



Information about Diabetes Mellitus: Review

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Abstract

Diabetes mellitus (DM), is a group of metabolic disorders characterized by a high blood sugar level in the blood. Diabetes can cause serious health complications including heart disease, blindness, kidney failure, Symptoms of marked hyperglycemia include polyuria, polydipsia, and sometimes with polyphagia. Acute life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis. Long-term complications of diabetes include retinopathy with loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers and ,Charcot joints; and cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased incidence of atherosclerotic cardiovascular, peripheral arterial, cerebrovascular disease and Hypertension in people with diabetes.

Key Words: Diabetes mellitus, Type 1, Type 2, Gestational, Signs and symptoms, Complications, Insulin

Introduction

Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time.^[1] Symptoms often include frequent urination, increased thirst, and increased appetite. If left untreated, diabetes can cause many complications.^[2] Acute complications can include diabetic ketoacidosis, hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, damage to the eyes and cognitive impairment.^[3]

As of 2019, an estimated 463 million people had diabetes worldwide (8.8% of the adult population), with type 2 diabetes making up about 90% of the cases. Rates are similar in women and men.^[4] Trends suggest that rates will continue to rise. Diabetes at least doubles a person's risk of early death. In 2019, diabetes resulted in approximately 4.2 million deaths.^[2]

Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus:^[5]

Type 1

Diabetes results from the pancreas' failure to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM). The loss of beta cells is caused by an autoimmune response. The cause of this autoimmune response is unknown.^[2] Type 1 diabetes is characterized by loss of the insulin-producing beta cells of the pancreatic islets, leading to insulin deficiency. This type can be further classified as immune-mediated. The majority of type 1 diabetes is of the immune-mediated nature, in which a T cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin it causes approximately 10% of diabetes mellitus cases in North America and Europe.^[6] Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages. The frequent onset in children, the majority of individuals living with type 1 diabetes are now adults. Type 1 diabetes can occur at any age, and a significant proportion is diagnosed during adulthood. Latent autoimmune diabetes of adults (LADA) is the diagnostic term applied when type 1 diabetes develops in adults; it has a slower onset than the same condition in children^[7].

Type 2

Diabetes is the most common type of diabetes mellitus. Begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non - insulin dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is a combination of excessive body weight and insufficient exercise.^[2] Type 2 diabetes involves maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding the use of tobacco. Type 2 diabetes may be treated with medications such as insulin sensitizers with or without insulin. Control of blood pressure and maintaining proper foot and eye care are important for people with the disease. Insulin and some oral medications can cause low blood sugar. Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes.^[8]

Type 2 diabetes is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion.^[9] The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Many people with type 2 diabetes have evidence of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) before meeting the criteria for type 2 diabetes. The progression of prediabetes to overt type 2 diabetes can be slowed or reversed by lifestyle changes or medications that improve insulin sensitivity or reduce the liver's glucose production.^[10]



Type 2 diabetes is primarily due to lifestyle factors and genetics. Several of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization.^[11] Excess body fat is associated with 30% of cases in people of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese may have a high ratio^[12]

Gestational Diabetes

Gestational diabetes usually resolves after the birth of the baby is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels.^[2] 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. It is recommended that all pregnant women are 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.^[12] However, after pregnancy approximately 5–10% of women with gestational diabetes are found to have another form of diabetes, most commonly type 2. Gestational diabetes is fully treatable, but required careful medical supervision throughout the pregnancy. Management may include dietary changes, blood glucose monitoring, and in some cases, insulin may be required. Though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother. Risks to the baby include macrosomia (high birth weight), congenital heart and central nervous system abnormalities, and skeletal-muscle malformations. Increased levels of insulin in a fetus's blood may inhibit fetal surfactant production and cause infant respiratory distress syndrome. A high blood bilirubin level^[13].

Signs and symptoms

The classic symptoms of untreated diabetes are unintended weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.^[14] Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurred vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Long-term vision loss can also be caused by diabetic retinopathy. Many of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes.^[15]

Complications

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20) but may be the first symptom in those who have otherwise not received a diagnosis before that time ^[16]. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in people with diabetes are due to coronary artery disease other macrovascular disease include stroke, and peripheral artery disease. ^[17]

The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. ^[18] Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems. Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. ^[18] The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle atrophy and weakness.

Table -1- Comparison of type 1 and 2 diabetes ^[19]

Feature	Type 1 diabetes	Type 2 diabetes
Onset	Sudden	Gradual
Age at onset	Mostly in children	Mostly in adults
Body size	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased
Concordance in identical twins	50%	90%
Prevalence	~10%	~90%



Insulin

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially the liver, adipose tissue and muscle^[20]

Insulin is released into the blood by beta cells (β -cells), found in the islets of Langerhans in the normal pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts oppositely manner to insulin.^[21]

If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin resistance), or if the insulin itself is defective, then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency.^[20]

When the glucose concentration in the blood remains high over time, the kidneys reach a threshold of reabsorption, and the body excretes glucose in the urine (glycosuria).^[22] This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume is replaced osmotically from water in body cells and other body compartments, causing dehydration and increased thirst (polydipsia).^[20] In addition, intracellular glucose deficiency stimulates appetite leading to excessive food intake (polyphagia).^[23]

Diagnosis

Table -2- WHO diabetes diagnostic criteria ^[24]

Condition	2-hour glucose		Fasting glucose		HbA _{1c}	
	<i>mmol/L</i>	<i>mg/dL</i>	<i>mmol/L</i>	<i>mg/dL</i>	<i>mmol/mol</i>	<i>DCCT %</i>
Normal	< 7.8	< 140	< 6.1	< 110	< 42	< 6.0
Impaired glycaemia	< 7.8	< 140	6.1–7.0	110– 125	42–46	6.0–6.4
fasting						
Impaired tolerance	≥ 7.8	≥ 140	< 7.0	< 126	42–46	6.0–6.4
Diabetes mellitus	≥ 11.1	≥ 200	≥ 7.0	≥ 126	≥ 48	≥ 6.5

Diabetes mellitus is characterized by recurrent or persistent high blood sugar, and is diagnosed by demonstrating any one of the following.^[25]

- Fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL)
- Plasma glucose ≥ 11.1 mmol/L (200 mg/dL) two hours after a 75 gram oral glucose load as in a glucose tolerance test (OGTT)
- Symptoms of high blood sugar and casual plasma glucose ≥ 11.1 mmol/L (200 mg/dL)
- Glycated hemoglobin (HbA_{1c}) ≥ 48 mmol/mol (≥ 6.5 DCCT %).^[26]

People with diabetes can benefit from education about the disease and treatment, dietary changes, and exercise Learning about the disease and actively participating in the treatment is important, since complications are far less common and less severe in people who have well-managed blood sugar levels.^[27] In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure.^[28] There is no known preventive measure for type 1 diabetes.^[2] Type 2 diabetes, which accounts for 85–90% of all cases worldwide can often be prevented or delayed by maintaining a normal body weight, engaging in physical activity, and eating a healthy diet.^[2] Higher levels of physical activity (more than 90 minutes per day) reduce the risk of diabetes by 28%.^[27] Dietary changes known to be effective in helping to prevent diabetes include maintaining a diet rich in whole grains and fiber, and choosing good fats, such as the polyunsaturated fats found in nuts, vegetable oils, and fish. Limiting sugary beverages and eating less red meat and other sources of saturated fat can also help prevent diabetes.^[27] Tobacco smoking is also associated with an increased risk of diabetes and its complications, so smoking cessation can be an important preventive measure as well. The relationship between type 2 diabetes and the main modifiable risk factors (excess weight, unhealthy diet, physical inactivity and tobacco use) is similar in all regions of the world. There is growing evidence that the underlying determinants of diabetes are a reflection of the

major forces driving social, economic and cultural change: globalization, urbanization, population aging, and the general health policy environment.^[29]

History of diabetes

Diabetes was one of the first diseases described, with an Egyptian manuscript from c. 1500 BCE mentioning "too great emptying of the urine."^[30] The Ebers papyrus includes a recommendation for a drink to take in such cases. The first described cases are believed to have been type 1 diabetes. Indian physicians around the same time identified the disease and classified it as *madhumeha* or "honey urine", noting the urine would attract ants.^{[30][31]}

The term "diabetes" or "to pass through" was first used in 230 BCE by the Greek Apollonius of Memphis. The disease was considered rare during the time of the Roman Empire, with Galen commenting he had only seen two cases during his career.^[30] This is possibly due to the diet and lifestyle of the ancients, or because the clinical symptoms were observed during the advanced stage of the disease. Galen named the disease "diarrhea of the urine" (diarrhea urinosa).^[30]

The Two types of diabetes were identified as separate conditions for the first time by the Indian physicians Sushruta and Charaka in 400–500 CE with one type being associated with youth and another type with being overweight. Effective treatment was not developed until the early part of the 20th century when Canadians Frederick Banting and Charles Herbert Best isolated and purified insulin in 1921 and 1922.^[30]

In 2017, 425 million people had diabetes worldwide^[32] up from an estimated 382 million people in 2013 and from 108 million in 1980.^[33] Accounting for the shifting age structure of the global population, the prevalence of diabetes is 8.8% among adults, nearly double the rate of 4.7% in 1980.^{[32][34]} Some data indicate rates are roughly equal in women and men, but male excess in diabetes has been found in many populations with higher type 2 incidence, possibly due to sex-related differences in insulin sensitivity, consequences of obesity and regional body fat deposition, and other contributing factors such as high blood pressure, tobacco smoking, and alcohol intake.^{[35][36]}

The WHO estimates that diabetes resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death.^[34] However another 2.2 million deaths worldwide were attributable to high blood glucose and the increased risks of cardiovascular disease and other associated complications (e.g. kidney failure), which often lead to premature death and are often listed as the underlying cause of death certificates rather than diabetes.^[37] For example, in 2017,

Diabetes occurs throughout the world but is more common (especially type 2) in more developed countries. The greatest increase in rates has however been seen in low- and middle-income countries, where more than 80% of diabetic deaths occur.^[37] The fastest prevalence increase is expected to occur in Asia and Africa, where most people with diabetes will probably live in 2030.^[38] The increase in rates in developing countries follows the trend of urbanization and lifestyle changes, including increasingly sedentary lifestyles, less physically demanding work, and the global nutrition transition,



marked by increased intake of foods that are high energy-dense but nutrient-poor (often high in sugar and saturated fats, sometimes referred to as the "Western-style" diet). The global number of diabetes cases might increase by 48% between 2017 and 2045.^[38]

Conclusion

Treatment involves both healthy diet and exercise as well as oral medications to regulate blood sugar. In all type 1 diabetics and in severe uncontrolled type 2 diabetics one or more injections of insulin a day may be needed.

Conflict of Interests.

There are non-conflicts of interest .

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الخلاصة

مرض داء السكر , او المعروف بأسم داء السكري (DM) Diabetes mellitus هو اضطراب الايض وارتفاع عالي في مستوى السكر على مدى فترة طويلة . ويسبب داء السكر مضاعفات صحية متمثلة عدد من الامراض كأمرض القلب والعمى والفشل الكلوي وتظهر اعراض مرض فرط سكر الدم غالبا بكثرة البول ,وزيادة العطش والشهية. كما يؤدي نمط الحياة الغير مسيطر على السكر بظهور مايسمى بالحماض الكيتوني السكري .وتسبب المضاعفات طويلة الامد الى الاصابة بعدد من الامراض منها اعتلال الشبكية السكري مع فقدان الرؤية واعتلال الكلوي السكري مؤديا الى الفشل الكلوي وايضا اعتلال الاعصاب المحيطية التي تسبب تقرحات القدم والتهاب مفصل شاركوت وامراض القلب الوعائية والعجز الجنسي. ان ترك المصاب بمرض السكر بدون معالجة يؤدي الى الاصابة بمرض تصلب الشرايين الاوعية القلبية وامراض الشرايين المحيطية وامراض الاوعية الدماغية وارتفاع ضغط الدم .