Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Review Article

AN OVERVIEW ON DIABETIS MELLITUS

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ABSTRACT

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Diabetes is a more variable disease than once thought and people may have combinations of forms. There is no known preventive measure for type 1 diabetes. Type 2 diabetes, which accounts for 85-90% of all cases - can often be prevented or delayed by maintaining a normal body weight, engaging in physical exercise, and consuming a healthful diet. Type 1 diabetes can only be treated with insulin, typically with a combination of regular and NPH insulin, or synthetic insulin analogs. Metformin is generally recommended as a first line treatment for type 2 diabetes, as there is good evidence that it decreases mortality.

Keywords: *metabolic disease, hyperglycemia, insulin, neutral protamine hagedorn (NPH) insulin, Metformin*

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both Normally our body breaks down the sugars and carbohydrates we eat into a special sugar called glucose. Glucose fuels the cells in our body. But the cells need insulin, a hormone, in our bloodstream in order to take in the glucose and use it for energy. With diabetes mellitus, either our body doesn't make enough insulin, it can't use the insulin it does produce, or a combination of both.

Since the cells can't take in the glucose, it builds up in our blood. High levels of blood glucose can damage the tiny blood vessels in our kidneys, heart, eyes, or nervous system. That's why diabetes - especially if left untreated - can eventually cause heart disease, stroke, kidney disease, blindness, and nerve damage to nerves in the feet Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced(1). There are three main types of diabetes mellitus:

Type 1 diabetes mellitus

Results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes"(2). The cause is unknown. However, it is believed to involve a combination of genetic and environmental factors. The underlying mechanism involves an autoimmune destruction of the insulin-producing beta cells in the pancreas . Diabetes is diagnosed by testing the level of sugar or A1C in the blood. There is no known way to prevent type 1 diabetes. Treatment with insulin is typically required for survival. Insulin therapy is usually given by injection just under the skin but can also be delivered by an insulin pump. A diabetic diet and exercise are an important part of management. Untreated, diabetes can cause

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many complications. Type 1 diabetes makes up an estimated 5–10% of all diabetes cases.

Type 2 diabetes mellitus

Begins with insulin resistance, a condition in which cells fail to respond to insulin properly(2). 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. Type 2 diabetes primarily occurs as a result of obesity and not enough exercise. Some people are more genetically at risk than others. Type 2 diabetes makes up about 90% of cases of diabetes, with the other 10% due primarily to diabetes mellitus type 1 and gestational diabetes. In diabetes mellitus type 1 there is an absolute lack of insulin due to breakdown of islet cells in the pancreas.

Gestational diabetes

Is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar levels(2). Gestational diabetes mellitus resembles type 2 DM in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy. Management may include dietary changes, blood glucose monitoring, and in some cases, insulin may be required.Now a days, natural products have been the main stay of treatment of various disorder on humans beings due to side effect of drugs. Numerous Ayurvedic herbal drugs have been indicated for their effectiveness in treatment of diabetes and related disorders. The advantages that herbal drug possess are numerous and multifaceted. An ever increasing number of patients suffering from diabetes around the world have shifted the research focus to find safe and effective herbal alternatives.

SYMPTOMS

Diabetes mellitus shows many types of symptoms. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome.

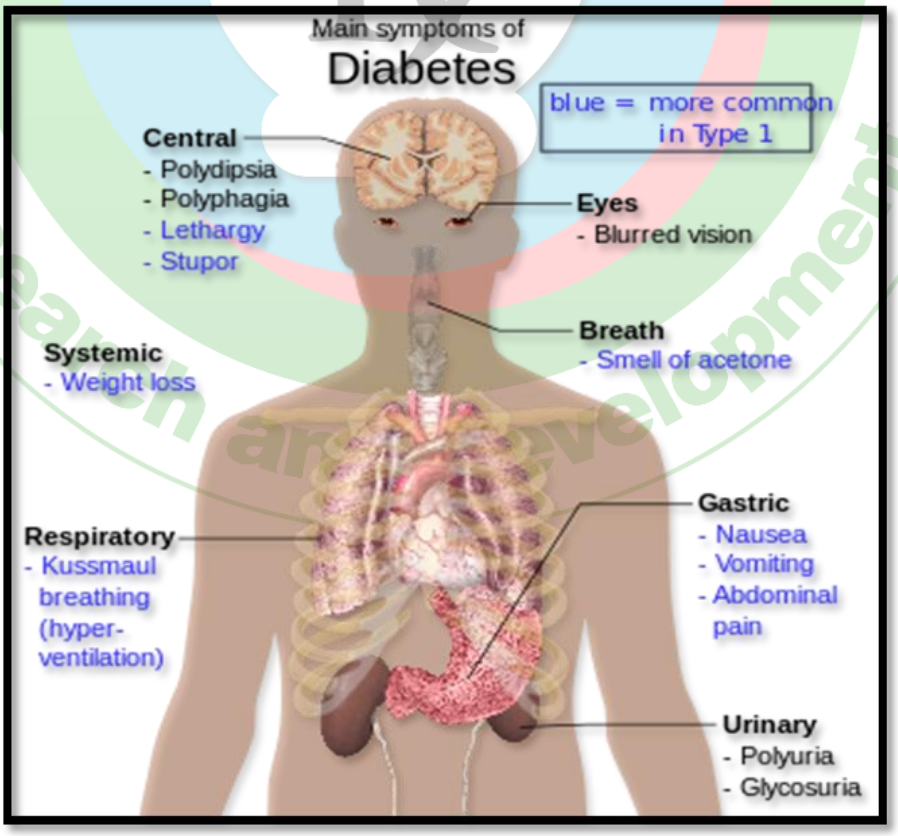

Fig.1 Overview of the most significant symptoms of diabetes

Acute symptoms

Low blood sugar is common in persons with type 1 and type 2 Diabetes mellitus. Most cases are mild and are not considered medical emergencies. Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious issues such as confusion, changes in behaviour such as aggressiveness, seizures, unconsciousness and (rarely) permanent brain damage or death in severe cases(3). Moderate hypoglycaemia may easily be mistaken for drunkenness, rapid breathing and sweating, cold, pale skin are characteristic of hypoglycemia but not definitive. Mild to moderate cases are self-treated by eating or drinking something high in sugar. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon..

CAUSES

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

Type 1 Diabetes Mellitus

Genetics

Type 1 diabetes is a disease that involves many genes. The risk of a child developing type 1 diabetes is about 5% if the father has it, about 8% if a sibling has it, and about 3% if the mother has it. If one identical twin is affected there is about a 50% chance the other will also be affected.[18] Some studies of heritability has estimated it at 80 to 86%.

More than 50 genes are associated with type 1 diabetes. Depending on locus or combination of loci, they can be dominant, recessive, or somewhere in between. The strongest gene, *IDDM1*, is located in the MHC Class II region on chromosome 6, at staining region 6p21. Certain variants of this gene increase the risk for decreased histocompatibility characteristic of type 1.such variants include of DRB1 0401, DRB1 0402, DRB1 0405, DQA 0301, DQB1 0302 and DQB1 0201, which are common in North Americans of European ancestry and in Europeans. Some variants also appear to be protective.

Environmental

Environmental factors can influence expression of type 1. For identical twins, when one twin has type 1 diabetes, the other twin only has it 30%-50% of the time. Thus for 50%-70% of identical twins where one has the disease, the other will not, despite having exactly the same genome; this suggests that environmental factors, in addition to genetic factors, can influence the disease's prevalence. Other indications of environmental influence include the presence of a 10-fold difference in occurrence among Caucasians living in different areas of Europe, and that people tend to acquire the rate of disease of their particular destination country.

Virus

One theory proposes that type 1 diabetes is a virus-triggered autoimmune response in which the immune system attacks virus-infected cells along with the beta cells in the pancreas. Several viruses have been implicated, including enteroviruses (especially coxsackievirusB), cytomegalovirus, Epstein–Barrvirus, mumps virus, rubellavirus and rotavirus, but to date there is no stringent evidence to support this hypothesis in humans. A 2011 systematic review and meta-analysis showed an association between enterovirus infections and type 1 diabetes, but other studies have shown that, rather than triggering an autoimmune process, enterovirus infections, as coxsackievirus B, could protect against onset and development of type 1 diabetes.

Chemicals and drugs

Some chemicals and drugs selectively destroy pancreatic cells. Pyrinuron (Vacor), a rodenticide introduced in the United States in 1976, selectively destroys pancreatic beta cells, resulting in type 1 diabetes after accidental poisoning. Pyrinuron was withdrawn from the U.S. market in 1979 and it is not approved by the Environmental Protection Agency for use in the U.S Streptozotocin (Zanosar),

an antineoplastic agent, is selectively toxic to the beta cells of the pancreatic islets. It is used in research for inducing type 1 diabetes on rodents and for treating metastatic cancer of the pancreatic islet cells in patients whose cancer cannot be removed by surgery. Other pancreatic problems, including trauma, pancreatitis, or tumors (either malignant or benign) can also lead to loss of insulin production.

Gluten

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. Increased intestinal permeability caused by gluten and the subsequent loss of intestinal barrier function, which allows the passage of pro-inflammatory substances into the blood, may induce the autoimmune response in genetically predisposed individuals to type 1 diabetes. Early introduction of gluten-containing cereals in the diet increases the risk of developing islet cell autoantibodies, which are responsible for the destruction of the insulin-producing beta cells in the pancreas.

Type 2 diabetes mellitus

Type 2 Diabetes Mellitus is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. 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.

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 due primarily to lifestyle factors and genetics 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. 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. Even those who are not obese often have a high waist–hip ratio(1).

Dietary factors also influence the risk of developing type 2 DM. 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 Eating lots of white rice also may increase the risk of diabetes. A lack of exercise is believed to cause 7% of cases.[43]

The development of type 2 diabetes is caused by a combination of lifestyle and genetic factors. While some of these factors are under personal control, such as diet and obesity, other factors are not, such as increasing age, female gender, and genetics. A lack of sleep has been linked to type 2 diabetes. This is believed to act through its effect on metabolismThe nutritional status of a mother during fetal development may also play a role, with one proposed mechanism being that of altered DNA methylation. The intestinal bacteriæ Prevotella copri and Bacteroides vulgatus have been connected with type 2 diabetes.

Lifestyle

Lifestyle factors are important to the development of type 2 diabetes, including obesity and being overweight (defined by a body mass index of greater than 25), lack of physical activity, poor diet, stress, and urbanization. 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 cases in Pima Indians and Pacific Islanders. Among those who are not obese, a high waist–hip ratio is often present. Smoking appears to increase the risk of type 2 diabetes mellitus.

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are important, with saturated fats and trans fatty acids increasing the risk, and polyunsaturated and monounsaturated fat decreasing the risk Eating a lot of white rice appears to play a role in increasing risk. A lack of exercise is believed to cause 7% of cases. Persistent organic pollutants may play a role.

Genetics

Most cases of diabetes involve many genes, with each being a small contributor to an increased probability of becoming a type 2 diabetic. If one identical twin has diabetes, the chance of the other developing diabetes within his lifetime is greater than 90%, while the rate for nonidentical siblings is 25–50%. As of 2011, more than 36 genes had been found that contribute to the risk of type 2 diabetes. All of these genes together still only account for 10% of the total heritable component of the disease. The TCF7L2 allele, for example, increases the risk of developing diabetes by 1.5 times and is the greatest risk of the common genetic variants. Most of the genes linked to diabetes are involved in beta cell functions.

There are a number of rare cases of diabetes that arise due to an abnormality in a single gene (known as monogenic forms of diabetes or "other specific types of diabetes").These include maturity onset diabetes of the young (MODY), Donohue syndrome, and Rabson-Mendenhall syndrome, among others. Maturity onset diabetes of the young constitute 1–5% of all cases of diabetes in young people.

Medical conditions

There are a number of medications and other health problems that can predispose to diabetes, Some of the medication include: glucocorticoids, thiazides, betablockers, a typical antipsychotics, and statins. Those who have previously had gestational diabetes are at a higher risk of developing type 2 diabetes. Other health problems that are associated include: acromegaly, Cushing'ssyndrome, hyperthyroidism, pheochromocytoma and certain cancers such as glucagonomas. Testosterone deficiency is also associated with type 2 diabetes.

Gestational diabetes

Gestational diabetes mellitus (GDM) resembles type 2 DM in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It is caused by not enough insulin in the setting of insulin resistance. 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. 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 respiratory distress syndrome. A high blood bilirubin level 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 dystoci

PATHOPHYSIOLOGY

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the insulin like growth factor (IGF-1). Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus.

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(1).

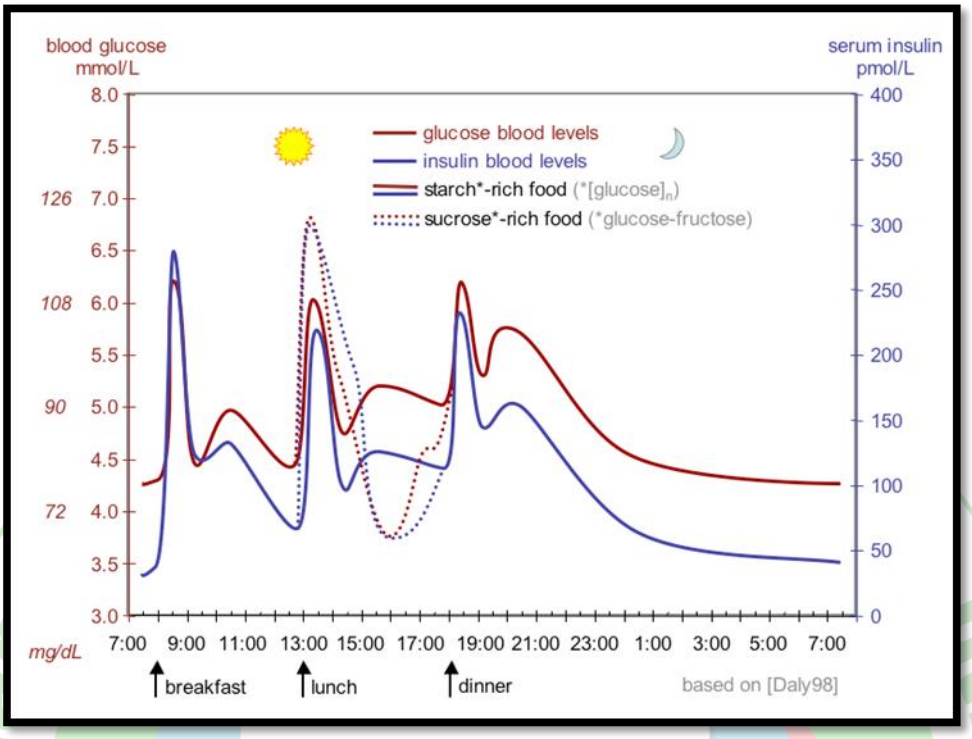

Fig.4.1 The fluctuation of blood sugar (red) and the sugar-lowering hormone insulin (blue) in humans during the course of a day with three meals — one of the effects of a sugar-rich vs a starch-rich meal is highlighted.

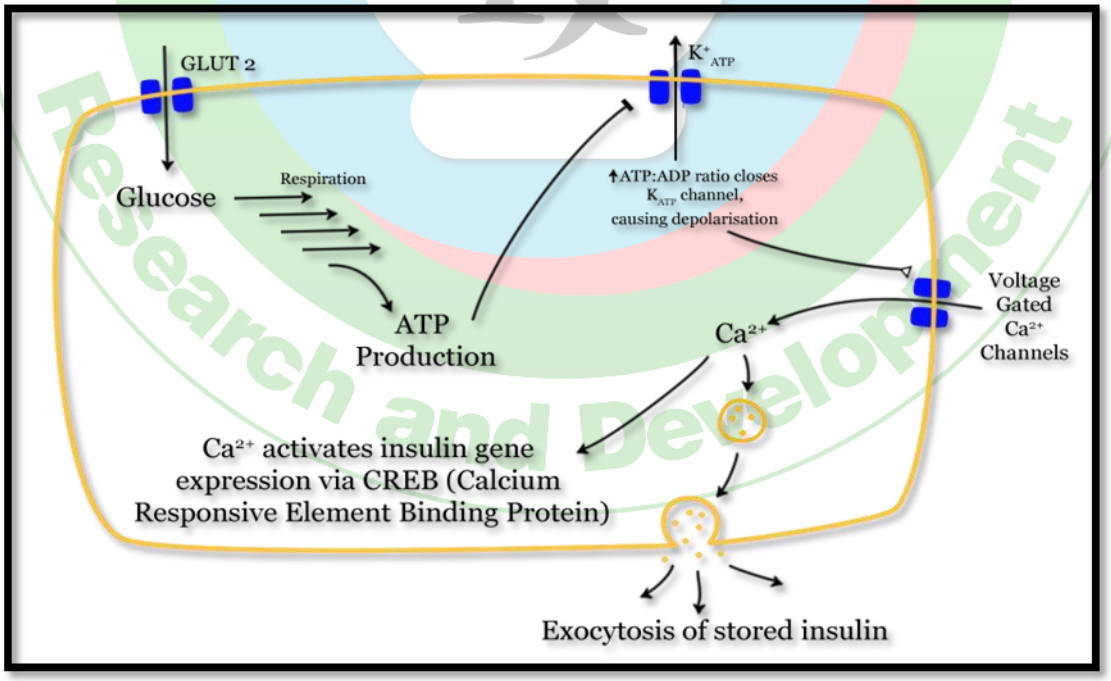

Fig.4.2 Mechanism of insulin release in normal pancreatic beta cells — insulin production is more or less constant within the beta cells. Its release is triggered by food, chiefly food containing absorbable glucose.

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(1).

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).

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.

The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease(7) and about 75% of deaths in diabetics are due to coronary artery disease. Other "macrovascular" diseases are stroke, and peripheral vascular disease.

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 . 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. 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. Being diabetic, especially when on insulin increases the risk of falls in older people(8).

Type 1 Diabetes

Complications of poorly managed type 1 diabetes mellitus may include cardiovascular disease, diabetic neuropathy, and diabetic retinopathy, among others. However, cardiovascular disease as well as neuropathy may have an autoimmune basis, as well. Women with type 1 DM have a 40% higher risk of death as compared to men with type 1 DM. The life expectancy of an individual with type 1 diabetes is 11 years less for men and 13 years less for women.

Diabetic retinopathy

It is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and blindness

Urinary tract infection

People with diabetes show an increased rate of urinary tract infection. The reason is bladder dysfunction that is more common in diabetics than in non-diabetics due to diabetic nephropathy. When present, nephropathy can cause a decrease in bladder sensation, which in turn, can cause increased residual urine, a risk factor for urinary tract infections.

Sexual dysfunction

Sexual dysfunction in diabetics is often a result of physical factors such as nerve damage and/or poor circulation, and psychological factors such as stress and/or depression caused by the demands of the disease.

Males

The most common sexual issues in diabetic males are problems with erections and ejaculation: "With diabetes, blood vessels supplying the penis's erectile tissue can get hard and narrow, preventing the adequate blood supply needed for a firm erection. The nerve damage caused by poor blood glucose control can also cause ejaculate to go into the bladder instead of through the penis during ejaculation, called retrograde ejaculation. When this happens, semen leaves the body in the urine." Another cause for erectile dysfunction are the reactive oxygen species created as a result of the disease. Antioxidants can be used to help combat this.

Females

While there is less material on the correlation between diabetes and female sexual dysfunction than male sexual dysfunction, studies have shown there to be a significant prevalence of sexual problems in diabetic women. Common problems include reduced sensation in the genitals, dryness, difficulty/inability to orgasm, pain during sex, and decreased libido In some cases diabetes has been shown to decrease oestrogen levels in females, which can affect vaginal lubrication.

Oral contraceptives can be taken by diabetics. Sometimes, contraceptive pills can cause a blood sugar imbalance, but this usually can be corrected by a dosage change. As with any medication, side effects should be taken into account and monitored to prevent serious complications with diabetes.

Women with type 1 diabetes show a higher than normal rate of polycystic ovarian syndrome (PCOS). The reason may be that the ovaries are exposed to high insulin concentrations since women with type 1 diabetes can have frequent hyperglycemia.

Type 2 diabetes

Diabetic coma

A diabetic coma could happen when your blood sugar gets too high -- 600 milligrams per deciliter (mg/dL) or more -- causing you to become very dehydrated.

It usually affects people with type 2 diabetes that isn't well-controlled. It's common among those who are elderly, chronically ill, and disabled. Doctors aren't sure why, but they think they these people may not realize they're thirsty or may not be able to get enough to drink.

This is a serious condition, and if it isn't spotted soon and treated quickly, it could be fatal.

Sleep problems

People who have diabetes often have poor sleep habits, including difficulty falling asleep or staying asleep. Some people with diabetes get too much sleep, while others have problems getting enough sleep. According to the National Sleep Foundation, 63% of American adults do not get enough sleep needed for good health, safety, and optimum performance.There are several causes of sleep problems for people with type 2 diabetes, including obstructive sleep apnea, pain or discomfort, restless legs syndrome, the need to go to the bathroom, and other problems associated with type 2 diabetes

Heart disease

Heart disease is common in people with diabetes. Data from the National Heart Association from 2012 shows 65% of people with diabetes will die from some sort of heart disease or stroke. In general, the risk of heart disease death and stroke are twice as high in people with diabetes.

While all people with diabetes have an increased chance of developing heart disease, the condition is more common in those with type 2 diabetes. In fact, heart disease is the number one cause of death among people with type 2 diabetes.

Stroke

Diabetes can also make it harder for your body to respond to a stroke. When your oxygen supply is cut off, other arteries can usually serve as a bypass. But if you have diabetes, those vessels may be hardened or clogged with plaque, a condition

known as atherosclerosis. This makes it harder for blood to get to your brain

It has also been associated with an increased risk of cognitive dysfunction and dementia through disease process such as Alzheimer's disease and vascular dementia. Other complications include acanthosis nigricans, sexual dysfunction, and frequent infections.

DIAGNOSIS

Diabetes mellitus is characterized by recurrent or persistent high blood sugar, and is diagnosed by demonstrating any one of the following:

Table.1: Diabetes mellitus is characterized by recurrent or persistent high blood sugar, and is diagnosed by demonstrating any one of the following

WHO diabetes diagnostic criteria				
Condition	2 hour glucose	Fasting glucose	HbA_{1c}	
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	mmol/mol	DCCT %
Normal	<7.8 (<140)	<6.1 (<110)	<42	<6.0
Impaired fasting glycaemia	<7.8 (<140)	≥6.1(≥110)&<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

- 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 %).

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(9). According to the current definition, two fasting glucose measurements above 126 mg/dl (7.0 mmol/l) is considered diagnostic for diabetes mellitus.

In 2009 an International Expert Committee that included representatives of the American Diabetes Association (ADA), the International Diabetes Federation (IDF), and the European Association for the Study of Diabetes (EASD) recommended that a threshold of ≥ 48 mmol/mol (≥ 6.5 DCCT %) should be used to diagnose diabetes. This recommendation was adopted by the American Diabetes Association in 2010. Positive tests should be repeated unless the person presents with typical symptoms and blood sugars >11.1 mmol/l (>200 mg/dl).

Threshold for diagnosis of diabetes is based on the relationship between results of glucose tolerance tests, fasting glucose or HbA_{1c} and complications such as retinal problems. A fasting or random blood sugar is preferred over the glucose tolerance test, as they are more convenient for people. HbA_{1c} has the advantages that fasting is not required and results are more stable but has the disadvantage that the test is more costly than measurement of blood glucose. It is estimated that 20% of people with diabetes in the United States do not realize that they have the disease.

TREATMENT

Prevention

There is no known preventive measure for type 1 diabetes(2). Type 2 diabetes, which accounts for 85-90% of all cases — can often be prevented or delayed by maintaining a normal body weight, engaging in physical exercise, and consuming a

healthful diet(2). Higher levels of physical activity (more than 90 minutes per day) reduce the risk of diabetes by 28%. 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. 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.

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, without causing low blood sugar. This can usually be accomplished with a healthy diet, exercise, weight loss, 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 important, since complications are far less common and less severe in people who have well-managed blood sugar levels(10). 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 negative effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise. Specialized footwear 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.

Lifestyle

People with diabetes can benefit from education about the disease and treatment, good nutrition to achieve a normal body weight, and 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 (11).

Medications

Medications used to treat diabetes do so by lowering blood sugar levels. There are a number of different classes of anti-diabetic medications. Some are available by mouth, such as metformin, while others are only available by injection such as GLP-1 agonists. Type 1 diabetes can only be treated with insulin, typically with a combination of regular and NPH insulin, or synthetic insulin analogs.

Metformin is generally recommended as a first line treatment for type 2 diabetes, as there is good evidence that it decreases mortality (12). It works by decreasing the liver's production of glucose. Several other groups of drugs, mostly given by mouth, may also decrease blood sugar in type II DM. These include agents that increase insulin release, agents that decrease absorption of sugar from the intestines, and agents that make the body more sensitive to insulin. When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially, while continuing oral medications (13). Doses of insulin are then increased to effect.

Since cardiovascular disease is a serious complication associated with diabetes, some have recommended blood pressure levels below 130/80 mmHg However, evidence supports less than or equal to somewhere between 140/90 mmHg to 160/100 mmHg; the only additional benefit found for blood pressure targets beneath this range was an isolated decrease in stroke risk, and this was accompanied by an increased risk of other serious adverse events. A 2016 review found potential harm to treating lower than 140

mmHg Among medications that lower blood pressure, angiotensin converting enzyme with DM while the similar medications angiotensin receptor blockers (ARBs) do not Aspirin is also recommended for people with cardiovascular problems, however routine use of aspirin has not been found to improve outcomes in uncomplicated diabetes.

Surgery

A pancreas transplant is occasionally considered for people with type 1 diabetes who have severe complications of their disease, including end stage kidney disease requiring kidney transplantation.

Weight loss surgery in those with obesity and type two diabetes is often an effective measure. Many are able to maintain normal blood sugar levels with little or no medications following surgery and long-term mortality is decreased (14). There however is some short-term mortality risk of less than 1% from the surgery. The body mass index cutoffs for when surgery is appropriate are not yet clear. It is recommended that this option be considered in those who are unable to get both their weight and blood sugar under control.

Support

In countries using a general practitioner system, such as the United Kingdom, care may take place mainly outside hospitals, with hospital-based specialist care used only in case of complications, difficult blood sugar control, or research projects. In other circumstances, general practitioners and specialists share care in a team approach. Home telehealth support can be an effective management technique (15).

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