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Review Article

DIABETES MELLITUS: AN OVERVIEW

Sunaina Sharma

Sanskar College of Pharmacy & Research, Ghaziabad, U.P., India

**Corresponding author: sunaina.sharma.6991@gmail.com*

ABSTRACT

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action or both. The condition itself introduces a need for patient's lifestyle adjustment to the disease and a number of everyday therapeutic and diagnostic restrictions. The main indication of diabetes mellitus is a hyperglycemia in blood which is due to inappropriate pancreatic insulin secretion or low insulin-directed fostering of glucose by target cells. It is silent killer disease and affects millions of people in the world. It is estimated that in 2010 there was globally 285 million people suffering from this disease. This number is estimated to increase to 430 million in the absence of better control or cure. Different types of diabetes mellitus, type 1, type 2, gestational diabetes and other types of diabetes mellitus are compared in terms of diagnostic criteria, etiology and genetics. As the disease progresses tissue or vascular damage ensures leading to severe diabetic complications such as retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration. Currently available pharmacotherapy for the treatment of diabetes mellitus includes insulin and hypoglycemic agents. These drugs act by increasing the secretion of insulin form pancreas or reducing plasma glucose concentrations by increasing glucose uptake and decreasing gluconeogenesis. Comobrid mental diseases can further negatively influence the course of diabetes. They are specially depression, anxiety disorders, eating disorders and cognitive disorders including dementia. Various herbal drugs have been also proved effective due to their beneficial contents in treatment of diabetes. This article focuses on the causes, types, diagnosis and treatment of diabetes.

Keywords: *Diabetes mellitus, Metabolic, Types, Causes, Diagnosis, Treatments*

1. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder when human body does not produce or properly uses insulin; a hormone that is required to convert sugar, starches and other food into energy. Absence or reduced insulin in turn leads to persistent abnormally high blood sugar and glucose in-tolerance. It is probably an oldest disease known to man. It is also referred as black-death from the 14th century [1].

In people with diabetes, blood sugar levels remain high. This may be due to insulin is not being produced at all, is not made at sufficient levels, or is not as effective as it should be. The most common forms of diabetes are, Type1 diabetes (5%); which is an autoimmune disorder, and Type 2 diabetes (95%); which is associated with obesity. Gestational diabetes is a form of diabetes that occurs in pregnancy, and other forms of diabetes are very rare and are caused by single gene mutation.

2. TYPES OF DIABETES

1. Type 1 diabetes
2. Type 2 diabetes
3. Gestational diabetes

Other types of diabetes are:

1. Diabetes LADA
2. Diabetes MODY
3. Double diabetes
4. Brittle diabetes
5. Diabetes Insipidus
6. Neonatal diabetes mellitus
7. Mixed pathologies in T1DM with obesity and insulin resistance

2.1. Type 1 Diabetes

It is a chronic auto-immune disease associated with selective destruction of insulin producing pancreatic β-cells [2]. When there is transplantation of pancreas from twin donors to chronic diabetic twin recipients in the absence of immune suppression is complicated due to elevated heterogenecity of pancreatic lesions of β-cells which are rapidly annihilated, and then there is development of massive insulitis by using infiltrating T lymphocytes which measures an amnestic autoimmune reaction [1]. Type 1 diabetes is often referred to as insulin- dependent (IDDM) or juvenile-onset diabetes.

2.1.1. Symptoms

Frequent urination, thirst, weight loss, extreme fatigue, acetone breath, nausea and vomiting, blurred vision and itchiness in the genital area are the common symptoms of diabetes.

2.2. Type 2 Diabetes

Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretary defect on the background of insulin resistance people with this type of diabetes frequently

are resistant to the action of insulin [3]. Globally, it affects 5-7% of the world's population. The disease is usually controlled through dietary therapy, exercise and hypoglycaemic agents [4]. This is the most common form of diabetes mellitus and is highly associated with a family history of diabetes, older age, obesity and lack of exercise [5].

2.3. Gestational Diabetes-

Pregnant women often develop diabetes. During pregnancy large quantities of hormones are produced, these hormones may reduce insulin action in the mother's body, causing insulin resistance. Women that develop diabetes mellitus during pregnancy and women with undiagnosed asymptomatic type 2 diabetes mellitus that is discovered during pregnancy are classified with gestational diabetes mellitus [5]. Clinical importance of GDM lies in the fact that it is associated with significant maternal and fetal morbidity [6].

2.4. Miscellaneous types of diabetes

2.4.1. Diabetes LADA

Latent Autoimmune Diabetes of the adults (LADA) is autoimmune diabetes defined by adult-onset, presence of diabetes associated auto-antibodies, and no insulin treatment requirement for a period after diagnosis [7]. It is becoming evident that a proportion of adults may have a slowly evolving kind of Type 1 diabetes, which is characterized by the presence of auto-antibodies. Some people diagnosed with type 2 diabetes soon find themselves dependent on insulin; these people may actually have a slowly progressive form of type 1 diabetes or LADA.

2.4.2. Diabetes MODY

Maturity onset diabetes of the young (MODY) is an autosomal dominantly inherited type of diabetes that results from heterozygous mutations in various transcription factors acting in the development and maturation of pancreatic β-cells. Characteristics features of MODY are autosomal inheritance, early onset of diabetes, no signs related to the autoimmune process or insulin resistance, and preservation of endogenous insulin secretion [8].

2.4.3. Double diabetes

Double diabetes is characterized by the occurrence of hyperglycaemia in children and young adolescents with the combination of markers typical of both type 1 and type 2 diabetes.

2.4.4. Brittle diabetes

Type 1 diabetes is an intrinsically unstable condition. A small group of patients with type 1 diabetes, mainly young women, suffer chronically by poor metabolic control, characterized by a severe instability of glycemia values with frequent and unpredictable hypoglycemic or diabetic ketoacidosis episodes which cannot be attributed to patients or clinicians errors. The quality of life of these patients is dramatically compromised in particular because of the frequency of acute events, hospital recoveries and precocious appearance of chronic complications. This clinical condition has been defined as brittle diabetes.

2.4.5. Diabetes Insipidus

Diabetes insipidus is a disease in which large volumes of dilute urine are excreted due to vasopressin deficiency, AVP resistance or excessive water intake. Polyuria is characterized by a urine volume in excess of 21/m2/24 h or approximately 150ml/kg/24h at birth, 100-110ml/kg/24h until the age of 2 years and 40-50 ml/kg/24h in the older child and adult [9].

2.4.6. Neonatal diabetes mellitus

- It occurs in first six months of life.
- Single gene defect
- Do not produce enough insulin
- Do not gain weight as quickly as expected
- High plasma glucose- mistake for T1DM

3. SYMPTOMS AND CAUSES OF DIABETES

Symptoms of diabetes include-

- Increased thirst and urination
- Increased hunger
- Fatigue
- Blurred vision
- Numbness or tingling in the feet or hands
- Sores that do not heal
- Unexplained weight loss
- Presence of ketones in the urine (ketones are a byproduct of the breakdown of muscle and fat that happens when there's not enough available insulin).
- Frequent infections, such as gums or skin infections and vaginal infections.
- Male sexual dysfunction.

3.1. Causes of diabetes

- Obesity
- Excess glucorticoids
- Excess growth hormone
- Polycystic ovary diseases
- Mutation of insulin receptor
- Lipodystrophy [2]

3.1.1. Causes of type 1 diabetes

- A genetic susceptibility to developing type 1 diabetes
- Certain viruses (e.g. German measles or mumps)
- Environmental factors

3.1.2. Causes of type 2 diabetes

Type 2 diabetes develops when the body becomes resistant to insulin or when the pancreas stops producing enough insulin.

3.2. Diagnostic tests for diabetes mellitus

Three blood tests are available to diagnose pre-diabetes and diabetes

1. Casual plasma (blood) glucose/ random plasma test
2. Fasting plasma glucose (FPG)
3. Oral glucose tolerance test

3.2.1. Casual plasma (blood) glucose/ random plasma test

The simplest test and doesn't require fasting before taking the test [6]. The criteria for diagnosis of diabetes with this test are the presence of diabetes symptoms and a blood glucose level of 200mg/dl or higher [10].

3.2.2. Fasting plasma glucose (FPG)

A fasting plasma glucose level of 7.0 mmol/L correlates most closely with a 2-hour plasma glucose value of ≥11.1mmol/L in a 75g oral glucose tolerance test (OGIT) and each predicts the development of retinopathy [11]. There should be 8hrs fasting before taking this. Blood glucose more than 126mg/dl on two or more tests conducted on different days confirms a diabetes diagnosis [5].

3.2.3. Oral glucose tolerance test

2hr blood glucose level of 200mg/dl or higher, prediabetes is diagnosed if the 2hr blood glucose level is 140-199mg/dl [10]

3.2.4. Hemoglobin A1C (HbA1c)

A1C can be measured at any time of day and is more convenient than FPG or 2hPG in a 75g OGIT. A1C also avoids the problem of day to day variability of glucose values as it reflects the average plasma glucose (PG) over the previous 2-3 months. [11].The specificity of HbA1c ≥6.5% is high enough to justify a diagnosis of diabetes and the sensitivity of HbA1c ≤5.7% is high enough to justify exclusion of a diagnosis of diabetes.

3.2.5. Diagnostic test for gestational diabetes

O'Sullivan test – This test is used to detect gestational diabetes. A 50g load of glucose is given to a fasting patient. Blood is drawn at one hour. Gestational diabetes is suggested by plasma levels above 1500mg/L. [12]

4. TREATMENT FOR DIABETES

Treatments on diabetes depend on the individual person and the type of diabetes.

4.1. Treatment of patients with type 1 diabetes

The patients with type 1 diabetes loose the ability to produce insulin and are therefore dependent upon extremely administered insulin without which they would die.

4.1.1. Insulin therapy

The use of insulin requires daily management of those factors that affect the insulin dose. Rapid- acting insulin may be given before, during, or immediately after a meal.

4.1.2. Conventional therapy

Daily 2 injections of mixed insulin contain rapid or short acting and intermediate acting drug taken before breakfast and the evening meal.

4.1.3. Conventional therapy with a split night-time dose

One injection of mixed insulin (rapid or short acting and intermediate acting) before breakfast, 1 injection of rapid-or-short acting insulin before the evening meal and 1 injection of intermediate acting insulin before the bedtime snack.

4.1.4. Multiple daily injections (MDI)

Multiple daily injections of rapid or short acting insulin before every meal with intermediate or long-acting insulin once or twice a day are advised.

4.1.5. Intensive therapy with a continuous subcutaneous insulin infusion (CSII or insulin pump)

A bolus dose of insulin is given before meals and snacks based on the amount of carbohydrate eaten and the measured level of blood glucose.

4.2. Treatment of patients with type 2 diabetes

The treatment depends on a number of factors.

- Body weight
- Current eating habits
- Current level of physical activity
- Severity of symptoms
- Blood glucose levels
- Time period of diabetes

Treatments include diet, exercise, medication and insulin therapy

Self-care: It includes Physical exercise, quitting smoking, weight loss, nutritional counseling, diabetic diet and dietary fiber.

Medications: Anti-diabetic medication, blood thinners, statin and insulin

Preventative: influenza vaccine and pneumococcal vaccine

4.2.1. Pharmacological treatments for diabetes

Oral anti-diabetic drugs: Blood glucose levels are mainly determined by absorption of glucose from gut, uptake of glucose by peripheral tissues, hepatic glucose output, and the insulin secretion from the pancreas.

4.2.1.1. Sulfonylureas

Sulfonylureas were the first widely used oral hypoglycemic medications [10]. The sulphonylureas bind to specific sulfonylurea receptors on pancreatic β cells and increase

insulin secretion. They are preferably given 15 to 30 minutes before meals.

4.2.1.2. Meglitinide analogues

Meglitinide analogues (repaglinide and netaglinide) are non-sulfonylurea insulin secretagogues. They are benzoic acid derivatives, which act on separate non-sulphonylurea receptor binding sites on β-cell and enhance insulin secretion.

4.2.1.3. Biguanides

Biguanides reduce hepatic glucose output and increase uptake of glucose by the periphery, including skeletal muscle. Motorman has become the most commonly used agent for type 2 diabetes in children and teenagers e.g. Metformin, Phenformin, Buformin. [10]. Metformin is the preferred biguanides.

4.2.1.4. Alpha-glucosidase inhibitors

Alpha-glucosidase inhibitors such as acarbose, acts by competitively inhibiting alpha-glucosidase, the enzyme in the small intestine brush border, which breakdowns oligosaccharides and disaccharides into mono-saccharides. The starting dosage is 25-50 mg once daily, which is increased to 50mg two to three times in a day. It must be ingested with the first bite of food.

4.2.1.5. Thiazolidinediones (Glitazone)

These agents act by improving insulin sensitivity in adipose tissue and skeletal muscle. It also inhibits hepatic glucose output. Pioglitazone has partial PPAR-alpha agonist activity. The dosage of rosiglitazone is 2-8mg on one to two divided doses while that of pioglitazone is 15 to 45mg once a day. The onset action of these drugs start from 2-4weeks of therapy and the maximum effect is observed after 8-12 weeks.

5. REFERENCES

1. Deepti B, Sowjanya K, Lidiya B, Bhargavi RS and Babu PS. *Journal of In silico and In vitro pharmacology,* 2017; **3:**1-14.
2. Ozougwu JC, Obimba KC, Belonwu CD and Unakalamba CB. *Journal of physiology and pathophysiology,* 2013; **4(4):**46-57.
3. Singh N, Kesherwani R, Kumar A and Patel DK. *The pharma innovation journal*, 2016; **5(7):**36-40.
4. Salim B. *International journal of diabetes and metabolism,* 2005; **13:**111-134.
5. Habetamu WB. *Journal of diabetes and metabolism*, 2015; **6:**5.
6. Siddiqui AA, Siddiqui SA, Ahmad S, Siddiqui S, Ahsan I and Sahu K. *International journal of drug development and research,* 2013; **5(2):**1-23.
7. Laugesen E, Ostergaard JA and Leeslie RDG. Latent autoimmune diabetes of the adult-current knowledge and uncertainty. Diabetic medicine 2015.
8. Ahmet A, Gonul L, Ayhan A and Ece B. *Journal of pediatric endocrinology and metabolism*, 2015; **28(3-4):**251-263.
9. Natascia D, Flavia N, Anna E, Maria A, Irene O, Enrica B et al. *Journal of hormone research in pediatrics,* 2012; **77:** 69-84.
10. Harikumar K, Kumar KB, Hemalatha GJ, Kumar BM, Steven FSL. *International journal of novel trends in pharmaceutical sciences,* 2015; **5**.
11. Ronald G and Zubin P. *Canadian journal of diabetes,* 2013; **37:** S8-S11.
12. Ngugi MP, Njagi JM, Kibiti CM, Ngeranwa JJN, Njagi ENM. *International journal of diabetes research*, 2012; **1(2):**24-27.