



Review Article

DIABETES MELLITUS AND GESTATIONAL DIABETES MELLITUS

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Abstract:

Diabetes mellitus (DM), also known as simply diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period Worldwide in 2012 and 2013 diabetes resulted in 1.5 to 5.1 million deaths per year, making it the 8th leading cause of death. Diabetes overall at least doubles the risk of death. This high blood sugar produces the symptoms of frequent urination, increased thirst, and increased hunger. Untreated, diabetes can cause many complications. Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma. Serious long-term complications include heart disease, stroke, kidney failure, foot ulcers and damage to the eyes. The number of people with diabetes is expected to rise to 592 million by 2035. The economic costs of diabetes globally were estimated in 2013 at \$548 billion and in the United States in 2012 \$245 billion. [3]Globally, as of 2013, an estimated 382 million people have diabetes worldwide, with type 2 diabetes making up about 90% of the cases. This is equal to 8.3% of the adults' population, with equal rates in both women and men. There are three main types of diabetes mellitus: In case of type 1 Diabetes mellitus, results from the body's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown. Another type is type 2 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 primary cause is excessive body weight and not enough exercise. Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop a high blood glucose level. Gestational diabetes usually resolves after the birth of the baby. It occurs in about 2–10% of all pregnancies and may improve or disappear after delivery. However, after pregnancy approximately 5–10% of women with gestational diabetes are found to have diabetes mellitus, most commonly type 2. Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy.

Key words: Insulin-dependent diabetes mellitus" (IDDM), non insulin-dependent diabetes mellitus" (NIDDM) & Gestational diabetes mellitus (GDM)

Introduction:

Diabetes mellitus (DM), also known as simply diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period.¹ This high blood sugar produces the symptoms of frequent urination, increased thirst,

and increased hunger. Untreated, diabetes can cause many complications. Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma. Serious long-term complications include heart disease, stroke, kidney failure, foot ulcers and damage to the eyes.² Worldwide in 2012 and 2013 diabetes resulted in 1.5 to 5.1 million deaths per year, making it the 8th leading cause of death. Diabetes overall at least doubles the risk of death. The number of people with diabetes is expected to rise to 592 million by 2035. The economic costs of diabetes globally were estimated in 2013 at \$548 billion and in the United States in 2012 \$245 billion. Globally, as of 2013, an estimated 382 million people have diabetes worldwide, with type 2 diabetes making up

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about 90% of the cases. This is equal to 8.3% of the adults' population, with equal rates in both women and men. [3] [4] 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: In case of type 1 Diabetes mellitus, results from the body's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown.⁵ Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic as the majority of type 1 diabetes is of the immune-mediated. T-cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin.⁵ It causes approximately 10% of diabetes mellitus cases in North America and Europe. 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. Type 1 diabetes can affect children or adults, but was traditionally termed "juvenile diabetes" because a majority of these diabetes cases were in children⁶. Brittle" diabetes, also known as unstable diabetes or labile diabetes is a term that was traditionally used to describe the dramatic and recurrent swings in glucose levels, often occurring for no apparent reason in insulin-dependent diabetes. This term, however, has no biologic basis and should not be used. [7] Another type is type 2 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 primary cause is excessive body weight and not enough exercise.⁸

A number 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 thirty), lack of physical activity, poor diet, stress, and urbanization. [11] Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific

Islanders. Those who are not obese often have a high waist–hip ratio.⁹

Dietary factors also influence the risk of developing type 2 diabetes. Consumption of sugar-sweetened drinks in excess is associated with an increased risk. The type of fats in the diet is also important, with saturated fats and trans fatty acids increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk.²⁹ Eating lots of white rice appears to also play a role in increasing risk. A lack of exercise is believed to cause 7% of cases. [10]

Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop a high blood glucose level. Gestational diabetes usually resolves after the birth of the baby.¹¹



The classic symptoms of untreated diabetes are weight loss, polyuria (frequent urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly within weeks or months in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.^{12,13}

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 blurry 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. A number of skin rashes that can occur in

diabetes are collectively known as diabetic dermadromes.¹⁴

Diabetic emergencies

People usually with type 1 diabetes may also experience episodes of diabetic ketoacidosis, a type of metabolic problems characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. A rare but equally severe possibility is hyperosmolar nonketotic state, which is more common in type 2 diabetes and is mainly the result of dehydration.¹⁵

All forms of diabetes increase the risk of long-term complications. These typically develop after many years like 10–20 years, but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in diabetics are due to coronary artery disease. Other "macrovascular" diseases are stroke, and peripheral vascular disease.¹⁶

The primary microvascular complications of diabetes 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 potentially blindness. 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 transplant. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes.¹⁷

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 wasting and weakness. There is a link between cognitive deficit and diabetes. Compared to those without diabetes, those with the disease have a 1.2 to 1.5-fold greater rate of decline in cognitive function.¹⁸

Comparison of type 1 and 2 diabetes

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%

Gestational diabetes

Gestational diabetes mellitus (GDM) 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. However, after pregnancy approximately 5–10% of women with gestational diabetes are found to have diabetes mellitus, most commonly type 2. Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy.¹⁹

Gestational diabetes occurs in women who have never had diabetes. This is not a disease, but rather a temporary condition in pregnancy in which the mother's hormonal system cannot maintain normal blood sugar levels. In the United States, it is annually diagnosed in about 4% of all pregnancies about 135,000 pregnancies. It is the most common pregnancy problem. Most women with gestational diabetes have healthy babies. If blood sugar levels can be kept within a safe range, the risks to mother and baby are about the same as for a woman without it. Gestational diabetes rarely has symptoms. In rare cases, high blood sugar levels may cause increased urination and excessive thirst.²⁰

The exact cause of gestational diabetes is unknown. Weight gain, hormonal changes, and hormones released from the placenta which block the action of insulin can cause insulin resistance. Insulin is a hormone responsible for removing glucose from the bloodstream. When insulin cannot do its job, blood sugar or glucose levels rise. When they rise high enough, gestational diabetes is diagnosed.²¹

The risk factors for gestational diabetes are as follows: Sibling or parent with diabetes, African American, Native American, Asian, Hispanic, or Pacific Islander, Over 25 years old, overweight, History of gestational diabetes, History of giving birth to multiples, a baby over 9 pounds or a baby with a birth defect, History of an unexplained miscarriage or stillbirth, Glucose in urine & Prediabetes. In case of high risk mother glucose level must be checked at the first antenatal visit and again between 24-28 weeks of pregnancy. Usually Oral Glucose tolerance test is done to check the glucose status. In case of oral Glucose tolerance test, blood sugar is checked before the test and 2 hours after 75gram glucose drink. Mother should be asked to remain fast for 8 hours prior to the test.²²

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 cardiac and central nervous system anomalies, and skeletal muscle malformations. Gestational diabetes is usually diagnosed later in pregnancy. The baby's body is formed, so there is not a high risk for developmental birth defects. Increased fetal insulin may inhibit fetal surfactant production and cause respiratory distress syndrome. Hyperbilirubinemia may result from red blood cell destruction. In severe cases, perinatal death may occur, most commonly as a result of poor placental perfusion due to vascular impairment. Labor induction may be indicated with decreased placental function. A Caesarean section may be performed if there is marked fetal distress or an increased risk of injury associated with macrosomia, such as shoulder dystocia. In case of mother risks are as follows: High blood pressure, increased chance for cesarean section, increased risk for Type 2 diabetes, increased risk for gestational diabetes in future pregnancies.²³

Treatment plan of Gestational Diabetes should be : Meal plan with nutritional counseling if possible, moderate exercise ,self-monitoring of blood sugar levels with a blood glucose meter, insulin if needed, regular blood pressure and urine protein testing, monitoring for urine ketones if needed ,Ultrasounds and non-stress tests may be used to monitor fetal well-being and growth, Kick counts to check the baby's activity, Gestational diabetes will most likely go away after delivery unless it has uncovered preexisting diabetes. Mother with gestational diabetes should be asked to return about six weeks after delivery to evaluate blood sugar levels.²⁴

Pathophysiology: The body obtains glucose from three main places: the intestinal absorption of food, the breakdown of glycogen, the storage form of glucose found in the liver, and gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body. Insulin plays a critical role in balancing glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen.²⁵

Insulin is released into the blood by beta cells (β -cells), found in the islets of Langerhans in the 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 for 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 in the opposite manner to insulin. If the amount of insulin available is insufficient, if cells respond poorly to the effects of insulin, insulin insensitivity or insulin resistance, or if the insulin itself is defective, then glucose will not be absorbed properly by the body cells that require it, and it will not be 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 acidosis. When the glucose concentration in the blood remains high over time, the kidneys will reach a threshold of reabsorption, and glucose will be excreted in the urine (glycosuria). 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 will be replaced osmotically from water held in body cells and other body compartments, causing dehydration and increased thirst (polydipsia).²⁶

Prevention: There is no known preventive measure for type 1 diabetes. Type 2 diabetes can often be prevented by a person being a normal body weight, physical exercise, and following a healthy diet. Dietary changes known to be effective in helping to prevent diabetes include a diet rich in whole grains and fiber, and choosing good fats, such as 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 in the prevention of diabetes. Active smoking is also associated with an increased risk of diabetes, so smoking cessation can be an important preventive measure as well.²⁷

Diagnosis: Glycated hemoglobin and Glucose tolerance test

Condition	WHO diabetes diagnostic criteria ^{28,29}		
	2 hour glucose	Fasting glucose	HbA _{1c}
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	%
Normal	<7.8 (<140)	<6.1 (<110)	<6.0
Impaired fasting glycaemia	<7.8 (<140)	> 6.1(>110) & <7.0(<126)	6.0–6.4
Impaired glucose tolerance	>7.8 (>140)	<7.0 (<126)	6.0–6.4
Diabetes mellitus	>11.1 (>200)	>7.0 (e"126)	e"6.5

Management: Diabetes mellitus is a chronic disease, for which there is no known cure except in very specific situations. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible, without causing hypoglycemia. This can usually be accomplished with diet, exercise, and use of appropriate medications, insulin in the case of type 1 diabetes; oral medications, as well as possibly insulin, in type 2 diabetes. Learning about the disease and actively participating in the treatment is vital for people with diabetes, since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar levels. The goal of treatment is an HbA_{1c} level of 6.5%, but should not be lower than that, and may be set higher. Attention is also paid to other health problems that may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise. Specialized is widely used to reduce the risk of ulceration, or re-ulceration, in at-risk diabetic feet. Evidence for the efficacy of this remains equivocal, however.²⁸

Lifestyle: People with diabetes can benefit from education about the disease and treatment, good nutrition to achieve a normal body weight, and sensible exercise, with the goal of keeping both short-term and long-term blood glucose levels within acceptable bounds. In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure.²⁹

Anti-diabetic medication: Metformin is generally recommended as a first line treatment for type 2 diabetes, as there is good evidence that it decreases mortality. Routine use of aspirin, however, has not been found to improve outcomes in uncomplicated diabetes. Angiotensin converting enzyme inhibitors (ACEIs)

improve outcomes in those with DM while the similar medications angiotensin receptor blockers (ARBs) do not. Type 1 diabetes is typically treated with a combination of regular and NPH insulin, or synthetic insulin analogs. When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially, while continuing oral medications. Doses of insulin are then increased to effect. In those with diabetes some recommend blood pressure levels below 120/80 mmHg; however, evidence only supports less than or equal to somewhere between 140/90 mmHg to 160/100 mmHg.³⁰

Research: Inhaled insulin has been developed. The original products were withdrawn due to side effects. Afrezza, under development by pharmaceuticals company Mankind Corporation, was approved by the FDA for general sale in June, 2014. There are several advantages of inhaled insulin: they are convenient and easy to use and provide a useful alternative therapy for patients who cannot use intravenous insulin.³¹

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