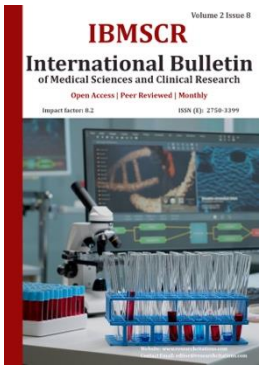

CAUSES AND TREATMENT PRINCIPLES OF DIABETES MELLITUS

Xasanova Nargis Qodirovna
Department of Fundamental Medical Sciences of the Asian International University, Bukhara, Uzbekistan
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Annotation : Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. It also predisposes to cardiovascular diseases. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.

Keywords : Diabetes mellitus, hyperglycemia, insulin, MODY, nanotechnology

Diabetes mellitus (DM) is a long-standing, complicated, and non-transmissible endocrine ailment that is growing rapidly and has posed clinical challenges globally, often linked with threats related to complicated metabolic development in patients. It is marked by elevated glucose and lipids in the blood as well as oxidative stress, which culminate in chronic complications involving diverse organs, mainly the kidneys, eyes, nerves, and blood vessels, among others, in the body. As reported by World Health Organization (WHO), DM is an outbreak prone to high malaise and death. Globally, approximately 387 million persons are affected by this disorder and it is estimated to be more than 640 million by 2040.

Etiologic Classification of Diabetes Mellitus:

I. Type 1 diabetes (beta cell destruction, usually leading to absolute insulin deficiency)
A. Immune mediated
B. Idiopathic
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)
III. Other specific types of diabetes
A. Genetic defects of beta cell function characterized by mutations in
1. Hepatocyte nuclear transcription factor (HNF) 4α (MODY 1)
2. Glucokinase (MODY 2)
3. HNF-1α (MODY 3)
4. Insulin promoter factor-1 (IPF-1; MODY 4)
5. HNF-1β (MODY 5)
6. NeuroD1 (MODY 6)
7. Mitochondrial DNA
8. Subunits of ATP-sensitive potassium channel
9. Proinsulin or insulin
B. Genetic defects in insulin action
1. Type A insulin resistance
2. Leprechaunism
3. Rabson-Mendenhall syndro

4. Lipodystrophy syndromes
C.Diseases of the exocrine pancreas—pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculous pancreatopathy, mutations in carboxyl ester lipase
D. Endocrinopathies—acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma
E. Drug or chemical induced—glucocorticoids, vacor (a rodenticide), pentamidine, nicotinic acid, diazoxide, β-adrenergic agonists, thiazides,
hydantoins, asparaginase, α-interferon, protease inhibitors, antipsychotics (atypicals and others), epinephrine
F. Infections—congenital rubella, cytomegalovirus, coxsackievirus
G. Uncommon forms of immune-mediated diabetes—"stiff-person" syndrome,
anti-insulin receptor antibodies
H. Other genetic syndromes sometimes associated with diabetes—Wolfram's syndrome, Down's syndrome, Klinefelter's syndrome, Turner's syndrome, Friedreich's ataxia, Huntington's chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome
IV. Gestational diabetes mellitus (GDM)

Other Types of DM:

Other etiologies for DM include specific genetic defects in insulin secretion or action, metabolic abnormalities that impair insulin secretion, mitochondrial abnormalities, and a host of conditions that impair glucose tolerance (Table 19-1). Maturity-onset diabetes of the young (MODY) is a subtype of DM characterized by autosomal dominant inheritance, early onset of hyperglycemia (usually >25 years), and impairment in insulin secretion (discussed below). Mutations in the insulin receptor cause a group of rare disorders characterized by severe insulin resistance.

DM can result from pancreatic exocrine disease when the majority of pancreatic islets are destroyed. Cystic fibrosis–related DM is an important consideration in this patient population. Hormones that antagonize insulin action can also lead to DM. Thus, DM is often a feature of endocrinopathies such as acromegaly and Cushing's disease. Viral infections have been implicated in pancreatic islet destruction but are an extremely rare cause of DM. A form of acute onset of type 1 diabetes, termed fulminant diabetes, has been noted in Japan and may be related to viral infection of islets.

Risk Factors of Diabetes:

There are several risk factors associated with diabetes. These risk factors contribute significantly to the progression of diabetes. They include but not limited to age; weight; family history of diabetes; smoking and race/ethnicity (Asiimwe et al., 2020; Noh et al., 2018). While T1DM is mostly found in the young, T2DM is an adult-related condition. The risk of T2DM increases with age which is due to the deficiency of insulin secretion which develops with age, and growing insulin resistance caused by a change in body composition . Increase in body weight which leads to obesity is closely associated with diabetes in a condition termed diabesity. This is because increase in body weight leads to increased insulin resistance.

According to the FDA, smokers are 30 to 40% more likely to come down with T2DM than nonsmokers. Smoking can also increase insulin resistance which makes the patients require more insulin for the control of their sugar level [19]. Diabetes is hereditary. Those with the family history are advised to adhere to lifestyles that reduce the risk of developing diabetes.

Treatment:

The treatment principles of diabetes mellitus (DM) aim to achieve and maintain optimal blood glucose levels, prevent complications, and enhance the quality of life. The approach depends on the type of diabetes and the individual patient's needs. Below are the core principles:

1. Lifestyle Modifications

•Dietary Management:

-Emphasize a balanced diet with controlled carbohydrate intake.

-Focus on high-fiber foods, lean proteins, healthy fats, and low glycemic index foods.

-Avoid sugary beverages and processed foods.

•Physical Activity:

-Regular exercise (e.g., 150 minutes of moderate aerobic activity per week) improves insulin sensitivity and helps manage weight.

•Weight Management:

-Encourage weight loss in overweight or obese patients to improve glycemic control.

2. Pharmacologic Therapy

•Type 1 Diabetes Mellitus (T1DM):

Insulin therapy is mandatory:

-Basal-bolus insulin regimen or insulin pumps.

-Regular monitoring of blood glucose levels.

•Type 2 Diabetes Mellitus (T2DM):

Oral or injectable antihyperglycemic agents are often the first-line therapy:

-Metformin: First-line medication for most patients.

-Other options: SGLT2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors, or sulfonylureas.

-Insulin therapy may be required in advanced stages or during acute illness.

•Gestational Diabetes:

-Lifestyle changes and, if needed, insulin or metformin.

3. Monitoring and Glycemic Targets

•Self-Monitoring of Blood Glucose (SMBG):

-Frequent monitoring to assess glucose control, especially for those on insulin.

•HbA1c Testing:

-Target levels: <7% for most patients, but individualized based on age, comorbidities, and risk of hypoglycemia.

•Continuous glucose monitoring (CGM) may be beneficial for some patients.

4. Management of Comorbidities

•Hypertension: ACE inhibitors or ARBs are commonly used.

•Dyslipidemia: Statins are often recommended.

•Obesity: GLP-1 receptor agonists or bariatric surgery in selected cases.

•Prevention of Complications:

-Regular screening for retinopathy, nephropathy, and neuropathy.

-Foot care to prevent ulcers and infections.

5. Patient Education and Support

•Provide comprehensive education on disease management.

•Psychological support to address stress, anxiety, or depression.

•Encourage active participation in care and goal setting.

6. Prevention of Acute and Chronic Complications

•Acute Complications:

-Prevent hypoglycemia with proper dosing and meal planning.
-Manage diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS) promptly.
•Chronic Complications:
-Control glucose, blood pressure, and lipids to reduce risks of cardiovascular disease, kidney disease, and nerve damage.
7. Regular Follow-Up
•Routine visits to monitor progress, adjust treatment plans, and address new issues.
•Coordination with a multidisciplinary team, including endocrinologists, dietitians, and diabetes educators.
Effective diabetes management relies on a tailored approach that considers the patient's age, type of diabetes, lifestyle, comorbid conditions, and preferences.
Conclusion: Diabetes mellitus (DM) underscores a rising epidemic orchestrating critical socio-economic burden on countries globally. Different treatment options for the management of DM are evolving rapidly because the usual methods of treatment have not completely tackled the primary causes of the disease and are laden with critical adverse effects.

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