetes is a long term (chronic) disease that affects how your body converts food into energy. Most of the consumed food is converted by the body into sugar (glucose), which is then released into blood circulation. Signals are sent to the pancreas to release insulin when blood sugar levels rise. Insulin works as a key to allow blood sugar to enter body's cells for energy production. In the case of diabetes, too much blood sugar remains in your circulation when there is insufficient insulin or when cells stop reacting to insulin. That can eventually lead to major health issues like renal disease, eyesight loss, and heart disease. “[6]”

- **Classification**

Diabetes is a complex disease that manifests itself in many ways. As well as the more common types of diabetes - type 1, type 2 and gestational diabetes, there are a range of other types of diabetes like

- Maturity onset diabetes of the young (MODY)
- Neonatal diabetes
- Wolfram Syndrome

- Alström Syndrome
- Latent Autoimmune diabetes in Adults (LADA)
- Type 3c diabetes
- Steroid-induced diabetes
- Cystic fibrosis diabetes “[7]”

In the case of **type 1 diabetes** pancreas stops producing insulin or releases very small amount so, cells of the body can't use blood sugar for energy production and glucose accumulates in the blood causing many of the problems and symptoms of diabetes. “[8]”

In **type 2 diabetes** or insulin resistance pancreas can release insulin but cells can't react effectively to it, so the blood sugar level is high. The pancreas releases more insulin to force cells to react, but the pancreas can't continue producing insulin leading to prediabetes and type 2 diabetes. “[9]”

Glucose intolerance that is first noticed during pregnancy is known as **gestational diabetes mellitus (GDM)**. The third trimester of pregnancy is when GDM often first manifests in women who have the illness. “[10]”

- **symptoms**

Researchers have found that blood sugar level influences diabetes symptoms. “[11]” Among people suffering from diabetes many symptoms have been detected, and the most important of them are the constant feeling of hunger and thirst, going to urinate many times, especially during the night, dry skin, noticeable weight loss and slow wound healing. “[12]” Depression also threatens diabetic patients. Therefore, when feeling depressed, they must go to a psychiatrist and receive treatment. “[13]” There are some differences between type1 and type2 diabetes symptoms “[12]”:

Type1	Type2
It can become severe in a few weeks or months.	It takes a long time to become severe.
Vomiting, nausea, and stomach pain are more likely to happen to type1 diabetic patients.	The symptoms are difficult to be detected and may not be present.

## • **Diagnosis**

- Early screening and diagnosis permit the identification of at-risk individuals (so that precautions, most importantly lifestyle changes, might not be taken seriously) and patients with early disease (so that the treatment steps can be started).
- Often used tests for diabetes diagnosis are fasting plasma glucose level of  $\geq 126$  mg/dl (7.0 mmol/l) or glycated hemoglobin (HbA1c) level of  $\geq 6.5\%$  (48 mmol/mol Hb).
- A fasting glucose level of 100 to 125 mg/dl (5.6 to 6.9 mmol/l) indicates prediabetes; the range of glycated hemoglobin levels that points to prediabetes is controversial, but the American Diabetes Association recommends a range between 5.7 - 6.4%.
- Hemoglobinopathies and conditions of altered red blood-cell turnover can give misleading results for glycated hemoglobin. “[14]”
- The blood sugar testing to diagnose type 1 diabetes is very similar to that for type 2 therefore doctors do **antibody serology test** (a blood test that looks for specific antibodies) like GAD, IA-2, ZnT8. That tells if it is either type 1 or 2. “[15]”
- In type 1 diabetes, the immune system makes antibodies that act against pancreatic cells ( $\beta$ -cells) that produce insulin.
- Doctors often suspect type 2 diabetes based on symptoms and risk factors, such as obesity and especially family history.

## • **Epidemiology**

Based on the most recent projections, 382 million individuals worldwide had diabetes in 2013, and that number is anticipated to climb to 592 million by 2035. The main types of diabetes are type 1 and type 2, with type 2 representing the majority (>85%) of all cases of diabetes.

### **Type 1:**

#### **Changes according to age, sex, and race**

Type 1 diabetes can develop at any age, the incidence is often highest between birth and 14 years of age. In most groups, the incidence rate rises steadily with age up to about 10-15 years. For ages over 35, there are no population-based incidence statistics available. The peak incidence occurs around puberty in most groups, and there is typically a male excess among young people. In populations of European ancestry, incidence is higher than in non-Europeans, mirroring the geographic pattern.

## **Type 2:**

### **Prevalence varies depending on place, race, age, and sex.**

There is significant geographic diversity, just like in type 1 diabetes, but the pattern is different. The incidence is lowest in rural parts of developing nations, generally intermediate in developed nations, and highest in some ethnic groups, especially those that have embraced Western living patterns. Obesity is associated with high prevalence rates. About 14 million more men than women estimated to have diabetes in 2013. According to research employing serial glucose tolerance testing, the annual prevalence in Western populations for Europeans is about 7 per 1000. Data from the US Centers for Disease Control reveal that the number of people with diabetes who had been diagnosed nearly quadrupled from 5.5 million in 1980 to 21.1 million in 2010.

Type 2 diabetes has started to occur in children and young people as a result of the rise in childhood obesity prevalence. In the United States, the prevalence of type 2 diabetes among youth (ages 10 to 19) increased generally from 0.34 per 1000 (95% confidence range, 0.31-0.37) in 2001 to 0.46 per 1000 (95% CI, 0.43-0.49) in 2009. It was greater in American Indian, black, and Hispanic kids than white youth. “[16]”

- **Causes**

#### **TYPE 1:**

Type 1 diabetes occurs when your immune system, the body's line of defense against infection, attacks and destroys the beta cells in your pancreas that make insulin. Scientists believe that environmental factors, such as infections and genetic predispositions, might cause type 1 diabetes. “[17]”

#### **TYPE 2:**

Numerous genetic and behavioral factors contribute to type 2 diabetes, which is the most common kind. “[17]”

- **Insulin resistance**

Type 2 diabetes frequently manifests as insulin resistance, a condition in which muscle, liver, and fat cells improperly utilize insulin. As a result, your body needs more insulin to help glucose enter cells. The pancreas first makes more insulin to satisfy the increased demand. Over time, the pancreas' failure to generate enough insulin causes blood glucose levels to increase. “[18]”

- **Risk Factors**

Each type of diabetes has specific risk factors.

**Type 1:**

- Family history is mainly genetic.
- Presence of diabetes immune system cells (which are autoantibodies) in family members of type 1 diabetes patients.

In case of existing, there will be an increasing risk of developing type 1 diabetes but it's not inevitable, some people have the cells but don't develop type 1 diabetes.

- Environmental and geographical factors.
- Obesity and overweight. “[17]”

**Type 2:**

- Race or ethnicity: People with black skin, from Spanish origin, American Indian and Asian American have higher risk of developing type 2 diabetes, however, the relation between race or ethnicity and type 2 diabetes isn't clear.
- Obesity and overweight. “[17]”
- Smokers have increased risk of developing type 2 diabetes.
- Inactive lifestyle and lack of physical work. “[19]”

- **complications**

In the last 20 years, rates of several major complications have decreased among US adults with diabetes.

**Type 1 diabetes complications:**

Type 1 diabetes can lead to other problems, especially if it is not well- controlled. They include:

- cardiovascular disease, diabetes can put you at higher risk of blood clot as well as high blood pressure and cholesterol.
- skin problems, people with diabetes are more likely to get bacterial and fungal infections.
- Gum disease, too much sugar in blood can lead to sugar in saliva.
- Eye damage, diabetes also leads to the destruction of blood vessels of the eye which is called diabetic retinopathy.

- Kidney damage, which happens because of high blood sugar and high blood pressure and is also called diabetic nephropathy. “[20]”

### **Type 2 diabetes complications:**

If you do not work hard to keep your blood glucose level under control, you run the risk of developing short - and long -term complications.

- Alzheimer's disease.
- Hearing problem.
- Depression.
- Nerve problems.
- Heart failure. “[17,21]”

### **• Prevention**

#### **DM Type 1:**

Prevention of type 1 diabetes is further subdivided into three types:

(Each type has its own method of prevention according to the stage of discovery)

1. Primary prevention takes place the moment the patient recognizes their autoimmune disease.  
This type should be started early in life, and it revolves around avoiding being exposed to triggers, such as cow milk that would stimulate the destruction of your  $\beta$  cells of Langerhans causing T1DM (type 1 diabetes).
2. Secondary prevention takes place after diagnosis with a significant number of the  $\beta$  cells left. This type takes a more confronting route, where we interfere with the autoimmune cascade during the process of  $\beta$  cells destruction.
3. Tertiary prevention takes place after a sever number of  $\beta$  cells have been destroyed. It takes a more repairing route, where we try to stop the process of  $\beta$  cells destruction or at least try to reverse it by making up for the destroyed cells.  
“[22]”

#### **DM Type 2:**

Methods of preventing this type revolves around a healthier lifestyle, these methods are:

1. Losing weight and not gaining it back
2. A healthy diet which involves: Staying away from sugar and fat as much as possible. Including plenty of white grains, fruits and veggies Limiting red and processed meat
3. If you consume alcohol stop or limit it
4. Do not smoke. “[23]”



- **Treatment**

There are various treatment options available for diabetes, including lifestyle changes, oral medications, insulin therapy, and non-insulin injectable therapies. “[24]”

Oral medications used to treat diabetes include sulfonylureas, metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and thiazolidinediones. “[25]”

During the last few years, newer medications such as glitazones, glinides and insulin analogues have enriched treatment options for type 2 diabetes.

In particular, non-insulin injectable therapies like glucagon-like peptide-1 receptor agonists have gained popularity in recent years due to their glucose-lowering effects, ability to induce insulin secretion in a glucose-dependent manner, and control of glucagon secretion. For patients whose type 2 diabetes is inadequately controlled with oral antihyperglycemic medications, injectable therapies such as insulin and GLP-1 receptor agonists are recommended. The American Diabetes Association and European Association for the Study of Diabetes recommend initial treatment with metformin, followed by intensifying treatment using dual therapy and triple therapy if needed. “[26]”

Treatment options for type 1 diabetes include insulin therapy via subcutaneous injection or pump infusion. However, there is currently no established therapy for lipotrophy in patients with type 1 diabetes. While lifestyle changes and oral medications are commonly used as first-line treatments for type 2 diabetes, more advanced therapies like insulin replacement therapy become necessary if these measures fail to control blood glucose levels. “[27]”

Despite the availability of various treatment options for diabetes, there are still limitations in their effectiveness and safety.

## ● References

1. Li S, Wang J, Zhang B, Li X, Liu Y. Diabetes mellitus and cause-specific mortality: A population-based study, *Diabetes & metabolism journal*. U.S. National Library of Medicine. [Online]. 2019 [cited 2023 Apr 27]; Available from: URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6581547/>
2. World Health Organization. Diabetes. [Online]. [cited 2023 Apr 27]; Available from: URL: [https://www.who.int/health-topics/diabetes#tab=tab\\_1](https://www.who.int/health-topics/diabetes#tab=tab_1)
3. Abouzid MR, Ali K, Elkhawas I, Elshafei SM. An overview of diabetes mellitus in Egypt and the significance of integrating preventive cardiology in diabetes management, *Cureus*. U.S. National Library of Medicine. [Online]. 2022 [cited 2023 Apr 27]; Available from: URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9390800/#REF1>
4. Karamanou M, Protogerou A, Tsoucalas G, Androutsos G, Poulakou-Rebelakou E. Milestones in the history of diabetes mellitus: The main contributors, *World journal of diabetes*. U.S. National Library of Medicine. [Online]. 2016 [cited 2023 Apr 27]; Available from: URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707300/#B1>
5. Sapra A, Bhandari P. *Diabetes Mellitus*, National Center for Biotechnology Information. StatPearls Publishing. [Online]. 2022 [cited 2023 Apr 27]; Available from: URL: <https://www.ncbi.nlm.nih.gov/books/NBK551501/>
6. CDC. What is diabetes? Centers for Disease Control and Prevention. [Online]. 2023 [cited 2023 Apr 18]; Available from: URL: <https://www.cdc.gov/diabetes/basics/diabetes.html>
7. Types of diabetes. Diabetes UK. [Online]. 2017 [cited 2023 Apr 20]; Available from: URL: <https://www.diabetes.org.uk/diabetes-the-basics/types-of-diabetes>
8. CDC. What is type 1 diabetes. Centers for Disease Control and Prevention. [Online]. 2022 [cited 2023 Apr 18]; Available from: URL: <https://www.cdc.gov/diabetes/basics/what-is-type-1-diabetes.html>
9. CDC. Type 2 diabetes. Centers for Disease Control and Prevention. [Online]. 2023 [cited 2023 Apr 24]; Available from: URL: <https://www.cdc.gov/diabetes/basics/type2.html>

10. Solis-Herrera C, Triplitt C, Reasner C, DeFronzo RA, Cersosimo E. Classification of Diabetes Mellitus [Internet]. Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al., editors. PubMed. South Dartmouth (MA): MDText.com, Inc.; 2000 [cited 2023 Apr 13]; Available from: URL: <https://www.ncbi.nlm.nih.gov/books/NBK279119/#class-diab-mellitus.toc-gestational-diabetes-mellitus-gdm>
11. Diabetes – Symptoms and causes [online]. 2023 Jan 20 [cited 2023 Apr 24]; Available from: URL: <https://www.mayoclinic.org/diseases-conditions/diabetes/symptoms-causes/syc-20371444>
12. CDC. Diabetes symptoms [online]. Centers for Disease Control and Prevention. 2023 [cited 2023 Apr 27]. Available from: URL: <https://www.cdc.gov/diabetes/basics/symptoms.html>
13. CDC. Diabetes and mental health [online]. Centers for Disease Control and Prevention. 2022 [cited 2023 Apr 27]. Available from: URL: <https://www.cdc.gov/diabetes/managing/mental-health.html>
14. Inzucchi SE. Diagnosis of Diabetes. New England Journal of Medicine 2012 Aug 9;367(6):542–50. Available from: URL: <https://www.nejm.org/doi/full/10.1056/NEJMcp1103643>
15. Genuth SM, Palmer JP, Nathan DM. Classification and Diagnosis of Diabetes. In: Cowie CC, Casagrande SS, Menke A, et al., editors. Diabetes in America. 3rd edition. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018 Aug. CHAPTER 1. Available from: URL: <https://www.ncbi.nlm.nih.gov/books/NBK568014/>
16. Forouhi NG, Wareham NJ. Epidemiology of diabetes [Internet]. Medicine (Abingdon, England: UK ed.). U.S. National Library of Medicine; 2014 [cited 2023 Apr 25]. Available from: URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4282306/>
17. Diabetes – Symptoms and causes [online]. 2023 Jan 20 [cited 2023 Apr 24]; Available from: URL: <https://www.mayoclinic.org/diseases-conditions/diabetes/symptoms-causes/syc-20371444>
18. Type 2 diabetes. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); 2016. Available from: URL: <https://www.niddk.nih.gov/health-information/diabetes/overview/symptoms-causes#causes>

19. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk Factors Contributing to Type 2 Diabetes and Recent Advances in Treatment and Prevention. *International Journal of Medical Sciences* [online]. 2014 Sep 6;11(11):1185–200. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4166864/>
20. Diabetes UK. Complications of diabetes [Online]. Diabetes UK. 2022. Available from: URL: <https://www.diabetes.org.uk/Guide-to-diabetes/Complications>
21. Diabetic hyperglycemic hyperosmolar syndrome: MedlinePlus Medical Encyclopedia [Online]. medlineplus.gov. Available from: URL: <https://medlineplus.gov/ency/article/000304.htm>
22. Wherrett DK, Daneman D. Prevention of type 1 diabetes [Online]. *Endocrinology and metabolism clinics of North America*. U.S. National Library of Medicine; 2009 [cited 2023Apr24]. Available from: URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2786901/#S5title>
23. Anon. How to prevent diabetes [Internet]. MedlinePlus. U.S. National Library of Medicine; 2017 [cited 2023Apr24]. Available from: URL: <https://medlineplus.gov/howtopreventdiabetes.html>
24. Singh S, Guerra J, Lazar P, Merchant A. The Effect of Social Determinants and Socioeconomic Status on Laparoscopic Roux-En-Y Gastric Bypass for Weight Loss: An Analysis of the National Inpatient Sample. *The Surgery Journal* [Online]. 2021 Jul 19; 7(3):147–53. Available from: <https://www.thieme-connect.de/products/ejournals/pdf/10.1055/s-0041-1734030.pdf>
25. Heo C, Choi C-I. Current Progress in Pharmacogenetics of Second-Line Antidiabetic Medications: Towards Precision Medicine for Type 2 Diabetes. *Journal of Clinical Medicine* [Internet] 2019;8(3):393. Available from: <http://dx.doi.org/10.3390/jcm8030393>
26. MacConell L, Gurney K, Malloy J, Zhou M, Kolterman O. Safety, and tolerability of exenatide once weekly in patients with type 2 diabetes: an integrated analysis of 4,328 patients. *Diabetes Metab Syndr Obes*. 2015; 8:241-253. Available from: <https://doi.org/10.2147/DMSO.S77290>
27. Jendle J, Buompiensiere MI, Holm AL. et al. The Cost-Effectiveness of an Advanced Hybrid Closed-Loop System in People with Type 1 Diabetes: A Health Economic Analysis in Sweden. *Diabetes Therapy*. 2021; 12:2977–2991. Available from: <https://doi.org/10.1007/s13300-021-01157-0>