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Review Article

Diabetes Mellitus: Understanding the Pathophysiology and Therapeutic Strategies

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Abstract:

Diabetes Mellitus (DM) affects approximately 100 million people worldwide, with both type 1 and type 2 diabetes causing significant health problems. Type 1 diabetes results from an autoimmune attack on pancreatic beta cells, resulting in inadequate insulin production; Type 2 diabetes is associated with insulin resistance and inadequate insulin secretion, which are mostly affected by genetics and lifestyle. Gestational diabetes also increases risk during pregnancy. Effective management requires lifestyle changes, medication, and sometimes insulin therapy. Complications include heart problems, kidney disease, neuropathy and eye problems. Many factors such as genetics, lifestyle and environmental factors can affect the development of diabetes. It is important to understand the pathophysiology of diabetes, including the role of insulin and glucagon. Lifestyle changes such as healthy eating, exercise and weight control are important. Pharmacological interventions, including insulin therapy and oral medications, are tailored to individual needs. Research is constantly exploring new avenues for future treatments, such as stem cells and gene therapy. Management strategies that integrate healthcare, lifestyle, and education are critical to reducing the burden of diabetes and improving patient outcomes.

Keywords: *Diabetes mellitus, Type 1 diabetes, Type 2 diabetes, Gestational diabetes, Hypoglycemia, Hyperglycemia*

Introduction

In the world, about 100 million people (6% of the population) suffer from diabetes mellitus (DM), a prevalent endocrine illness. It is brought on by insufficient or inefficient insulin synthesis by the pancreas, which alters blood sugar levels. Numerous bodily systems have been discovered to be harmed by it, including the heart, blood vessels, kidneys, eyes, and nerves. [1] Diabetes mellitus, popularly known as diabetes, is a disease caused by high blood sugar shown in figure 1. This condition is caused by the body's inability to effectively use or produce insulin, an important hormone in controlling diabetes. Insulin is produced in the pancreas and helps cells absorb glucose from the blood to produce energy. [2]

In type 1 diabetes, the immune system mistakenly destroys the beta cells of the pancreas, causing insufficient insulin production. Type 2 diabetes has a combination of insulin resistance and inadequate insulin production and is often related to genetics and lifestyle. [3] Diabetes requires constant monitoring to control blood sugar to prevent complications. Common symptoms include excessive thirst, frequent urination, unexplained weight gain, fatigue and blurred vision. Blood tests include blood tests such as fasting blood sugar, oral glucose tolerance test, and glycated haemoglobin test. [1]

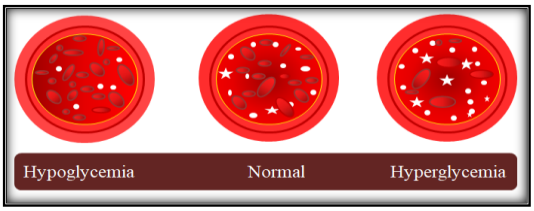

Fig. 1: Blood Glucose Levels

Treatment includes lifestyle changes, including a healthy diet, regular exercise, medication and, in some cases, insulin therapy. Proper control of diabetes is important to prevent complications such as heart disease, kidney disease and neurological disease. Education, regular monitoring, and collaboration with healthcare professionals are components of a good strategy for people with diabetes. [4]

Although both type 1 and type 2 diabetes are the two main types of diabetes, this strict classification may not apply to some people. The clinical presentation of a diagnosis is often the deciding factor in classification, and the following are commonly used to classify individuals in healthcare:

- Age of onset of diabetes
- Sudden occurrence of hyperglycemia
- Ketosis at presentation
- Obesity Degree
- Insulin is required at the time of diagnosis [5]

Types of diabetes:

Diabetes can be divided into three types: type 1, type 2 and gestational diabetes. Each has its own characteristics and requires different management strategies. [6]

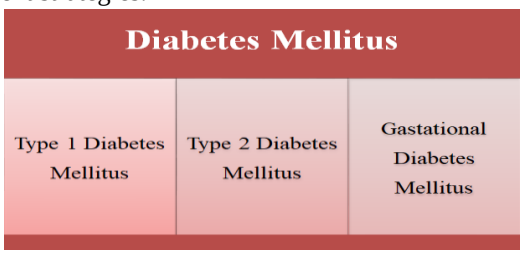

Fig. 2: Types of diabetes mellitus

- **Type 1 diabetes:** Type 1 diabetes is a chronic autoimmune disease characterized by the immune system's erroneous attack on insulin-producing beta cells in the pancreas. Insulin plays a vital role by facilitating the absorption of sugar into cells for energy and regulating blood sugar (glucose) levels. However, in individuals with type 1 diabetes, the destruction of beta cells leads to insufficient insulin production, resulting in elevated blood sugar levels, a condition known as hyperglycemia. Without proper insulin function, cells are unable to utilize glucose effectively, leading to various complications. To manage type 1 diabetes, individuals rely on external insulin administration, typically through injections or an insulin pump, to regulate blood sugar levels. Alongside insulin therapy, careful monitoring of blood sugar levels, adherence to a balanced diet, regular physical activity, and frequent medical check-ups are essential for effectively managing the condition and reducing the risk of complications associated with uncontrolled blood sugar levels. [7]
- **Type 2 diabetes:** Type 2 diabetes is a chronic disease caused by insulin resistance, poor response of cells to insulin and insufficient insulin production by the pancreas. Although it usually occurs in adults, it can also affect young people, as it is influenced by genetics and lifestyle choices such as diet and physical activity. Symptoms include excessive thirst, frequent urination, fatigue and blurred vision. Managing type 2 diabetes involves a number of approaches, including lifestyle changes such as healthy eating, regular exercise and weight control. Medications such as oral hypoglycemic medications or insulin may also be prescribed to help control diabetes. Some people with type 2 diabetes may need insulin therapy in addition to insulin. Regular blood sugar monitoring and regular physical exams are important to maintain good control and prevent complications associated with uncontrolled diabetes. [8]
- **Gestational diabetes:** Gestational diabetes is a type of diabetes in which the body does not produce enough insulin during pregnancy to meet demand, causing blood sugar levels to rise. Although this condition usually disappears after birth, it increases the risk of both mother and child developing type 2 diabetes later in life. Management of gestational diabetes involves monitoring blood sugar levels, following a healthy and nutritious diet, and, if necessary, administering insulin during pregnancy to control diabetes. Regular physical examinations are important in protecting the health of the mother and baby and reducing complications related to gestational diabetes. By keeping your blood sugar under control and following your doctor's recommendations, women with gestational diabetes have a higher chance of getting pregnant and a reduced risk of health problems by drinking clean water for both themselves and their children for a long time. [9]

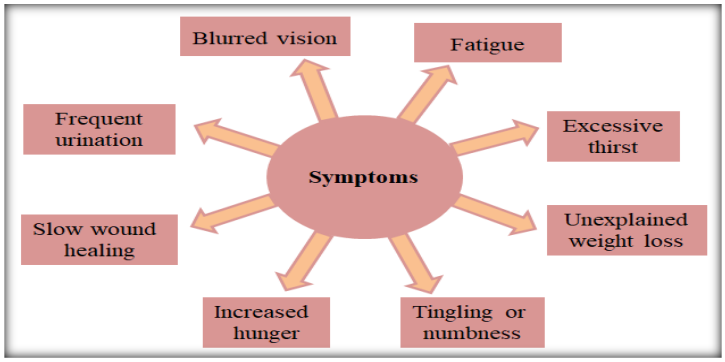

Fig. 3: Symptoms of diabetes

Factors affecting diabetes mellitus:

There are many factors that affect the development and treatment of diabetes, and these factors are often interrelated and can lead to depression. Key topics include genetics, lifestyle choices such as diet and exercise, stress levels, access to healthcare, health and social support. Understanding and addressing these issues is critical to managing diabetes and related mental health issues. [10]

- Genetics
- Lifestyle and Behavior
- Obesity
- Age
- Ethnicity
- Gestational Diabetes
- Hormonal Factors
- Medical Conditions
- Environmental Factors
- Social and Economic Factors
- Psychological Factors
- Sleep Patterns
- Medications

Pathophysiology of Diabetes:

Normal glucose metabolism depends on the interaction between insulin and glucagon, a pancreatic hormone important in the control of diabetes. After a meal, insulin secretion increases and cellular glucose is stimulated to produce and store energy. Conversely, when blood sugar levels drop, glucagon release causes the liver to release glucose into the bloodstream to maintain high levels. This balance provides stable cellular energy while preventing hyperglycemia or hypoglycemia. While insulin promotes glucose utilization, glucagon acts as an antidote to maintain glucose homeostasis by promoting glucose uptake in the liver. Together they regulate glucose metabolism, which is important for overall health.[11]

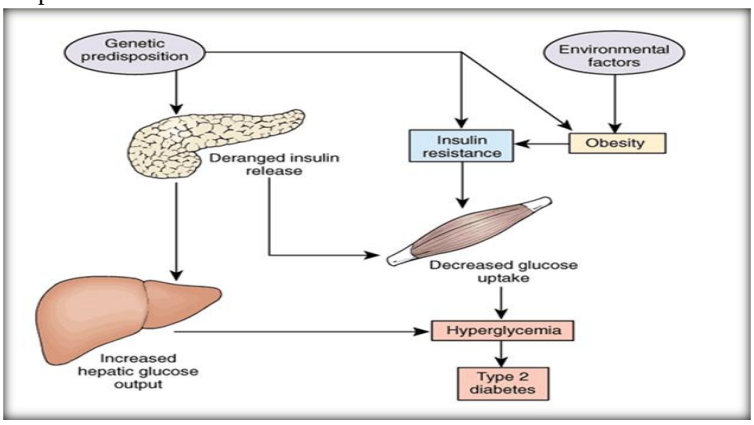

Fig. 4: Pathophysiology of diabetes mellitus

Type 1 diabetes (T1DM) pathogenesis:

a) **Autoimmune destruction of pancreatic beta cells:** Type 1 diabetes (T1DM) is associated with the failure of the immune system's pancreatic beta cells, which are responsible for insulin production. This autoimmune attack leads to insulin deficiency, causing blood sugar to rise. Therefore, patients with T1DM require exogenous insulin to maintain normal blood sugar levels.
b) **Cenetic Predispositions and Environmental Triggers:** Type 1 diabetes (T1DM) has a genetic predisposition and some genes affect the autoimmune attack of pancreatic beta cells. Environmental factors, especially infections, can trigger this autoimmune response in genetically susceptible individuals. The interaction of genetics and environment contributes to many aspects of T1DM etiology; This suggests the interaction of genetic and environmental factors in the development of the disease. [12]

Pathogenesis of type 2 diabetes (T2DM):

a) **Insulin Resistance:** In type 2 diabetes (T2DM), cells develop insulin resistance, reducing insulin signaling efficiency, thus hindering health and productivity. Therefore, the body needs to increase the amount of insulin in order to compensate for this protection and control blood sugar. Despite the pancreas' efforts to produce more insulin, the cells still fail to respond, causing the high blood sugar that is characteristic of T2DM. Lifestyle factors such as diet and physical activity are associated with the development and progression of insulin resistance in T2DM. [13]
b) **Beta Cell Dysfunction:** In type 2 diabetes (T2DM), beta cells in the pancreas gradually lose their ability to produce enough insulin to meet the body's needs. This beta cell activity causes insufficient insulin production, causing blood sugar levels to rise. As T2DM progresses, decreased β-cell capacity can lead to hyperglycemia, leading to chronic diseases and complications. Factors such as genetic predisposition, obesity, and lifestyle choices may increase β-cell dysfunction in T2DM patients.
c) **Genetic and environmental risk factors:** T2DM has a strong genetic component, and a variety of different diseases contribute to insulin resistance and beta cell dysfunction. Environmental factors such as obesity, sedentary lifestyle and malnutrition also play an important role in the pathogenesis of T2DM.[14]

Pathogenesis of Gestational Diabetes: Gestational diabetes is an option caused by insulin resistance caused by placental hormones, maternal obesity, genetics and lifestyle. Beta cell dysfunction and inflammation lead to glucose intolerance. Race and family history of GDM increase the risk. Recognition of these conditions is important for prevention and management during pregnancy. Lifestyle changes such as diet and exercise are important interventions. Blood sugar monitoring and, if necessary, insulin treatment are important in the treatment of GDM to avoid negative consequences for mother and child. [15]

Role of insulin and glucagon in glucose homeostasis:

Insulin promotes the cellular uptake of glucose for energy production or storage as glycogen or fat. It also prevents the release of sugar from the liver. On the other hand, when blood sugar drops, glucagon stimulates the liver to release glucose into the blood. Insulin and glucagon work together to keep blood sugar within a narrow range, ensuring cells have enough energy. [16]

Effect of dysregulated glucose metabolism on various organs and systems:

a) **Cardiovascular disease:** Acute hyperglycemia in diabetes can cause vascular damage and increase atherosclerosis, heart disease, heart disease and stroke.
b) **Kidney System:** Diabetes is the cause of chronic kidney disease (diabetic nephropathy) due to damage to the small blood vessels in the kidney. This can lead to kidney failure.
c) **Nervous System:** Diabetes can cause neuropathy, or nerve damage, and cause symptoms such as numbness, tingling, and pain, especially in the extremities. It can also cause autonomic dysfunction, affecting the nerves that control involuntary functions such as digestion, bladder control, and heart rate.
d) **Eye problems:** Diabetes can damage the blood vessels in the retina, causing diabetic retinopathy, a type of diabetic retinopathy. It causes blindness in adults. It also increases the risk of other eye diseases such as cataracts and glaucoma. [17]

Lifestyle Changes:

a) **Health and Fitness:** Eating a healthy diet that includes a variety of healthy foods such as fruits, vegetables, whole grains, lean protein and healthy fats is important for diabetes management. Counting carbohydrates or checking the glycemic index can help control blood sugar.
b) **Exercise:** Regular exercise increases insulin sensitivity and cellular uptake of glucose, thus reducing blood sugar levels. Strength training, as well as aerobic exercises such as walking, running, swimming and cycling, are also beneficial for people with diabetes.
c) **Weight management:** Weight management through diet and exercise is important in controlling diabetes, especially for people who are overweight or obese. Even a small amount of weight can improve insulin sensitivity and control diabetes. [18][19]

Drug intervention: Drug interventions employ medications to manage various medical conditions, often targeting specific pathways or mechanisms in the body. These interventions aim to alleviate symptoms, improve health outcomes, and sometimes even cure diseases. They play a crucial role in modern healthcare, complementing other therapeutic approaches like lifestyle modifications and surgery.

Insulin therapy:

a) **Insulin Types:** There are different types of insulin: rapid-acting, short-acting, intermediate-acting and long-acting. The choice of insulin type depends on factors such as meal times, diabetes, and personal needs.
b) **Method of administration:** Insulin can be administered by injection via syringe, insulin pen or insulin pump. Some types of insulin are also available in inhaled form. [20]

Oral hypoglycemic drugs:

a) **Metformin:** Metformin, the main treatment for type 2 diabetes, increases insulin sensitivity and lowers glucose levels in the liver, thereby lowering blood sugar levels. This medication is considered the first line because it controls glucose metabolism with a low risk of hypoglycemia compared to other treatments. [21][22]
b) **Sulfonylureas:** Sulphonylureas are drugs that stimulate the release of insulin from the pancreas and help reduce diabetes. They help control blood sugar by stimulating insulin release, and are useful in the treatment of type 2 diabetes by promoting glucose uptake into cells. [23][24]
c) **DPP-4 Inhibitors:** DPP-4 inhibitors stimulate insulin production by preventing the degradation of incretin hormones, thus helping to control diabetes. They also lower blood sugar levels by reducing glucagon secretion. This dual use makes DPP-4 inhibitors effective in treating type 2 diabetes by improving insulin sensitivity and preventing excessive glucagon release. [25][26]
d) **SGLT2 inhibitors:** SGLT2 inhibitors increase urinary glucose excretion and reduce blood glucose by blocking renal glucose reabsorption. These drugs inhibit the SGLT2 protein in the kidney, promoting the removal of excess sugar from the body, providing a good way to control and cure type 2 diabetes. [27]
e) **GLP-1 receptor agonists:** GLP-1 receptor agonists mimic the effects of the incretin hormone, stimulating insulin production, inhibiting glucagon release, and slowing digestion, all of which reduce blood sugar. Focusing on different ways to control blood sugar, these medications are effective in treating type 2 diabetes, improving blood sugar control, and helping control weight. [28]

New Treatments and Scientific Research:

- **Stem Cell Therapy:** Researchers are investigating the potential of stem cell therapy to regenerate pancreatic beta cells or improve insulin resistance in diabetics. This new approach holds the promise of restoring normal glucose levels and improving disease control. Researchers aim to develop effective treatments against diabetes and its complications by taking advantage of the regenerative power of stem cells. [29]
- **Gene Therapy:** Gene therapies aim to solve genetic problems associated with diabetes or improve insulin production in the pancreas. This new therapy, which teaches genes to work or replaces existing genes, has the potential to correct the underlying genetic disease and improve insulin secretion. It represents a potential breakthrough in the treatment of diabetes and its associated complications. [30]

Conclusion

In summary, diabetes is an important health problem worldwide, including type 1 and type 2 diabetes, as well as gestational diabetes. Effective management requires a variety of approaches, including lifestyle changes, medications, and sometimes insulin therapy. Comorbidities such as heart problems, kidney disease, neuropathy, and eye problems highlight the importance of quality care. Understanding the pathophysiology of diabetes is important for tailoring management strategies. Lifestyle changes and pharmacological interventions play an important role in diabetes management. Ongoing research into new treatments such as stem cells and gene therapy holds promise for the future. Successful management strategies are important to improve patient outcomes and reduce the burden of diabetes.

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Competing Interest

The authors have declared that no competing interest exists.

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