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A Review on Diabetics

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Abstract:

One of the most prevalent non-communicable diseases in the world is "diabetes mellitus". Diabetes management in India is complicated by a number of factors, such as an increase in both urban and rural incidence, a lack of public awareness of the condition, a lack of available healthcare resources, a high cost of care, and subpar treatment outcomes. management of blood sugar and an increase in the frequency of diabetes complications. Insulin treatment is the most common type of Up to four times each day, subcutaneous injections are typically used for delivery. Long-term insulin therapy has a negative impact on patient outcomes because of issues with patient compliance and the invasiveness of its administration. The prevalence of type 1 diabetes has also increased, however Type 2 diabetes mellitus is the primary contributor to the diabetic epidemic and affects more than 90% of all cases of diabetes. A dangerous and prevalent chronic condition that results from a complicated set of interaction between the environment and inheritance as well as additional risk factors like obesity and sedentary behaviour.

Keywords: Diabetes mellitus, diagnosis, cause and treatment.

Introduction: -

A chronic condition of the metabolism of proteins, lipids, and carbohydrates is known as diabetes mellitus. A hallmark of diabetes mellitus is a poor or insufficient insulin secretory response, which results in impaired utilisation of carbohydrates (glucose) and the subsequent hyperglycemias.[1] The most prevalent type of diabetes is called diabetes mellitus (DM), also known as “sugar” Endocrine condition that often manifests as a lack or deficit of insulin, but occasionally, Insulin resistance, a condition that impairs insulin activity [2]. The International Federation of Diabetes (IDF) calculates that there are approximately 40.9 million diabetes individuals in India. By 2025, number is projected to increase to 69.9 million [3].

Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the beta (ß) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan’s. Insulin decreases the blood glucose level by the glycogenesis and transport glucose into the muscles, liver and adipose tissue. Neural tissue and erythrocytes do not required insulin for glucose utilization whereas alpha (α) cells play an important role in controlling blood glucose by producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis Diabetes mellitus is a long-term disorder that affects how proteins, lipids, and carbohydrates are metabolised. A weak or insufficient insulin secretory response, which leads to impaired glucose utilisation and the associated hyperglycemias, is a defining feature of diabetes mellitus.[1] Diabetes mellitus, also known as "sugar," is the most common kind of diabetes. endocrine disorder that frequently shows signs as an insulin deficiency or shortage, but sporadically, insulin action is hampered by the condition of insulin resistance [2]. Diabetes International

Federation According to the Indian Diabetes Foundation (IDF), India has 40.9 million people who have diabetes. The number is anticipated to rise to 69.9 million by 2025 [3].In diabetes, there is an aberration either in the synthesis or secretion of insulin as seen in Type 1 diabetes mellitus (T1DM) and stenosis in the pancreatic duct, or the development of resistance to insulin or its subnormal production as in the case of Type 2 diabetes (T2DM) and certain secondary diabetes. Diabetes affected 8.5 percent of persons aged 18 and above in 2014. Diabetes was the direct cause of 1.5 million fatalities in 2019, with 48 percent of all diabetes-related deaths occurring before the age of 70. Diabetes caused a 5% increase in premature mortality rates (death before the age of 70) between 2000 and 2016.

Diabetes-related premature mortality dropped in high-income nations from 2000 to 2010, but then climbed from 2010 to 2016. Diabetes-related premature mortality increased in lower-middle-income nations over both eras.Between 2000 and 2016, the global risk of dying from any of the four major noncommunicable diseases (cardiovascular diseases, cancer, chronic respiratory diseases, or diabetes) between the ages of 30 and 70 fell by 18%.[5]

Diabetes mellitus (DM) is commonest endocrine disorder that affects more than 100 million people worldwide (6% population). It is caused by deficiency or ineffective production of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. It is found to of body systems particularly blood vessels, eyes, kidney, heart and nerves1. Diabetes mellitus has been classified into two types i.e., insulin dependent diabetes mellitus (IDDM, Type I) and non-insulin dependent diabetes mellitus (NIDDM, Type II).[8]

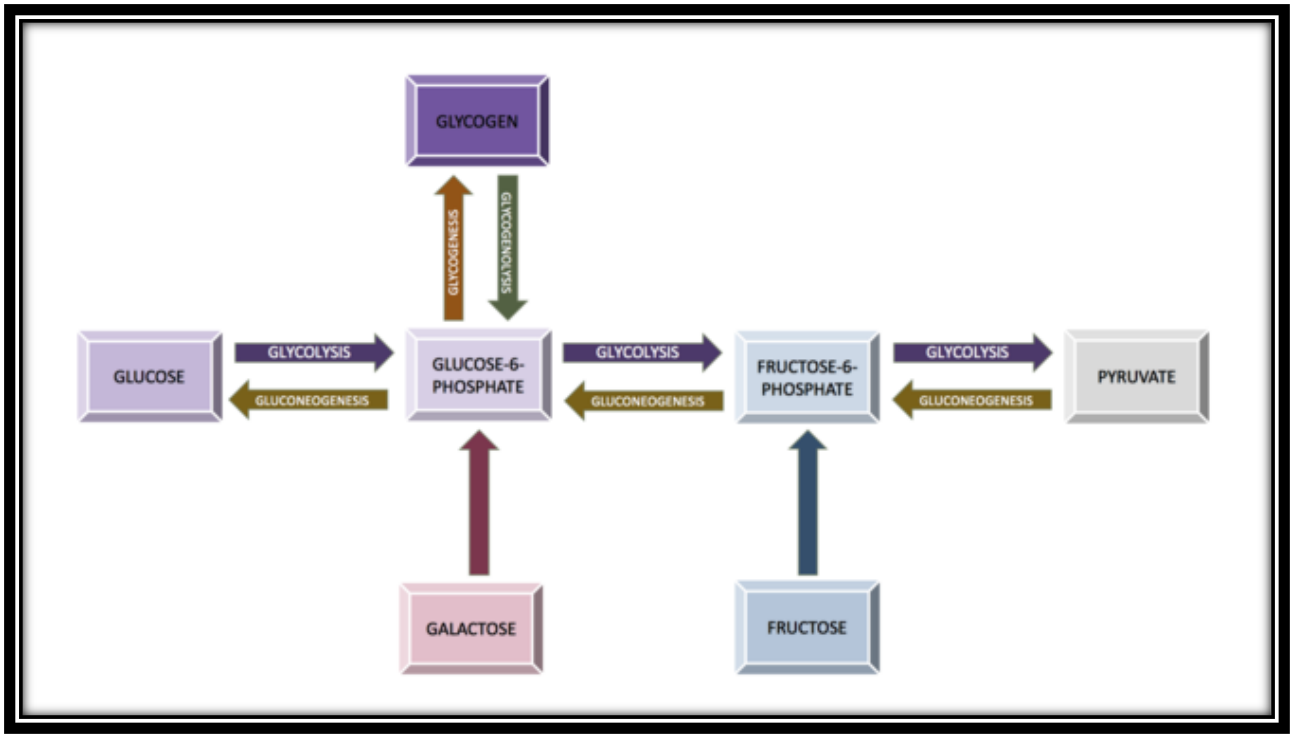


Fig 1: carbohydrate (glucose) metabolism

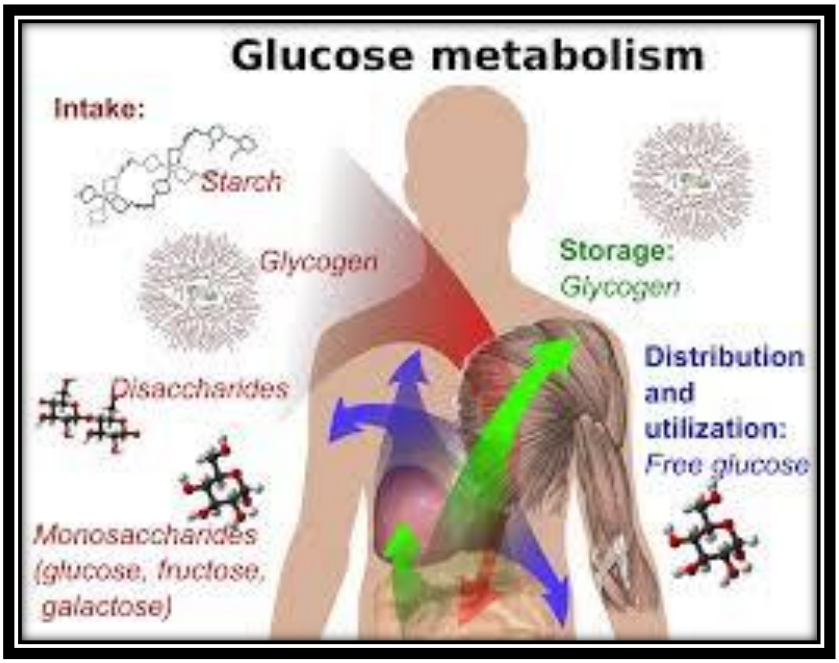


Fig 2 :(glucose) metabolism

➢ **Classification of Diabetes Mellitus**

The first mostly accepted classification of diabetes mellitus was published by WHO in the year 1980 and, it is modified in the year 1985, The most common and important form of Primary or idiopathic diabetes mellitus, which is focus of our discussion. It must be different From secondary diabetes mellitus which includes forms of hyperglycemia associated with identifiable causes in which destruction of pancreatic islets is induced by inflammatory Pancreatic diseases, surgery, tumors, certain drugs, iron overloaded (Hemochromatosis) and certain acquired or genetic endocrinopathies [1].

The classification encompasses both clinical stages and aetiological types of diabetes mellitus and other categories of hyperglycemia . Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, and many diabetic individuals do not easily fit into a single class, diabetes mellitus probably represents a heterogeneous group of disorders that have hyperglycaemia as a common feature [1].

Fig 3: Classification of diabetes mellitus

1. Insulin Dependent Diabetes Mellitus (Type1 IDDM) s

Previously known as juvenile-onset or ketosis-prone diabetes, this type of diabetes mellitus is now classified as autoimmune diabetes. The person could also look for help from others. autoimmune diseases including Hashimoto's thyroiditis and Graves' Addison's illness, thyroiditis, and kind of diabetes is sometimes referred to as IDDM, or insulin-dependent diabetic mellitus this primarily affects children and young people, and the beginning is generally unexpected and perhaps fatal.

Type 1 typically Anti-glutamic acid is a characteristic feature. Detecting decarboxylase, islet cell, or insulin antibodies the autoimmune reactions that result in beta-cell death, Type 1 diabetes, which is brought on by the death of b-cells, is resulting typically in complete insulin insufficiency) (American 2014 Diabetes Association. Beta-cell degeneration occurs at a number of different rates; in some people, it happens quickly and slowly in others, there is a serious shortage. or lack of insulin secretion as a result of ß-islet breakdown the pancreas' cells. Treatment utilising insulin injections is necessary [4].

Immune destruction markers, such as islet insulin auto-antibodies, cell auto-antibodies, and auto There are antibodies to glutamic acid decarboxylase (GAD) when people with Type 1 diabetes mellitus (85–90%) Initial detection of fasting diabetes hyperglycemia. The Although the precise origin of diabetes mellitus is yet uncertain There is evidence of an autoimmune disease in most people auto-antibody-based process that destroys the beta-the islet cells.

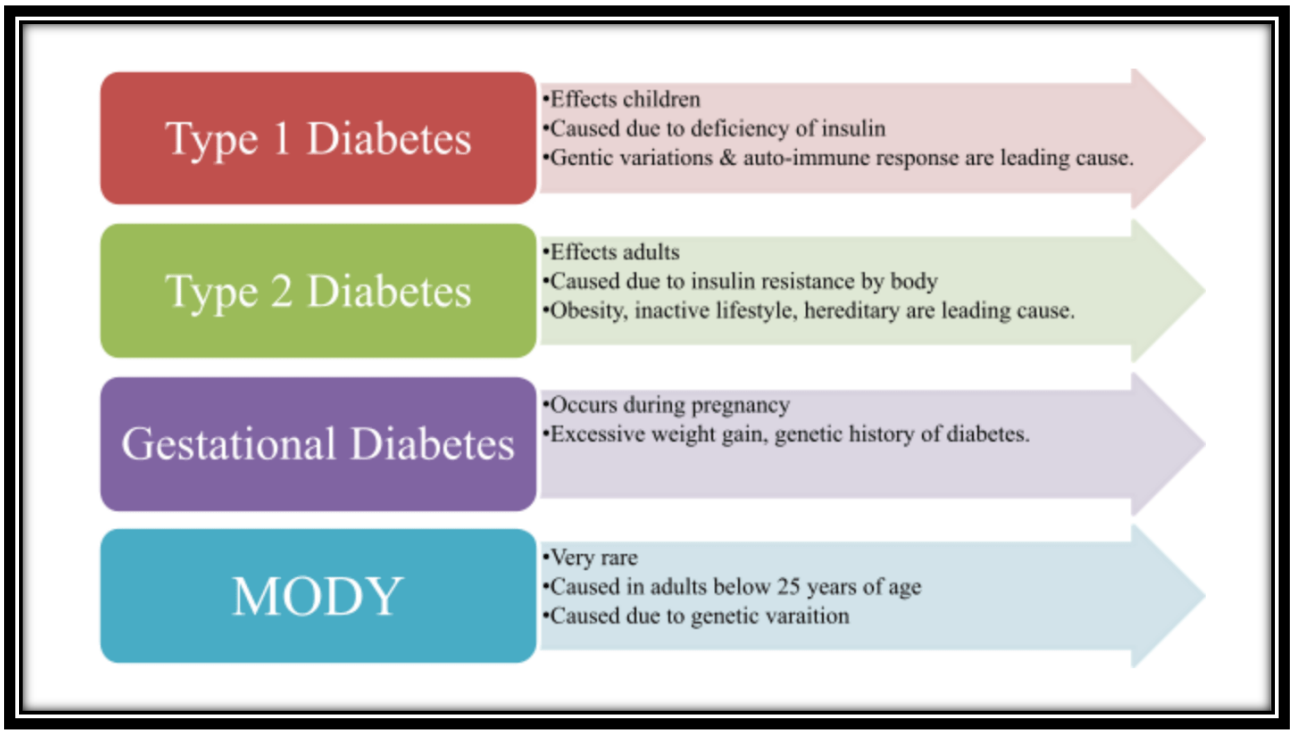


Fig No (4): - Type of diabetes mellitus

2. Non-Insulin Dependent Diabetes Mellitus (Type2 Nidd)

Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretary defect on the background of Insulin resistance (American Diabetes Association, 2014) People with this type of diabetes frequently are resistant to the Action of insulin. The long-term complications in blood Vessels, kidneys, eyes and nerves occur in both types and are the major causes of morbidity and death from diabetes [1]. The Causes are multifunctional and predisposing factor includes: Obesity, Sedentary

lifestyle, increasing age (affecting middle-Aged and older people), Genetic factor (Ross and Wilson 2010), such patients are at increased risk of developing macro-Vascular and micro vascular complications

3. Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is the term used to describe glucose intolerance that develops for the first time or is diagnosed during pregnancy. Women with Type 1 diabetes ladies who have diabetes mellitus during pregnancy and unidentified Type 2 diabetes mellitus that is asymptomatic found during pregnancy are categorised as Gestational Type 2 Diabetes (GDM). pregnant women with type 1 diabetes (GDM) (uncontrolled pregnancy-related diabetes) Diabetes are certainly over). pregnancy-related diabetes mellitus During pregnancy, several conditions may arise and then recede. extended period of time, children born to moms with GDM are more likely to develop type 2 diabetes and obesity in the future. Life is a phenomenon that is linked to intrauterine exposure to high blood sugar [21]

4. Other Specific Type (Monogenic Types)

The most common form of monogenic types of diabetes is developed with mutations on chromosome 12 in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1 They also referred to as genetic defects of beta cells. These forms of diabetes are frequently characterized by onset of hyperglycemia at an early age (generally before age of 25 years). They are also referred to as maturity onset diabetes of the young (MODY) [12] or maturity-onset diabetes in youth or with defects of insulin action; persons with diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; persons with dysfunction associated with other endocrinopathies (e.g. acromegaly); and persons with pancreatic dysfunction caused by drugs, chemicals or infections, Some drugs also used in the combination with the treatment of HIV/ AIDS or after organ transplantation. Genetic abnormalities that result in the inability to convert proinsulin to insulin have been identified in a few families, and such traits are inherited in an autosomal dominant pattern. They comprise less than 10% of DM cases [11]

➢ Some Common Sign and Symptoms

Cells with diabetes mellitus virtually starve because they are unable to metabolise glucose normally. Diabetes melilotus's long-term effects, which include escalating development of the particular retinopathy problems with possible blindness, renal failure-causing nephropathy and neuropathy, Charcot joint, and risk of foot ulcer characteristics of sexual dysfunction and autonomic dysfunction, Diabetes raises a person's risk for disease.

Other, various symptoms are observed due to-

I. . Gluconeogenesis from amino acids and body protein, causing muscle wasting, tissue breakdown and further increases the blood glucose level.

II. Catabolism of body fat, releasing some of its energy and excess production of ketone bodies [2]

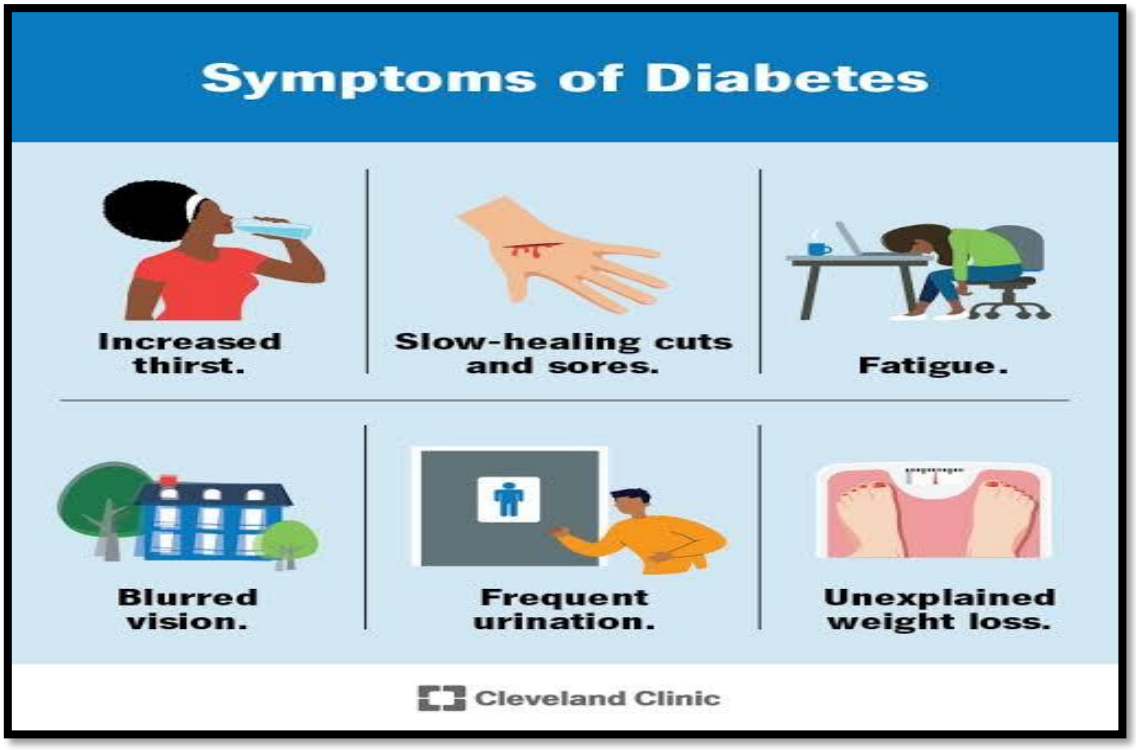


Fig No (5): - Sign and symptoms of diabetes mellitus

➢ **Etiology of Diabetes Mellitus**

The word etiology is derived from Greek word "aetiologia". Hence, etiology is defined as the science of finding causes andorigins in which a disease is arise, it includes –

1. It is currently believed that the juvenile-onset (insulin dependent) form has an auto immune etiology.
2. Viruses may also play a role in the etiology of diabetes like coxsackieB.
3. Mumps and rubella viruses all have been shown to produce morphologic changes in the islet-cell structure.
4. The genetic role in the etiology of diabetes is controversial. Possibly a genetic trait makes an = individual's pancreas more susceptible to one of the above viruses [15].

Type	Etiology
Type 1	Diabetes (cell destruction, usually leading to absolute insulin deficiency) immune mediated, idiopathic
Type 2	Diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
Others	Genetic defects of cell function
	Genetic defects in insulin action
	Diseases of the exocrine pancreas
	Drug or chemical-induced
	Infections
	Uncommon forms of immune-mediated diabetes
	Gestational DM

DM: Diabetes mellitus

Fig no. 6: Etiology of diabetes mellitus

➢ **Causes of Diabetes Milliteus**

ß cell gluco-receptor disturbances or abnormalities that cause them to respond to greater glucose concentrations or a relative ß cell deficit. Insulin secretion is compromised either way; may eventually lead to ß cell failure. The principal-agent hypothesis in micro brain hypoxia brought on by vascular disease, and the direct metabolic consequences of hyperglycaemia on neurons.

1. Reduced sensitivity of peripheral tissues to insulin: reduction in number of insulin receptors, 'down regulation' of insulin receptors. Many hypersensitive and hyperinsulinaemic, but normal glycaemic; and have associated dyslipidaemia, hyperuricaemia, abdominal associated dyslipidaemia, hyperuricaemia, abdominal obesity. Thus, there is relative insulin resistance, particularly at the level of liver, muscle and fat. Hyperinsulinaemic has been implicated in causing angiopathy [14].

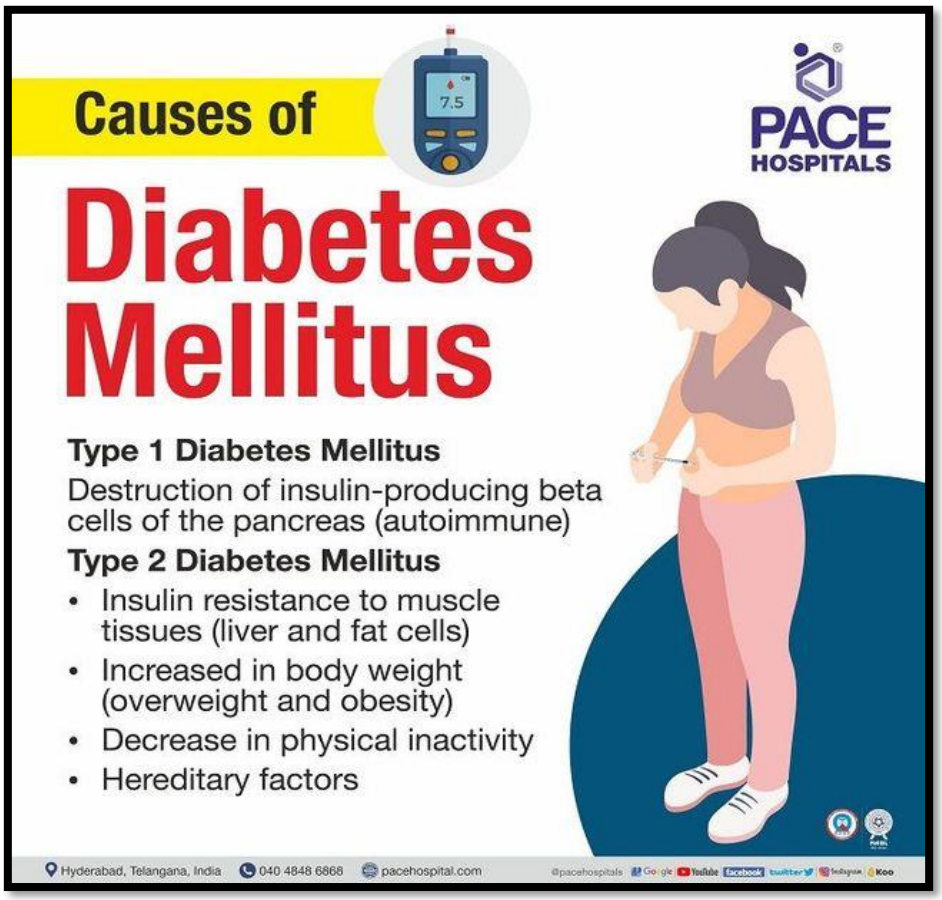


Fig no. 7 causes of diabetes mellitus

2. Excess of hyperglycaemia hormone (glucagon) etc. /obesity; causes relative insulin deficiency –the ß cells lag behind. Two theories have demonstrated abnormalities in nitric oxide metabolism, resulting in altered perineural blood flow and nerve damage [15].

3. Other rare forms of diabetes mellitus are those due to specific genetic defects (type 3) like "maturity onset diabetes of young" (MODY) other endocrine disorders, pancreatectomy and gestational diabetes mellitus (GDM). [14].

4. Due to imbalance of specific receptor can cause diabetes mellitus. Some specific receptors are Glucagon-like peptide-1(GLP-1) receptor, peroxisomes proliferator-activated (γ) receptor (PPARγ), beta3 (ß3) ardent-receptor some enzymes like α glycosidase, dipeptidyl peptidase IV enzyme etc [14].

5. Current research on diabetic neuropathy is focused on oxidative stress, advanced glycation-end products, protein kinase C and the polyol pathway [16].

➢ **Diagnosis of Diabetes Mellitus**

Never base a diabetes diagnosis in a client who is asymptomatic on a single abnormal blood glucose reading. When diabetes is identified, the doctor must consider the diagnosis to be fully established because the the effects on the person are severe and long-lasting. Diabetes mellitus diagnosis criteria include urine sugar, glucose tolerance test, renal glucose threshold, blood sugar a reduced tolerance to glucose, an enhanced tolerance to glucose, prolonged glucose tolerance curve, corticosteroids, and renal glycosuria glucose tolerance test under stress and intravenous glucose tolerance glucose tolerance test administered orally**.**

TABLE 2

DIAGNOSING DIABETES

	A1C (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes*	6.5 or above	126 or above	200 or above
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Normal	About 5	99 or below	139 or below

Fig no. 7 diagnosing diabetics

➢ **Treatment**

The treatment is to overcome the precipitating cause and to give high doses of regular insulin. The insulin requirement comes back to normal once the condition has been controlled, the aims of management of diabetes mellitus can be achieved by:

1. To restore the disturbed metabolism of the diabetic as nearly to normal as is consistent with comfort and safety.
2. To prevent or delay progression of the short-term and long-term hazards of the disease.
3. To provide the patient with knowledge, motivation and means to undertake this own enlightened care.

A. Types of Therapy Involved in Diabetes Mellitus

1. Stem cell therapy

Monocytes and macrophages may have a major role in these chronic inflammations and insulin resistance in T2DM patients, according to research [28]. educator for stem cells Therapy is a cutting-edge technique intended to prevent or reverse immunological system issues [29]. The process entails collection. in which the blood of patients is circulated in a closed loop, co-culture, lymphocyte purification from whole blood of them with adherent multi-potent stem cells obtained from cord blood injection of the educated cells (CB-SCs) in vitro lymphocytes into the patient's circulation, but not CB-SC [19].

2. Antioxidant therapy

A variety of antioxidants, such as vitamins, supplements, plant-derived active substances and drugs with antioxidant effects, have been used for oxidative stress treatment in T2DM patients. Vitamin C, vitamin E and β carotene are ideal supplements against oxidative stress and its complications. [30] Antioxidant which play an important role in lowering the risk of developing diabetes and its complications.

3. Anti-inflammatory treatment

The changes indicate that inflammation plays a pivotal role in the pathogenesis of T2DM and its complications [31, 32]. In T2DM, especially in adipose tissue, pancreatic islets, the liver, the vasculature and circulating leukocytes, [33] which include altered levels of specific cytokines and chemokines, the number and activation state of different leukocyte populations, increased apoptosis and tissue fibrosis. [33, 34] immunomodulatory drug is provided.

B. Dietary Management

Adequate caloric value Dietary management should be taken properly by the both diabetic and non-diabetic patient such as:

1. Balanced in regard to protein, carbohydrate and fats, in all cases it is necessary to restrict carbohydrate intake.
2. Should conform as closely as possible to normal
3. Food intake should be divided into regularly spaced meals of similar size
4. Reduce total calorie intake by decreasing both fat and carbohydrate
5. Patient must be advised to be constant in his dietary habits from day to day.

C. Newer Insulin Delivery Devices

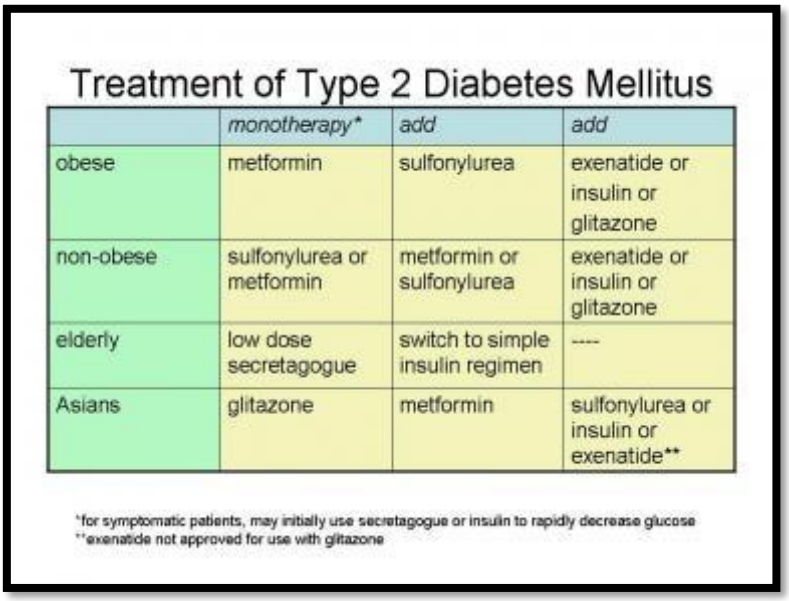
A number of innovations have been made to improve ease and accuracy of insulin administration as well as to achieve tight glycaemia control. These are insulin syringes, pen devices, inhaled insulin, insulin pumps, implantable pumps, other routes of insulin delivery.

D. Oral Hypoglycaemic or Antidiabetic Agents

The goal of insulin therapy should be to replicate nature, which is very effective at preventing between-meal hypoglycaemia and minimising postprandial hyperglycemia26. The location of the insulin injection is crucial for the efficient and secure action of the drug, and it can be administered intravenously or intramuscularly route. There are numerous insulin formulations available, including human, beef, and pork insulin. The use of insulin is not without risks and side effects. The most significant negative effects include weight gain and low blood sugar when an incorrect insulin dose is used and when there is an imbalance between a meal and an insulin shot. Weight gain after starting insulin therapy for uncontrolled diabetes is an inevitable consequence and is the result of increased truncal fat and muscle bulk. This is also due to reduced energy losses through glycosuria 29,30. Sulphonyl urea's such as glibenclamide, glipizide and biguanides such as metformin, phenformin are oral hypoglycemic drugs.

Sulfonylureas cause hypoglycaemia by stimulating insulin release from pancreatic ß-cells. They bind to sulfonylurea (SUR) receptors on the ß-cell plasma membrane, causing closure of adenosine triphosphate (ATP)-sensitive potassium channels, leading to depolarization of the cell membrane. This in turn opens voltage-gated channels, allowing influx of calcium ions and subsequent secretion of preformed insulin

granules. Acute administration of sulfonylureas to type 2 DM patient's increases insulin release from the pancreas and also may further increase insulin levels by reducing hepatic clearance of the hormone. Initial studies showed that a functional pancreas was necessary for the hypoglycemic actions of sulfonylureas31. Biguanides such as metformin is antihyperglycaemic, not. hypoglycemic. It does not cause insulin release from the pancreas and does not cause hypoglycaemia, even in large doses33. It has been shown to increase peripheral uptake of glucose, and to reduce hepatic glucose output by approximately 20-30% when given orally but not intravenously. Impaired absorption of glucose from the gut has also been suggested as a mechanism of action.



- **Herbal treatment of diabetes**

In the last few decades eco-friendly, bio-friendly, cost effective and relatively safe, plant-based medicines have moved from the fringe to the main stream with the increased research in the field of traditional medicine. There are several literature reviews by different authors about anti-diabetic herbal agents, but the most informative is the review by Atta-are-Rahman who has documented more than 300 plant species accepted for their hypoglycaemicproperties. This review has classified the plants according to their botanical name, country of origin; parts used and nature of active agents. One such plant is Momordicacharantia (Family: Cucurbitaceae)37. WHO has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called the botanical garden of the world38.

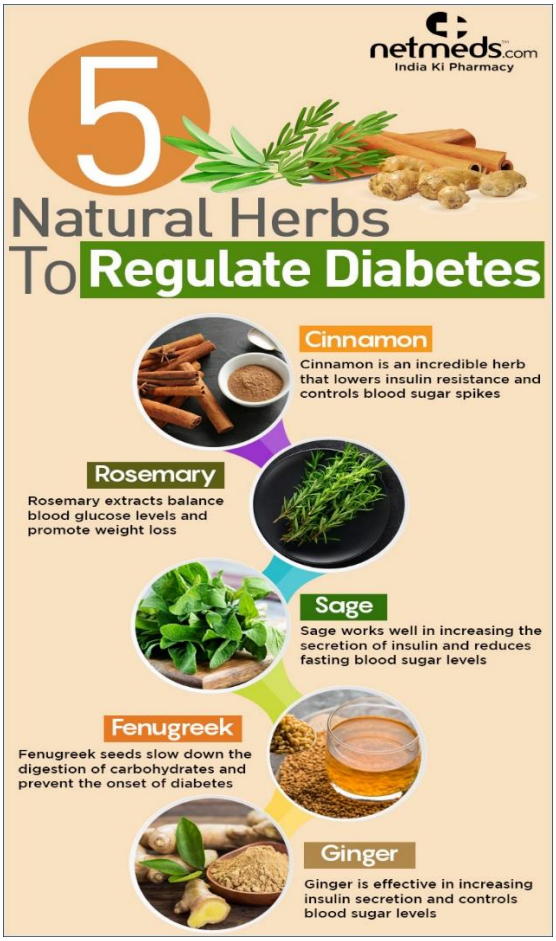


Fig no 8: herbal treatment

➢ **Market Overview:**

IMARC's new report "**Indian Diabetes Market Report: Patients, Prevalence, Oral Antidiabetics, Insulin and Diagnostics**" provides an analytical and statistical insight into the Indian diabetes market. The report provides both current and future trends in the prevalence, demographical breakup, diagnosis and treatment of diabetes in India. The report has segmented the Indian diabetes market into three segments - Oral Antidiabetics, Insulin and Diabetes Diagnostics. For each of the aforementioned categories, the report provides historical and future market sales, performance of key classes and the performance of top players.

The research study serves as an exceptional tool to understand the epidemiology, market trends, therapeutic structure, competitive structure and the outlook of the Indian diabetes market. This report can serve as an excellent guide for investors, researchers, consultants, marketing strategists and all those who are planning to foray into the Indian diabetes market in some form or the other.

Fig no. 9 marketed formulation

➢ CONCLUSION

The term diabetes mellitus includes several different metabolic disorders that all, if left untreated, result in abnormally high concentration of a sugar called glucose in the blood. Diabetes mellitus type 1 results when the pancreas no longer produces significant amounts of the hormone insulin, usually owing to the autoimmune destruction of the insulin-producing beta cells of the pancreas. Diabetes mellitus type 2, in contrast, is now thought to result from autoimmune attacks on the pancreas and/or insulin resistance. The pancreas of a person with type 2 diabetes may be producing normal or even abnormally large amounts of insulin. The main goal of diabetes management is, as far as possible, to restore carbohydrate metabolism to a normal state. To achieve this goal, individuals with an absolute deficiency of insulin require insulin replacement therapy, which is given through injections or tablets. Insulin resistance, in contrast, can be corrected by dietary modifications and exercise. Other goals of diabetes management are to prevent or treat the many complications that can result from the disease itself and from its treatment. By keeping the blood sugar level under control, diabetes can become patient's companion and he/she can enjoy life joyfully.

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