



DIABETES MELLITUS: AN OVERVIEW

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ABSTRACT

Diabetes mellitus is an endocrinological and/or metabolic disorder marked by elevated levels of sugar in the blood. It is a silent killer disease and affects millions of peoples in the world. It is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by ineffectiveness of the insulin produced. High blood glucose levels are symptomatic of diabetes mellitus as a consequence of inadequate pancreatic insulin secretion or poor insulin-directed mobilization of glucose by target cells. It is the second leading cause of blindness and renal disease worldwide. Impaired insulin secretion and increased insulin resistance, the main pathophysiological features of type 2 diabetes. The goal of diabetes treatment is to secure a quality of life (QOL) and lifespan comparable to those of healthy people, and a prerequisite for this is the prevention of onset and progression of vascular complications. This article focuses on the causes, types, factors affecting DM, incidences, preventive measures, treatment and future perspectives of the acute and chronic complications of diabetes directly associated with hypoglycemia and severe metabolic disturbances.

KEYWORDS: Diabetes mellitus, endocrinology, insulin, hypoglycemia, metabolism.

INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects of insulin secretion and increased cellular resistance to insulin. Chronic hyperglycemia and other metabolic disturbances of DM lead to long-term tissue and organ damage as well as dysfunction involving the eyes, kidneys and nervous and vascular system.^[1,2,3]

CLASSIFICATION OF DIABETES MELLITUS

1. β - cell destruction (Type 1 diabetes - IDDM)
 - Immune mediated
 - Idiopathy
2. Insulin resistance (Type 2 diabetes - NIDDM)
3. Genetic defects of β - cell function
 - Glucokinase
 - Hepatocyte nuclear transcription factor – 4 α
 - Insulin promoter factor
 - Mitochondrial DNA
 - Proinsulin or insulin conversion
4. Genetic defects in insulin processing or insulin actions defects in
 - Proinsulin conversion.
 - Insulin gene mutation
 - Insulin receptor mutation
5. Exocrine pancreatic defects
6. Endocrinopathy

- Acromegaly
- Cushing syndrome
- Hyperthyroidism
- Pheochromocytoma
- Glucocanoma
- 7. Infections
 - Cytomegalovirus
 - Coxsackievirus
- 8. Drugs
 - Glucocorticoid
 - Thyroid hormone
 - Thiazides
 - Phenytoins
- 9. Genetic syndrome associated with diabetes
 - Down's syndrome
 - Klinefelter's syndrome
 - Turner's syndrome
- 10. Gestational diabetes mellitus^[36,37]

Signs and Symptoms of diabetes?

The classic symptoms of untreated diabetes are weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger).^[7] Symptoms may develop rapidly (weeks or months) in type 1 DM, while they usually develop much more slowly and may be subtle or absent in type 2 DM.

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.^[8]

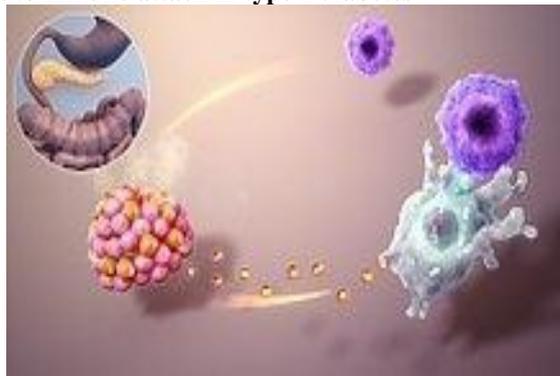
CAUSES

Diabetes mellitus is classified into four broad categories: type 1, type 2, gestational diabetes, and "other specific types".^[5] The "other specific types" are a collection of a few dozen individual causes.^[5] Diabetes is a more variable disease than once thought and people may have combinations of forms.^[9] The term "diabetes", without qualification, usually refers to diabetes mellitus.

Diabetes mellitus type 1

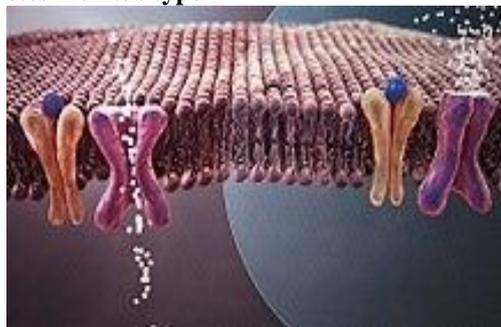
- Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the pancreatic islets, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, in which a T cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin.^[10] 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 children.
- "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.^[11] Still, type 1 diabetes can be accompanied by irregular and unpredictable high blood sugar levels, frequently with ketosis, and sometimes with serious low blood sugar levels. Other complications include an impaired counter regulatory response to low blood sugar, infection, gastroparesis (which leads to erratic absorption of dietary carbohydrates), and endocrinopathies (e.g., Addison's disease).^[11] These phenomena are believed to occur no more frequently than in 1% to 2% of persons with type 1 diabetes.^[12]

Autoimmune attack in type 1 diabetes



- Type 1 diabetes is partly inherited, with multiple genes, including certain HLA genotypes, known to influence the risk of diabetes. In genetically susceptible people, the onset of diabetes can be triggered by one or more environmental factors,^[13] such as a viral infection or diet. Several viruses have been implicated, but to date there is no stringent evidence to support this hypothesis in humans.^{[13][14]} Among dietary factors, data suggest that gliadin (a protein present in gluten) may play a role in the development of type 1 diabetes, but the mechanism is not fully understood.^{[15][16]}

Diabetes mellitus type 2



Reduced insulin secretion and absorption leads to high glucose content in the blood

- Type 2 DM is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion.^[5] 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. Type 2 DM is the most common type of diabetes mellitus.^[4]
- In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, high blood sugar can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce the liver's glucose production.
- Type 2 DM is primarily due to lifestyle factors and genetics.^[17] A number of lifestyle factors are known to be important to the development of type 2 DM, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet,

stress, and urbanization.^[6] 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.^[5] Even those who are not obese often have a high waist–hip ratio.^[5]

is associated with an increase risk^[18,19] the type of fat in the diet is also important, with saturated fats and trans fat increase risk and polyunsaturated and monounsaturated fat decreased the risk.^[17] eating lots of white rice also may increase the risk of diabetes.^[20] A lack of physical activity is believed to cause 7% of cases.^[21]

Dietary factor also influence the risk of developing type 2 DM. Consumption of sugar sweetend drinks in excess

DIAGNOSIS

WHO diabetes diagnostic criteria^[29, 30]

Condition	2 hour glucose	Fasting glucose	HbA1c	
			mmol/mol	DCCT%
Unit	mmol/L(mg/dl)	mmol/L(mg/dl)		
Normal	<7.8(<140)	<6.1(<110)	<42	<6.0
Impaired Fasting glycaemia	<7.8(<140)	>6.1(>110) and <7.0(<126)	42-46	6.0-6.4
Impaired glucose 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.^[22]

- 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 g oral glucose load as in a glucose tolerance test.
- 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 %).^[23]

from any cause.^[28]

A positive result, in the absence of unequivocal high blood sugar, should be confirmed by a repeat of any of the above methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test.^[24] According to the current definition, two fasting glucose measurements above 126 mg/dl (7.0 mmol/l) is considered diagnostic for diabetes mellitus.

Per the World Health Organization people with fasting glucose levels from 6.1 to 6.9 mmol/l (110 to 125 mg/dl) are considered to have impaired fasting glucose.^[25] people with plasma glucose at or above 7.8 mmol/l (140 mg/dl), but not over 11.1 mmol/l (200 mg/dl), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two prediabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus, as well as cardiovascular disease.^[26] The American Diabetes Association since 2003 uses a slightly different range for impaired fasting glucose of 5.6 to 6.9 mmol/l (100 to 125 mg/dl).^[27]

Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death

TREATMENT OF DIABETES^[31,32,33,34,35]

ALLOPATHIC DRUGS	HERBAL DRUGS
<p>Diabetes Medications Many different types of medications are available to help lower blood sugar levels in people with type 2 diabetes. Each type works in a different way. It is very common to combine two or more types to get the best effect with fewest side effects.</p> <p>Sulfonylurea These drugs stimulate the pancreas to make more insulin.</p> <p>Biguanides These agents decrease the amount of glucose produced by the liver.</p> <p>Alpha-glucosidase inhibitors These agents slow absorption of the starches and glucose.</p> <p>Thiazolidinediones These agents increase sensitivity to insulin.</p> <p>Meglitinides: These agents stimulate the pancreas to make more insulin.</p> <p>D-phenylalanine derivatives These agents stimulate the pancreas to produce more insulin more quickly.</p> <p>Amylin synthetic derivatives Amylin is a naturally occurring hormone secreted by the pancreas along with insulin. An amylin derivative, such as pramlintide (Symlin), is indicated when blood sugar control is not achieved despite optimal insulin therapy.</p> <p>Incretin mimetics Exenatide (Byetta) was the first incretin mimetic agent approved in the United States. It is indicated for diabetes mellitus type 2 in addition to metformin or a sulfonylurea when these agents have not attained blood sugar level control alone.</p> <p>Insulins Synthetic human insulin is now the only type of insulin. It is less likely to cause allergic reactions than animal-derived varieties of insulin used in the past. Different types of insulin are available and categorized according to their times of action onset and duration. Examples of rapid-acting insulins – Regular insulin (Humulin R, Novolin R) Insulin lispro (Humalog) Insulin aspart (Novolog) Insulin glulisine (Apidra) Prompt insulin zinc (Semilente, slightly slower acting)</p>	<p>Herbs for diabetes treatment are not new. Since ancient times, plants and plant extracts were used to combat diabetes. Here are some herbs that have been confirmed by scientific investigation, which appear to be most effective, relatively non-toxic and have substantial documentation of efficiency.</p> <p>Cinnamon Cinnamon is the inner bark and has insulin-like properties, which able to decrease blood glucose levels as well as triglycerides and cholesterol, all of which are important especially for type 2 diabetes patients.</p> <p><i>Pterocarpus marsupium</i> It demonstrates to reduce the glucose absorption from the gastrointestinal tract, and improve insulin and pro-insulin levels. It also effective in β cell regeneration.</p> <p>Bitter melon (<i>Momordica charantia</i>) It lower blood glucose concentrations and acts on both the pancreas and in nonpancreatic cells, such as muscle cells. These include charantin and an insulin-like protein referred to as polypeptide-P, or plant insulin.</p> <p><i>Gynema Sylvestre</i> It improves the ability of insulin to lower blood sugar in both type I and type II diabetes. This herb is showing up in more and more over the counter weight loss products and blood sugar balancing formulas.</p> <p>Onion It consists of an active ingredient called APDS (allyl propyl disulphide) and it block the breakdown of insulin by the liver and possibly to stimulate insulin production by the pancreas, thus increasing the amount of insulin and reducing sugar levels in the blood.</p> <p>Fenugreek (<i>Trigonella foenum-graecum</i>) The fiber-rich fraction of fenugreek seeds can lower blood sugar levels in people with diabetes, and to a lesser extent, for lowering blood cholesterol, weight control.</p> <p>Blueberry (<i>Vaccinium myrtillus</i>) Blueberry is a natural method of controlling or lowering blood sugar levels in the blood. It is a good astringent and helps relieve inflammation of the kidney, bladder and prostate.</p> <p>Asian Ginseng It has been shown to enhance the release of insulin from the pancreas and to increase the number of insulin receptors. It also has a direct blood sugar-lowering effect and improves psycho-physiological performance.</p> <p>Ginkgo Biloba The extract may prove useful for prevention and treatment of early-stage diabetic neuropathy. It has also been shown to prevent diabetic retinopathy.</p>

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