Review Article

Diabetes Mellitus: A Comprehensive Review of Pathophysiology, Diagnosis, and Management Strategies

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ABSTRACT

Persistent hyperglycemia brought on by deficiencies in insulin secretion, action, or both is a hallmark of diabetes mellitus (DM), a chronic metabolic disease. It is one of the most common endocrine disorders in the world, and its prevalence is rising quickly, especially in developing nations like India. The classification, epidemiology, pathophysiology, clinical manifestations, diagnostic standards, and related complications of diabetes mellitus are all covered in detail in this review. Type 1 diabetes mellitus, type 2 diabetes mellitus, and gestational diabetes mellitus are the three main types of diabetes mellitus; each has a different etiology, onset, and management approach. Complex mechanisms are involved in the pathophysiology, such as insulin resistance coupled with β-cell dysfunction in type 2 diabetes and autoimmune destruction of pancreatic β-cells in type 1 diabetes. Polyuria, polydipsia, polyphagia, exhaustion, and weight loss are typical clinical symptoms. Standardized tests like the oral glucose tolerance test, fasting plasma glucose, and glycated hemoglobin (HbA1c) are used to make the diagnosis. Serious acute problems like hypoglycemia and diabetic ketoacidosis, as well as long-term problems like retinopathy, nephropathy, neuropathy, and cardiovascular diseases, can result from uncontrolled diabetes.

Keywords: Insulin resistance, hyperglycemia, diabetes mellitus, epidemiology, complications, diagnosis.

INTRODUCTION

Over 100 million people worldwide (6% of the population) suffer from diabetes mellitus (DM), the most prevalent endocrine disorder. It is brought on by insufficient or inefficient insulin production by the pancreas, which causes blood glucose concentrations to rise or fall. Numerous bodily systems, including the blood vessels, eyes, kidneys, heart, and nerves, are found to be harmed[1].

The most prevalent endocrine condition is diabetes mellitus (DMD), which is predicted to affect over 200 million people globally by 2010 and another 300 million by 2025. 15–17 volts. estimates and forecasts through 2010. Diabetic Medicine, 14:S1-S85, 1997[2].

The World Health Organization (WHO) first proposed the diagnostic criteria and classification of diabetes in 196518, followed by the National Diabetes Data Group (NDDG) in 197919. The WHO then released simplified recommendations in 1980. 20 Diabetes is the most prevalent endocrine condition; by 2010, it is predicted that over 200 million people will have the condition globally, and by 2025, 300 million will have it 15–17. Diabetes is a metabolic disorder caused by a defect in insulin secretion, action, or both. The World Health Organization (WHO) first proposed the diagnostic criteria and classification of diabetes in 196518, followed by the National Diabetes Data Group (NDDG) in 197919 and the WHO in 198020. 1-4 Chronic hyperglycemia and disruptions in the metabolism of carbohydrates, fats, and proteins result from insulin deficiency. 1.4 As the condition worsens, vascular or tissue damage results, which can cause serious diabetic complications like retinopathy[3,4].

TYPES:

In general, diabetes mellitus can be divided into three categories:

1. T1DM, or type 1 diabetes mellitus

Cause: Little or no insulin production due to autoimmune destruction of pancreatic β-cells

Onset: Can happen at any age, but it usually happens in childhood or adolescence.

Treatment: requires lifelong insulin therapy

Important characteristic: Patients require insulin[5].

2. T2DM, or type 2 diabetes mellitus

Cause: Insulin resistance plus decreased insulin secretion

Onset: Increasingly observed in younger individuals, but typically in adults

Genetics, sedentary lifestyle, and obesity are risk factors[6].

Treatment: Oral drugs, lifestyle modifications, and occasionally insulin

The most prevalent form (approximately 90–95% of cases)[7].

3. Diabetes mellitus during pregnancy (GDM)

Cause: Insulin resistance due to hormonal changes during pregnancy

Onset: In the second or third trimester of pregnancy.

Result: Usually goes away after delivery, but it raises the risk of Type 2 later.

Importance: If unchecked, may have an impact on both mother and child[8].

EPIDEMIOLOGY

In 2011, there were an estimated 366 million people with DM; by 2030, that number would have increased to 552 million[9]. Every country is seeing an increase in the number of people with type 2 diabetes, with 80% of those affected residing in low- and middle-income nations. Due to environmental and lifestyle risk factors, type 2 diabetes caused 4.6 million deaths worldwide in 2011[10]. Over the next 20 years, the prevalence of diabetes mellitus (DM) in adults-of which type 2 DM is becoming more common—is expected to rise. A large portion of this increase is expected to occur in developing nations, where the majority of patients are between the ages of 45 and 64[11].

In India, diabetes Recent estimates indicate that 285 million people (6.6%) in the 20–79 age group will have diabetes globally in 2010, and 438 million people (7.8%) of the adult population will have the disease by 2030. India has the highest number of diabetic subjects worldwide, earning it the dubious title of "diabetes capital of the world." The International Diabetes Federation's Diabetes Atlas 2006 states that unless immediate preventive measures are taken, India's current diabetes population of 40.9 million is predicted to increase to 69.9 million by 2025 [11,14.]

The "Asian Indian Phenotype" refers to specific clinical and biochemical abnormalities in Indians, such as increased insulin resistance, increased abdominal adiposity (higher waist circumference despite lower BMI), lower adiponectin, and higher high sensitive C-reactive protein levels[10]. Diabetes mellitus is frequently associated with changes in dietary patterns and decreased physical activity in urban populations. Diabetes is quickly gaining the status of a potential epidemic in India, with over 62 million diabetics currently diagnosed 12-13.[12] In 2000, India (31.7 million) led the world in the number of people with diabetes mellitus, followed by China (20.8 million) and the United States (17.7 million) in second and third place, respectively[13.]

According to diabetes prevalence is expected to double globally from 171 million in 2000 to 366 million by 2030, with India seeing the greatest increase. Diabetes mellitus is projected to affect 79.4 million people in India by 2030, with significant increases in China (42.3 million) and the United States (30.3 million)[11,14.]

PATHOPHYSIOLOGY:

The pathogenesis and pathophysiology of Diabetes Mellitus:

Hyperglycemia is directly linked to physiological and behavioral responses. When hyperglycemia occurs, the brain recognizes it and sends a message to the pancreas and other organs via nerve impulses to reduce its effects[17,18].

Type 1 diabetes mellitus is caused by the autoimmune destruction of insulin-producing cells in the pancreas by CD4+ and CD8+ T cells, as well as macrophages infiltrating the islets[19]. Several characteristics distinguish type 1 diabetes as an autoimmune disease:

1. The infiltrated pancreatic islets contain immunocompetent and accessory cells.

2. A correlation between the major histocompatibility complex's class II (immune response) genes and disease susceptibility (MHC; human leucocyte antigens HLA)[19,21].

3. Autoantibodies specific to islet cells are present.

4. Modifications in immunoregulation mediated by T cells, specifically in the CD4+ T cell compartment.

5. The role of TH1 cells that produce interleukins and monokines in the course of the illness.

6. Frequent occurrence of other organ-specific auto-immune diseases in affected individuals or family members.

Prior to insulin therapy, approximately 85% of patients have circulating islet cell antibodies, with the majority also having detectable anti-insulin antibodies. Most islet cell antibodies target pancreatic B cells' glutamic acid decarboxylase (GAD)[19]. T1DM is caused by the autoimmune destruction of pancreatic β-cells, resulting in insulin secretion deficiencies and metabolic abnormalities. T1DM patients experience abnormal pancreatic α-cell function, excessive glucagon secretion, and loss of insulin secretion. Hyperglycemia typically reduces glucagon secretion; however, in T1DM patients, hyperglycemia does not suppress glucagon secretion. The resulting inappropriately elevated glucagon levels exacerbate metabolic defects caused by insulin deficiency.

Insulin deficiency is the primary cause of type 1 diabetes, but there is also a problem with the way insulin is given. Deficiency in insulin leads to uncontrolled lipolysis and elevated levels of free fatty acids in the plasma, which suppresses glucose metabolism in peripheral tissues such as skeletal muscle. Impaired glucose, lipid, and protein metabolism are the primary metabolic abnormalities resulting from insulin deficiency in type 1 diabetes. This is due to the fact that insulin deficiency also lowers the expression of a number of genes necessary for target tissues to react to insulin normally, including the GLUT 4 class of glucose transporters in adipose tissue and glucokinase in the liver[17,18]. Type 2 diabetes Impaired insulin action due to insulin resistance and impaired insulin secretion due to pancreatic β-cell dysfunction are the two main pathological defects in type 2 diabetes[20,21]. The mass of β-cells changes in a way that can increase the supply of insulin and compensate for the excessive and abnormal demand when insulin resistance is prevalent. Both fasting and meal stimulation usually result in an absolute increase in the plasma insulin concentration.

Despite this, the plasma insulin concentration is insufficient to sustain normal glucose homeostasis "relative" to the

degree of insulin resistance. It is nearly impossible to separate the role of each in the etiopathogenesis of DM2 due to the close relationship between insulin secretion and the sensitivity of hormone action in the complex control of glucose homeostasis. Impaired glucose tolerance is ultimately caused by insulin resistance and hyperinsulinemia. The mode of inheritance for type 2 diabetes mellitus is unknown, with the exception of maturity onset diabetes of the young (MODY)[18]. Mutations in the glucokinase gene on chromosome 7p may cause MODY, an autosomal dominant trait. When islet cell antibodies (ICA) are negative, MODY is defined as hyperglycemia that is diagnosed before the age of twenty-five and can be treated without insulin for more than five years. Insulin resistance: The main causes of peripheral insulin resistance are thought to be an initial deficiency in insulin secretion and, in many patients, a relative insulin deficiency. Impaired insulin-mediated peripheral glucose uptake (by muscle and fat), insufficient hepatic glucose output suppression, and impaired triglyceride uptake by fat are all consequences of insulin resistance. Islet cells will secrete more insulin in order to overcome insulin resistance. Patients with impaired fasting glucose or type 2 diabetes have increased endogenous glucose production. Hepatic insulin resistance is the primary cause of hyperglycemia in type 2 diabetes because this increase happens in the presence of hyperinsulinemia, at least in the early and intermediate stages of the disease[18,21].

DIABETES MELLITUS COMPLICATIONS:

1. Acute issues

1.1 Low blood sugar

1.2 Crises of hyperglycemia Ketoacidosis of Diabetes (DKA) HHS, or hyperglycemic hyperosmolar state

2. Persistent issues:

2.1 Microvascular issues

2.1.1 Retinopathy caused by diabetes

2.1.2 Nephropathy caused by diabetes

2.1.3 Neuropathy caused by diabetes

Symptoms:

1.Polyuria: Frequent urination due to osmotic diuresis caused by hyperglycemia[25.]

2.Polydipsia: Excessive thirst resulting from dehydration secondary to fluid loss[23.]

3.Polyphagia: Increased appetite due to impaired glucose utilization by cells[22.]

4.Fatigue: Persistent weakness due to reduced cellular energy availability[25.]

5.Unintentional weight loss: More common in Type 1 diabetes mellitus, due to breakdown of fat and muscle for energy[26].

DIAGNOSIS:

1. FPG, or fasting plasma glucose:

After a minimum of eight hours of fasting, fasting plasma glucose is measured[27].

Normal: less than 100 mg/dL

Diabetes: greater than 126 mg/dL

2. Blood glucose after meals (PPBS):

Two hours after eating, this test is conducted.

A glucose level of at least 200 mg/dL is indicative of diabetes[27].

3. RPG, or random plasma glucose:

It is possible to measure blood glucose at any time of day.

Diabetes is confirmed by ≥ 200 mg/dL and symptoms (polyuria, polydipsia, weight loss)[28].

4. The OGTT, or oral glucose tolerance test:

Blood glucose is measured two hours after a standard 75 g glucose load is administered orally[27].

Normal: less than 140 mg/dL

140–199 mg/dL is considered prediabetes.

Diabetes: 200 mg/dL or higher

5. HbA1c, or glycated hemoglobin:

The average blood glucose levels over the previous two to three months are reflected in this test[27].

Typical: less than 5.7%

5.7–6.4% have prediabetes

Diabetes: at least 6.5%

SIDE EFFECTS:

Short-term adverse effects:

1. High blood sugar or hyperglycemia: causes thirst, exhaustion, and frequent urination.

2. Low blood sugar or hypoglycemia: causes perspiration, lightheadedness, disorientation, and fainting.

3. Diabetic ketoacidosis (DKA), which is more common in type 1, can be fatal and cause vomiting, abdominal pain, and fruity breath.

Long-term issues:

1. Damage to the eyes: Diabetic Retinopathy

can result in blindness or blurred vision.

2. Damage to the kidneys: Diabetic Kidney Disease

may develop into renal failure.

3. Damage to the nerves: Diabetic Neuropathy.

causes burning, tingling, and numbness, particularly in the feet.

4. Vascular and cardiac conditions: Elevated risk of hypertension, heart attack, and stroke.

5. Issues with the feet: Infections, ulcers, and occasionally amputation due to poor healing.

6. Skin problems: Bacterial and fungal infections.

7. Reproductive and sexual issues: Menstrual irregularities in women and erectile dysfunction in men.

Additional consequences:

- weakened immunity (repeated infections).

- changes in weight and fatigue.

- Mental health problems (depression, stress) Weak immunity (repeated infections).

RESULTS AND DISSCUSION

Epidemiological data analysis reveals a sharp increase in diabetes cases worldwide, and forecasts suggest that the number of affected populations will rise significantly over the next several decades. The prevalence is especially high in developing nations like India, where the incidence of the disease is greatly influenced by changes in lifestyle, urbanization, and genetic predisposition.[29,30] Type 2 diabetes mellitus (T2DM) is the predominant form of the disease, accounting for 90–95% of cases[31].

According to pathophysiological findings, the primary cause of Type 1 diabetes mellitus (T1DM) is the autoimmune destruction of pancreatic β-cells, which results in a complete lack of insulin. On the other hand, insulin resistance and decreased insulin secretion are the hallmarks of type 2 diabetes. Chronic hyperglycemia and related metabolic problems involving proteins, lipids, and carbohydrates are the outcome of these mechanisms[32].

Clinical analysis shows that fatigue, weight loss, polyuria, polydipsia, polyphagia, and other common symptoms are consistently seen in diabetic patients. Fasting plasma glucose (≥126 mg/dL), postprandial glucose (≥200 mg/dL), and HbA1c (≥6.5%) are still common and trustworthy diagnostic criteria for disease detection[33].

Additionally, the review identifies chronic complications (retinopathy, nephropathy, neuropathy, cardiovascular diseases) and acute complications (hypoglycemia, diabetic ketoacidosis, hyperosmolar hyperglycemic state) as significant causes of morbidity and mortality in diabetic patients[34].

CONCLUSION

Diabetes mellitus has major clinical, social, and economic ramifications and is a rapidly expanding global health concern[35]. The growing incidence emphasizes the critical need for efficient management and prevention techniques, especially in developing nations like India[36]. This review highlights the fact that diabetes is a complex metabolic disease marked by persistent hyperglycemia brought on by deficiencies in either insulin action or secretion, or both[35].

Although type 1, type 2, and gestational diabetes are classified according to different etiologies and pathophysiological mechanisms, if left untreated, all forms of the disease can lead to serious acute and long-term complications[37].

In summary, combating diabetes necessitates a comprehensive strategy that includes public health regulations, awareness campaigns, and ongoing research to create innovative treatment approaches. In order to lessen the worldwide burden of diabetes and enhance the lives of those who are affected, early intervention and preventive measures continue to be crucial[35].

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