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Review Article

DECODING DIABETES: PATHOPHYSIOLOGY, PREVENTION, AND PROGRESS

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Abstract:

Diabetes and the advancements in food and nutrition needed to prevent or manage all forms of diabetes were the main topics of the systematic review. High blood sugar levels over an extended period of time are a hallmark of diabetes. Diabetes leads to numerous health issues if treatment is not received. Diabetic ketoacidosis, hyperosmolar hyperglycemia, and even mortality are examples of acute complications. Chronic kidney disease, foot ulcers, eye damage, cardiovascular disease, and stroke are examples of serious long-term health issues. Either the pancreas cannot make enough insulin, or the body cells do not react appropriately to the insulin that is produced, which results in diabetes. There are several distinct forms of diabetes mellitus, but the three main ones are type 1, type 2, and gestational diabetes. The reason is not known. Insulin resistance, a disorder in which cells do not react to insulin as intended, is the first sign of type 2 diabetes. A shortage of insulin may also arise as the illness worsens. This kind was once known as “adult-onset diabetes” or “non-insulin-dependent diabetes mellitus” (NIDDM). Diabetes can be prevented or managed by adhering to a healthy diet, low-fat, low-calorie, paleolithic, very low carbohydrate, raw foodist, and/or ketogenic diets.

Keywords: diabetes, decoding diabetes, pathophysiology, ketoacidosis etc.

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INTRODUCTION:

Diabetes mellitus is a condition of macromolecule metabolism that is characterized by a compromised body's capacity to respond to hormones and maintain appropriate blood sugar (glucose) levels. (1). The endocrine system transports blood sugar into your cells for storage or energy use. Untreated high blood glucose from polygenic illness can harm your kidneys, nerves, eyes, and other organs. In polygenic disease, your body either won't produce enough endocrine or will use the endocrine it does produce efficiently. (2). Insufficient endocrine output (produced by the duct gliding and lowering blood glucose) or insufficient cell receptivity to endocrine activity. (3).Hyperglycemia, either during fasting or postprandial periods, is a hallmark of diabetes. The ongoing elevated blood sugar levels In addition to tissues including the kidney, heart, nerves, retina, and blood vessels, diabetes mellitus (DM) is associated with the end of organ failure, damage, and dysfunction. The total number of diabetics is determined by the International Federation of Diabetes (IDF). There were 366 million Tus in 2011, and that number is expected to rise to 552 million by 2030.(4).A consensus statement issued by the World Health The most recent diabetes diagnostic criteria were published by the World Health Organization (WHO).(5).which are found in accordance with the consensus declaration of the American Diabetes Association(6).from the Canadian Diabetes Association (CDA).(7).

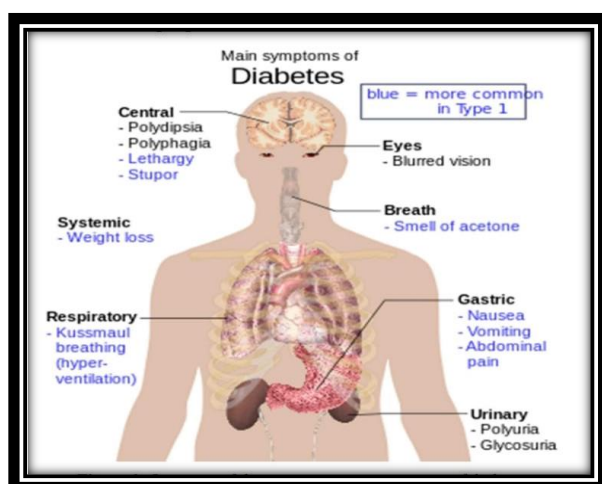


Fig No 1. : Clinical Manifestations and Systemic Symptoms of Diabetes Mellitus

Definition of Diabetes

Diabetes mellitus is a long-term metabolic disease marked by elevated blood glucose (sugar) levels brought on by either insufficient pancreatic synthesis of insulin or inefficient cell utilization of insulin. A condition known as diabetes is characterized by hyperglycemia in either.(8).

Postprandial or fasting states. End-organ damage, dysfunction, and failure in organs and tissues such as the retina, kidney, nerves, heart, and blood vessels are linked to the chronic hyperglycemia of diabetes mellitus (DM).According to the International Diabetes Federation (IDF), 366 million people worldwide had diabetes mellitus in 2011, and by 2030, that number is predicted to increase to 552 million.(9).Hemoglobin A1c (HbA1c) has recently been included by the American Diabetes Association (ADA) as a diagnostic test for DM as well as a gauge of the effectiveness of therapies and the management of hyperglycemia (American Diabetes Association,(2010a).(10).The World Health Organization (WHO) first proposed the diagnostic standards and classification of diabetes in 1965(11). The National Diabetes Data Group (NDDG) then proposed similar recommendations in 1979(12), and the WHO again did so in 1980.(13).

Classification of Diabetes mellitus

In 1980, a United Nations body unveiled the first widely recognized classification of diabetes (14). This was modified in 1985. (15).Our presentation will center on the most prevalent and essential type of primary or upset diabetes. It should differ from secondary diabetes, which includes symptoms associated with identifiable causes, such as inflammatory exocrine gland diseases, surgery, tumors, certain medications, iron overload (hemochromatosis), and certain acquired or genetic endocrinopathies, which all cause the destruction of exocrine gland islets.(16).All clinical stages, aetiological types of diabetes, and various kinds of hyperglycemia are included in the classification.(17).

Type1 Diabetes mellitus

Only 5–10% of people with diabetes have this kind of diabetes, which was formerly referred to as juvenile-onset diabetes or insulin-dependent diabetes. It is caused by an autoimmune cellular-mediated death of the pancreatic β -cells. Autoantibodies to insulin, GAD (GAD65), islet cell autoantibodies, and autoantibodies to the tyrosine phosphatases IA-2 and IA-2b are indicators of the immunological destruction of the β -cell. Immune modification in high-risk individuals has been the subject of clinical trials investigating the possibility of avoiding or postponing autoimmune type 1 diabetes. Patients with recent-onset type 1 diabetes, for instance, within 6 weeks of clinical presentation, when an estimated 80% to 90% of the β -cell mass has already been destroyed, have been included in numerous preventative studies.(18).

Previously known as juvenile-onset or ketosisprone polygenic illness, this form of diabetes is often referred to as response diabetes. The person may also inquire about several autoimmune conditions, such as Graves' disease, Addison's disease and Hashimoto's thyroiditis.(19).The rate at which

betacells are destroyed varies somewhat; it frequently happens quickly for some people and slowly for others.(18).Hormone production is severely lacking or absent due to the duct gland's β -islets cells being destroyed. Hormone injections are necessary for treatment.(19).Immune destruction markers, island cell auto-antibodies, and/or motorcar hormone antibodies, as well as auto-antibodies When fasting diabetic hyperglycemia is initially identified, you treat individuals with type 1 diabetes using the amino acid enzyme (GAD) area unit gift in 85–90.(20).

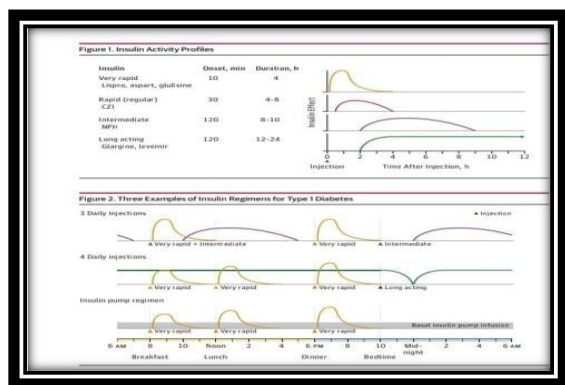


Fig No 2 . Comparison of Insulin Types and Their Duration of Action

Type 2 Diabetes mellitus

The most prevalent kind of diabetes, type 2, is characterized by problems with insulin production and insulin resistance. 28 Up to 7% of people in Western nations are afflicted by the illness. (21). It impacts 5–7% of the world's population worldwide.(22).This prevalence is underreported. Because a large number of cases—possibly 50% in some populations—go undetected. The prevalence of type 2 diabetes varies greatly across the globe, ranging from less than 1% in some developing country populations, such as rural Chinese and Melanesians in Papua New Guinea, to more than 50% among Arizona's Pima Indians.(23).Compared to rural areas, type 2 diabetes is more common in metropolitan settings.(24).Ketosis-resistant diabetes mellitus is another name for type 2 diabetes. Insulin resistance as a backdrop for the progressive hypoglycemic agent secretory malfunction (American Polygenic Disorder Association, 2014). (25).Individuals with this type of polygenic disorder frequently exhibit resistance to the effects of hypoglycemic medications.(26).The primary causes of morbidity and mortality from polygenic disorders are semi-permanent problems in the kidneys, eyes, nerves, and blood vessels, which affect all kinds.(27).

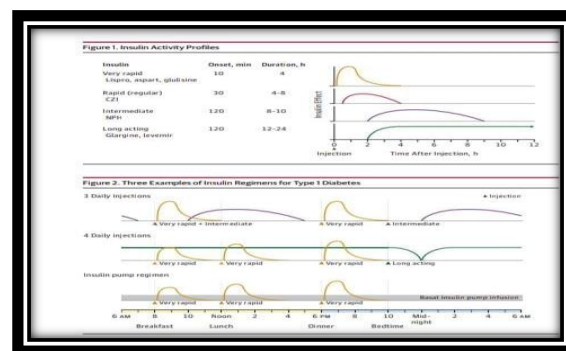


Fig NO 3 . Insulin Secretion and Glucose Regulation Profiles in Diabetes

Etiology

1. The juvenile-onset (insulindependent) type is currently thought to have an associate degree autoimmune origin.
2. Viruses might also contribute to the genesis of polygenic illnesses like coxsackie B.
3. It has been demonstrated that the German measles virus and epidemic parotitis both cause morphologic alterations in the islet-cell structure.
4. There is debate on the genetic component of polygenic illness genesis. The exocrine gland of a person is likely more susceptible to one of the viruses due to a genetic characteristic.(28).
5. Milliteus disturbances, a polygenic illness, or deviation in the β cell's gluco-receptor so that they respond to increased aldohexose concentration or relative β cell deficiency. In any approach, hypoglycaemic agent secretion is compromised; could lead to β cell failure.(29).Principal's concept in small vascular neurological drive brought on by illness, and hence the direct consequences of hyperglycemia on metabolism of vegetative cells. (30). diminished insulin sensitivity of peripheral tissues: decrease in hypoglycemic range Agent receptors, hypoglycemic agent receptors, and "down regulation." A number of supersensitive Despite being conventionally glycaemic, hyperinsulinemia is also linked to abdominal obesity, hyperuricemia, and dyslipidemia. Thus, a relative hypoglycemic agent is present. Resistance, especially in the areas of fat, muscle, and liver. The use of hyperinsulinaemic responsible for causing angiopathy. (31).
6. Obesity; results in relative hypoglycemic agent deficiency; the β cells lag behind; far over hyperglycemia; internal secretion (glucagon), etc. Two theories contend that abnormalities in nitric oxide metabolism

cause nerve damage and changed perineural blood flow. (32).

7. Protein kinase C, advanced glycation-end products, oxidative stress, and therefore the polyol pathway are the focus of current research on diabetes pathophysiology. (33).

PATHOPHYSIOLOGY

The pathogenesis of diabetes mellitus Hyperglycemia, or increased blood glucose levels, is a hallmark of diabetes mellitus, a chronic metabolic disease caused by deficiencies in either insulin secretion, insulin action, or both. Diabetes comes in two main forms: Types 1 and 2.

1. Diabetes Mellitus Type 1 (T1DM) Absolute insulin insufficiency is caused by the autoimmune destruction of pancreatic β -cells in the islets of Langerhans. Caused by environmental variables (such viral infections) and genetic predispositions (like HLA-DR3/DR4). Hyperglycemia, lipolysis, ketone formation, and metabolic acidosis result from glucose's inefficient entry into cells in the absence of insulin.
2. Diabetes Mellitus Type 2 (T2DM) caused by relative insulin insufficiency and insulin resistance in peripheral tissues (liver, muscle, and fat). First, β -cells make up for it by secreting more insulin.

Mechanism of action

Action mechanism Sulfonylureas stimulate the release of insulin from pancreatic β -cells, which results in hypoglycemia. They attach to β -cell plasma membrane sulfonylurea (SUR) receptors, which closes adenosine triphosphate (ATP)-sensitive potassium channels and causes the cell membrane to depolarize. Consequently, voltage-gated channels are opened, permitting the inflow of calcium ions and the subsequent release of insulin granules that have already been produced. When sulfonylureas are given acutely to patients with type 2 diabetes, the pancreas releases more insulin, and this may also raise insulin levels by decreasing the hormone's hepatic clearance. According to preliminary research, sulfonylureas' hypoglycemic effects required a functioning pancreas. (34).

Symptoms

Both forms of diabetes have comparable symptoms, albeit they differ in severity. In type 1 diabetes, symptoms appear more frequently and more quickly. Polyuria, polydipsia, polyphagia, weariness, weight loss, cramps, constipation, hazy eyesight, and candidiasis are some of the symptoms. (35). One Patients with long-standing type 1 diabetes are at risk for macrovascular disease (heart, peripheral vascular, and coronary

artery disorders) as well as microvascular consequences (36).

Prevention

There is no proven preventive intervention for type 1 diabetes (37).. A good diet, regular exercise, and keeping a normal body weight can typically avoid or delay type 2 diabetes, which makes up 85 to 90% of all cases globally (38). More than 90 minutes a day of physical activity lowers the risk of diabetes by 28% (39). Maintaining a diet high in fiber and whole grains, as well as selecting healthy fats such polyunsaturated fats from nuts, fish, and vegetable oils, are effective dietary modifications that are known to help prevent diabetes (40). The development of early diabetic retinopathy is not stopped by the aldose reductase inhibitors ponalrestat and sorbinil. (41). Epalrestat significantly reduced deterioration, as measured by fluorescein angiography, in 214 diabetic patients with either nonproliferative retinopathy or preproliferative retinopathy (defined as the presence of microaneurysms, retinal hemorrhages and exudates, and intraaretinal vascular abnormalities). However, visual function was not reported in the epalrestat-treated patients compared to the placebo-treated group. (42). A significant, extensive prospective study conducted in China looked at how food and exercise affected the rate at which IGT progressed to diabetes; either by themselves or in combination, the interventions slowed the disease's progression by 40% after six years. (43). Similar research conducted in Sweden also shows how well lifestyle modifications might prevent diabetes. (44). A lifestyle intervention lowered the risk of type 2 diabetes progression in participants with IGT by 58%, according to a more recent Finnish Diabetes Prevention Study. (45).

TREATMENT

High dosages of a typical hypoglycemic medication are used as part of the treatment to combat the underlying cause. Once the situation is under control, the demand for hypoglycemic agents returns to normal (46). The following will help to accomplish the goals of DM management:

1. To restore the diabetic's disrupted metabolism as close to its original state as possible while maintaining safety and comfort.
2. To prevent or postpone the development of the illness's immediate and long-term risks.
3. To provide the patient with information, inspiration, and resources to carry out this self-enlightened care.

1. Somatic cell medical aid

Medical assistance for somatic cells According to research, monocytes and macrophages may also be major contributors to the hypoglycemic medication resistance and chronic inflammations seen in T2DM patients. (47). A novel technology called somatic cell professional medical aid is designed to

control or even reverse immunological dysfunctions.(48).

2. Inhibitor medical care

Patients with type 2 diabetes are treated for aerophilous stress using a range of antioxidants, including vitamins, supplements, active ingredients derived from plants, and medications having inhibitory effects. The best supplements to prevent aerophilous stress and its aftereffects are vitamin C and tocopherol tocopherol carotene. (49).

3. Newer endocrine Delivery Devices

To improve the precision and ease of endocrine administration and achieve strict glycaemia control, several innovations are developed. These include endocrine syringes, pen devices, inhaled hormones, implantable pumps, and other endocrine administration methods.

In the ETDRS, 3711 patients with macular edema who had either mild-to-severe nonproliferative retinopathy or mild early proliferative retinopathy were treated with panretinal photocoagulation followed by treatment with either aspirin (650 mg per day) or placebo.(50). One eye of each patient was treated with panretinal photo-Coagulation by argon laser at the beginning of the study, and the other eye was examined every four

months and treated with photocoagulation only if high-risk proliferative retinopathy was detected. During five years of follow-up, early panretinal photocoagulation resulted in a slightly lower rate of severe visual loss (2.6 Percent) than deferred treatment (3.7 percent). Early vitrectomy increased the likelihood of excellent vision in the Diabetic Retinopathy Vitrectomy Study as compared to delaying vitrectomy for a year. In the milder phases of severe proliferative retinopathy, vitrectomy was beneficial before the onset of severe visual loss from retinal detachment or hemorrhage, but not in the most advanced stages. (51).

Management strategies

People with or without diabetes are generally advised to take the same precautions when it comes to alcohol and drug use, according to management recommendations. It is not recommended to encourage nondrinkers to start drinking alcohol for its cardiometabolic benefits, even though people with type 2 diabetes who consume alcohol at low risk levels (variously defined in national guidelines but generally less than 20 g alcohol daily) shouldn't necessarily be advised to stop. Unintentionally encouraging alcohol use is expected to have a detrimental impact on other health and social outcomes, negating any potential benefits, given the unclear advantages of moderate drinking and the obvious harm connected to increasing alcohol intake. Individuals with diabetes must understand how frequent heavy drinking and binge drinking affect their health. Although there

is currently little evidence, studies have started to evaluate the efficacy of drug and alcohol therapies for individuals with diabetes and substance use disorders.(52). In both individuals with and without diabetes, intensive psychosocial interventions to change substance use seem to be equally effective. Despite the fact that comorbid depression and diabetes have been demonstrated to benefit from integrated care approaches, aggressive case discovery, and expedited referrals to social and psychiatric therapies. According to a short research of 119 patients receiving therapy with opioid agonists, methadone prescribers had a 3-4 times higher risk of diabetes than buprenorphine users. According to this research, buprenorphine may be the better choice for this group because methadone negatively impacts blood glucose metabolism.(53)

CONCLUSION:

A high blood sugar level for an extended length of time is a hallmark of diabetes mellitus, a group of metabolic illnesses. Diabetes mellitus can lead to numerous consequences if treatment is not received. Diabetic ketoacidosis, hyperosmolar hyperglycemia, or even mortality are examples of acute consequences. Chronic kidney disease, foot ulcers, cardiovascular illness, eye impairment, and stroke are examples of serious long-term consequences. Diabetes is brought on by either insufficient insulin production by the pancreas or improper cell response to insulin. Type 1, Type 2, and gestational diabetes are the three primary forms of diabetes mellitus. When beta cells are lost, the pancreas is unable to make enough insulin, which leads to type 1 diabetes. While brief therapies work well for alcohol consumption, more comprehensive interventions and cooperation with addiction specialists are probably needed for those with substance use problems.

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