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DIABETES: A DISEASE OR CRISIS

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ABSTRACT

"One of the most prevalent non-communicable diseases is diabetes mellitus. Globally, the prevalence of diabetes mellitus, a chronic metabolic condition, has been gradually rising. Due to this trend, the disease is quickly spreading to other parts of the world and is predicted to affect twice as many people in the next ten years as a result of an aging population. This will increase the burden already placed on healthcare providers, particularly in less developed nations. India confronts a number of obstacles in managing diabetes, including an increase in both urban and rural prevalence, low public awareness of the disease, a lack of healthcare facilities, high treatment costs, inadequate glycaemic control, and an increase in the prevalence of diabetic complications. The most popular way to administer insulin therapy for diabetes is by subcutaneous injections up to four times per day. Long-term insulin therapy has led to issues with patient compliance, which has an impact on patient outcomes. These issues are further exacerbated by the intrusive nature of insulin delivery. Type-2 diabetes mellitus, which accounts for more than 90% of all diabetes occurrences, is the primary cause of the diabetic epidemic, while type-1 diabetes incidence is also on the rise. Type-2 diabetes is a dangerous and prevalent chronic illness that is brought on by a complicated interplay between genetics, environment, and other risk factors like obesity and a sedentary lifestyle.

KEYWORDS: Diabetes, Insulin, Abnormalities of ß-cell's gluco-receptor.

INTRODUCTION

Over 100 million people worldwide suffer with diabetes mellitus, a prevalent endocrine illness that affects approximately 6% of the population. It is brought on by insufficient insulin synthesis from the pancreas, which causes variations in blood glucose levels. Numerous body systems are shown to be harmed by it, specifically the blood vessels, eyes, kidneys, heart, and nerves. Insulin-dependent diabetes mellitus (Type-1) and non-insulin-dependent diabetes mellitus (Type-2) are the two forms of diabetes mellitus. In contrast to Type-2 diabetes, which is defined by peripheral insulin resistance and decreased insulin secretion, Type-2 diabetes is an autoimmune illness that is characterized by a local inflammatory reaction in and surrounding islets that is followed by the selective death of insulin secreting cells. Diabetes mellitus increases the chance of developing a number of problems, including peripheral vascular disease, stroke, neuropathy, renal failure, retinopathy, blindness, and amputations. Mostly, drugs are used to treat symptoms and preserve lives. The secondary goals are to prolong longevity by removing different risk factors and to prevent long-term diabetic problems.

A chronic illness involving the metabolism of proteins, lipids, and carbohydrates is diabetes mellitus. Diabetes mellitus is characterized by a poor or insufficient insulin secretary response, which results in impaired utilization of carbohydrates (glucose), as well as the hyperglycemias that follow.4 Diabetes mellitus, also called "sugar diabetes," is the most prevalent endocrine illness. It normally arises from an insufficient or absent amount of insulin, or in rare cases, from an impairment in the activity of insulin. According to estimations from the International Diabetes Federation, there are approximately 40.9 million diabetic people in India, and by 2025, that number is expected to increase to 69.9 million. Both glucagon and insulin hormones are released by the pancreas. The beta (ß) cells and alpha (α) cells are found in the islets of Langerhan's and release insulin and glucagon, respectively. Insulin transfers glucose into the muscles, liver, and adipose tissue, lowering blood glucose levels through glycogenesis. While erythrocytes and neural tissue do not require insulin for glucose use, alpha (α) cells are crucial for blood glucose regulation because they produce glucagon, which raises blood glucose levels by speeding up the process of glycogenolysis.

In addition to a higher chance of obesity, metabolic, cardiovascular, and cancer in the fetus's postnatal life.

Eighty to ninety percent of cases of diabetes mellitus are type II. Geographic variation can influence total morbidity and mortality as well as the severity of the issues. Furthermore, the risk of death is not significantly higher for diabetics who moderately exercise than for those who do not. It is now well recognized that the occurrence of such an event necessitates a particular genetic composition. One of the biggest health obstacles to economic development facing the states of the WHO African Region is the rising prevalence of diabetes and other non-communicable diseases. Patients with type-1 diabetes mellitus are treated primarily with insulin replacement therapy, whereas type-2 diabetes mellitus is treated and managed mostly with diet and lifestyle changes. For the treatment of diabetes, a variety of hypoglycemic medications are also available, including biguanides and sulfonylureas.

However, none of these drugs are perfect because of their harmful side effects, and long-term usage might occasionally result in a reduction in response. The primary drawback of the medications that are already on the market is that they have adverse effects and must be taken continuously. Worldwide, medicinal plants and their bioactive components can be utilized to treat diabetes mellitus, particularly in nations with limited access to traditional anti-diabetic medications. There are also numerous experimental models available to evaluate a plant's antidiabetic properties. Therefore, the goal of this review is to gain a deeper understanding of diabetes mellitus, including its clinical manifestation, epidemiological information, complications, and current treatment options.

Diabetes in India
India is the second most affected country in the world, after China, with an estimated 77 million people living with diabetes. India accounts for one in six (17%) of the global diabetes population. As of October 2018, India's population accounted for roughly 17.5% of the world's total. The International Diabetes Federation predicts that by 2045, there would be 134 million people with the condition. Compared to western nations, type-1 diabetes is less common in India. In India, only around one-third of those with type-2 diabetes are obese or overweight. According to a 2004 study, industrialization and the migration of Indians from rural to urban areas may have changed their lifestyles and the environment, which may have contributed to the high prevalence of type-2 diabetes among them. These changes also occur earlier in life, which means chronic long-term complications are more common.

EPIDEMIOLOGY
The most recent data, statistics, and predictions on diabetes globally may be found in the IDF Diabetes Atlas, Tenth Edition 2021. An estimated 537 million persons (30–80 years old) have diabetes in 2021. By 2030, there will be 643 million individuals worldwide with diabetes, and by 2045, there will be 783 million.

Due to environmental and behavioral risk factors, the incidence of type-2 diabetes mellitus varies greatly between geographic regions. According to predictions, within the next 20 years, there will be a significant increase in the prevalence of diabetes mellitus in adults, with type-2 diabetes becoming more common. Most of these cases will occur in developing nations, where the majority of patients are between the ages of 45 and 64.

COMMON INDICATES AND SYMPTOMS
When cells in diabetes mellitus are unable to metabolize glucose in a normal way, they essentially starve to death. Diabetes mellitus's long-term effects include the progressive development of certain complications such as retinopathy, which can result in blindness, nephropathy, which can cause renal failure, neuropathy, which can cause foot ulcers, Charcot joints, and symptoms of autonomic dysfunction and sexual dysfunction. Diabetes raises a person's risk of illness.

Among the common signs of diabetes are
- Blurred eyesight.
- Non-healing ulcer.
- Increasing thirst and hunger.
- Losing weight.
- Frequently micturating.
- Extreme weariness.
- In females, urinary tract infections and itchy skin.
- In males, erectile dysfunction and weak muscular mass.

CAUSES OF DIABETES MILLITEUS
Abnormalities or disturbances in the ß cell's gluco-receptor that cause them to react to increased glucose concentrations or a relative ß cell shortage. Either way, there is a reduction in insulin secretion, which could lead to ß cell failure. the hypothesis of direct effects of hyperglycemia on neuronal metabolism and the role of microvascular illness in causing cerebral hypoxia.

1. Diminished insulin sensitivity in peripheral tissues due to "down regulation" and a decrease in the number of insulin receptors. Many have normal glycemic levels but are hypersensitive and hyper-insulinaemic; they are also linked to dyslipidemia, hyperuricemia, and abdominal fat. Relative insulin resistance therefore exists, especially at the liver, muscle, and fat levels. It has been suggested that hyper insulinemia can lead to angiopathy.
2. Relative insulin shortage, or the ß cells lagging behind, is brought on by an excess of the hormone (glucagon) associated with hyperglycemia and obesity. Nitric oxide metabolism anomalies leading to altered perineural blood flow and nerve injury have been shown by two theories.
3. Certain genetic flaws (type-3) that cause diabetes mellitus in rare instances include "maturity onset diabetes of young," other endocrine problems, pancreatectomy, and gestational diabetes mellitus (GDM).
4. Diabetes mellitus may be brought on by an imbalance of a particular receptor. A few examples of particular

receptors are the dipeptidyl peptidase IV enzyme, α glycosidase, beta3 (ß3) ardent-receptor, peroxisomes proliferator-activated (γ) receptor (PPARγ), and glucagon-like peptide-1 (GLP-1) receptor.

5. Advanced glycation-end products, polyol pathway, protein kinase C, and oxidative stress are the main areas of current study on diabetic neuropathy.

CLASSIFICATION OF DIABETES MELLITUS

The World Health Organization released the first widely recognized categorization of diabetes mellitus in 1980, and it was updated in 1985. The primary kind of idiopathic diabetes mellitus, which is the subject of our discussion, is the most prevalent and significant kind. It must be distinct from secondary diabetes mellitus, which encompasses hyperglycemia with known causes, such as inflammatory pancreatic diseases, surgery, tumors, some medications, iron overload (hemochromatosis), and specific acquired or genetic endocrinopathies that cause the destruction of pancreatic islets. This categorization includes hyperglycemia in other categories as well as the clinical stages and aetiological kinds of diabetes mellitus. The circumstances that exist at the moment of diagnosis are generally used to determine the type of diabetes that a person has, and many diabetics find it difficult to fall into a single class.

Hyperglycemia is a common trait across a broad set of illnesses that most likely constitutes primary diabetes mellitus. The World Health Organization used to classify diabetes mellitus into four categories: type-1, type-2, "other specific types," and gestational diabetes. These terms have since been superseded and replaced by a new classification system (WHO Expert Committee 1999). These were taken into consideration for the next International Nomenclature of Diseases (IND) in 1991 and the International Classification of Diseases (ICD-10) tenth edition in 1992. Hence, classification of diabetes mellitus is described as below.

1. Insulin Dependent Diabetes Mellitus (Type-1)

Formerly known as juvenile-onset or ketosis-prone diabetes, this type of diabetes mellitus is also known as autoimmune diabetes. The patient may also seek treatment for other autoimmune diseases, including Addison's disease, Hashimoto's thyroiditis, and Graves disease. Insulin-dependent diabetes mellitus, sometimes referred to as type-1 diabetes mellitus, is primarily seen in children and young people. Its onset is typically abrupt and can be fatal. Anti-glutamic acid decarboxylase, islet cell, or insulin antibodies that recognize the autoimmune mechanisms that result in beta-cell death are typically present in type-1 patients. Type-1 diabetes (caused by b-cell loss, which typically results in complete insulin insufficiency). The rate at which beta cells are destroyed varies greatly; in certain cases, it might happen quickly. The pancreatic ß-islets cells are destroyed, resulting in a significant shortage or absence of insulin production. Insulin injections are necessary for treatment. When fasting diabetic hyperglycemia is first discovered, 85–

90% of people with Type-1 diabetes mellitus have markers of immunological damage, such as islet cell auto-antibodies, auto antibodies to insulin, and auto antibodies to glutamic acid decarboxylase (GAD). Although the precise origin of diabetes mellitus is still unknown, auto-antibodies that damage beta-islet cells in most cases have been linked to an autoimmune process.

Causes of type-1 diabetes

It is unknown what specifically causes type-1 diabetes. It is known that your immune system, which often battles dangerous bacteria or viruses, targets and kills the cells in your pancreas that produce insulin. You end up with little to no insulin as a result. Rather than being absorbed by cells, sugar accumulates in the circulation. It is believed that a combination of environmental conditions and genetic predisposition causes type-1, yet it is still unknown exactly what those factors are. Type-1 diabetes is not thought to be influenced by weight.

2. Non-Insulin Dependent Diabetes Mellitus(Type-2)

Adult-onset diabetes is another name for type-2 diabetes mellitus. insulin resistance as a backdrop for the increasing insulin secretor malfunction (American Diabetes Association, 2014). Insulin resistance is a common symptom in people with this kind of diabetes. Both forms of diabetes are associated with long-term issues in the kidneys, eyes, nerves, and blood vessels, which are the main sources of morbidity and death from the disease. The predisposing factors are multifaceted and include obesity, sedentary lifestyle, ageing (affecting middle-aged and older persons), and genetics. Patients with these conditions are more likely to experience macrovascular and microvascular problems.

Causes of type-2 diabetes

The pancreas is unable to produce enough insulin to overcome cell resistance to the action of insulin in both type-2 diabetes and prediabetes, conditions that can progress to the disease. Rather from entering cells to be used as fuel, sugar accumulates in the circulation. Although the exact cause of this is unknown, type-2 diabetes is thought to be influenced by both genetic and environmental factors. Though not everyone with type-2 diabetes is overweight, there is a clear correlation between being overweight and the development of the disease.

3. Gestational Diabetes Mellitus

Gestational diabetes mellitus is the term used to describe glucose intolerance that develops or is diagnosed during pregnancy. Gestational Diabetes Mellitus is the term used to describe women who acquire Type-1 diabetes mellitus during pregnancy as well as women who have undetected asymptomatic Type-2 diabetes mellitus that is identified during pregnancy. diabetes mellitus during pregnancy. Long-term effects of prenatal exposure to hyperglycemia include an increased risk of obesity and type-2 diabetes in offspring born to mothers with gestational diabetes mellitus, which can develop

throughout pregnancy and go away after delivery.

Causes of gestational diabetes
The placenta makes hormones to keep your pregnancy going during pregnancy. Your cells become more insulin-resistant as a result of these hormones. In order to overcome this resistance, the pancreas often produces enough additional insulin in response. Occasionally, though, the pancreas cannot cope. This results in gestational diabetes because too little glucose enters the cells and too much remains in the blood.

4. Monogenic diabetes
Mutations in a hepatic transcription factor known as hepatocyte nuclear factor on chromosome 12 result in the most prevalent type of monogenic types of diabetes. They also called them beta cell genetic abnormalities. The early start of hyperglycemia (usually before the age of 20) is a common characteristic of several kinds of diabetes. These conditions are also known as maturity-onset diabetes of the young, maturity-onset diabetes in youth, or defects of insulin action; exocrine pancreas diseases, such as pancreatitis or cystic fibrosis; other endocrinopathies-related dysfunction; and pancreatic dysfunction brought on by medications, chemicals, or infections. Certain medications are also used in conjunction with HIV/AIDS treatment or following organ transplantation. A few families have been found to have genetic defects that prevent proinsulin from being converted to insulin; these features are inherited in an autosomal dominant way. Less than 10% of DM cases consist of these.

Causes of Monogenic diabetes
Monogenic diabetes is a rare kind of the disease caused by mutations or alterations in a single gene. Approximately 1 to 4 percent of all occurrences of diabetes in the US are monogenic types. The gene mutation that causes monogenic diabetes is typically inherited from one or both parents. There are situations where a gene mutation arises on its own, in which case neither parent carries the mutation. The majority of mutations that result in monogenic diabetes impair the body's capacity to synthesise insulin, a pancreatic protein that aids in the body's use of glucose as an energy source.

PATHOPHYSIOLOGICAL ASPECTS
Insulin insensitivity resulting from insulin resistance, decreased insulin production, and ultimately pancreatic beta-cell loss characterize type-2 diabetes mellitus. As a result, there is less glucose transported into the adipose, muscle, and liver tissues. Hyperglycemia causes an increase in the breakdown of fat. Patients with type-1 diabetes are typically not obese when their symptoms initially appear and are rather young (children or teens). There is an inherent propensity that is strongly correlated with specific histocompatibility antigens (HLA types) and has a 10-fold greater incidence in first-degree relatives of an index case. Research on identical twins has demonstrated that genetically inclined people need to be exposed to environmental factors like viral infections in addition to their genetic makeup. A viral infection can harm B cells in the pancreas and reveal antigens that trigger an autoimmune reaction that keeps happening to itself. It is not until more than 90% of the B cells are destroyed that the patient is diagnosed as having diabetes.

This kind of insulin insufficiency weakens long-term potentiation and may result in cognitive and memory impairments. Insulin resistance and decreased insulin production are associated with type-2 diabetes, both of which play significant roles in the disease's etiology. These patients are typically obese and appear in adulthood, with an increasing prevalence as B-cell activity progressively declines with age. In this case, tau hyperphosphorylation and Aβ plaque development are caused by insulin resistance. Plaque development and Aβ buildup result from insulin and Aβ competing for the insulin-degrading enzyme during hyperinsulinemia. Reduced insulin receptor signaling causes tau hyperphosphorylation, GSK-3β dephosphorylation (activation), and inhibition of Akt.
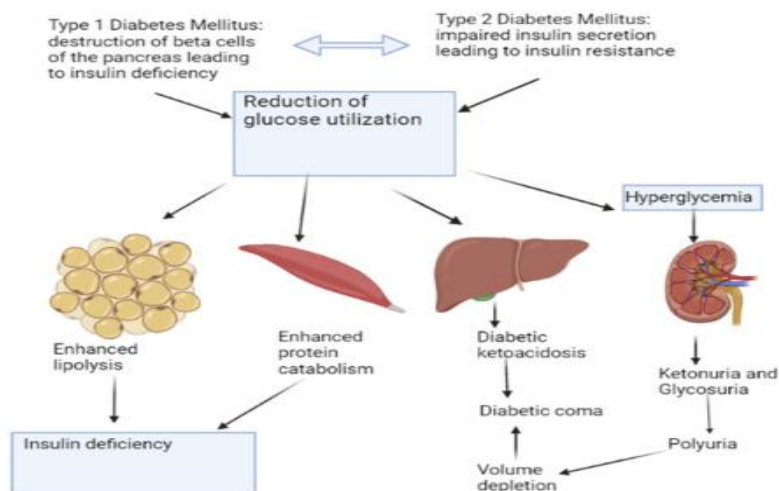

Fig. 1: Pathophysiological of Diabetes.

CONCLUSION

In modern times, diabetes mellitus is a major complication. The way of life and the conditions of the modern world are key factors in the development of these kinds of serious difficulties. When untreated, all of the metabolic conditions together referred to as diabetes mellitus cause an abnormally high blood glucose content. When the pancreas stops producing substantial amounts of the hormone insulin, it is known as diabetes mellitus type-1. This is typically caused by the autoimmune death of the pancreatic beta cells that create insulin. On the other hand, diabetes mellitus type-2 is currently believed to be caused by insulin resistance or autoimmune attacks on the pancreas. A person with type-2 diabetes may have normal, or even unusually high, insulin production from their pancreas. We learn some information about diabetes mellitus from this review. Numerous plants have been used separately or in combination to treat diabetes and its aftereffects. The lack of clarity on the active ingredients in this herbal mixture is one of its main issues. Understanding the active ingredient and its molecular interactions is crucial for both standardizing the product and analyzing its therapeutic efficacy. Currently, efforts are being made to use model systems to look at the mechanisms of action of some of these plants.

For those who have diabetes, understanding diabetes management is crucial since it aids in both disease control and the avoidance of complications.

In individuals with type-1 diabetes, maintaining normal blood glucose levels inhibits the development and progression of vascular and neurological problems. It is highly advised to follow and implement strategies like stress reduction, exercise, and diet to control type-2 diabetes. Among them, nutrition has received substantial consideration in the management of hyperglycemia in type-2 diabetes. Refined food consumption, polished cereal consumption, and fat consumption have been found to impact the early establishment of impaired glucose tolerance, which ultimately results in diabetes without any warning signs. The concomitant hyperglycemic situation may be alleviated in these cases by treating them with "insulin sensitizers" like metformin. An expert consensus statement on the management of hyperglycemia in people with type-2 diabetes was released by the American Diabetic Association and the European Association for the research of Diabetes. Type-2 diabetic patients frequently feel hopeless, have low self-esteem, and are consequently less likely to stick to their treatment plans. It is advised that hospitals set up educational programs to teach diabetic patients about food, hygiene, and following their doctors' orders about exercise, medication, and nutrition.

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