Diabetes Mellitus: The Silent Sweet Enemy

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Abstract

Diabetes mellitus, a group of metabolic disorders characterized by defective insulin secretion or either insulin action, is becoming more and more common worldwide. It is primarily caused by the pancreas not producing enough insulin or by the body becoming resistant to the insulin, which results in hyperglycaemia (increased blood glucose) and disrupts the metabolism of fat, carbohydrates, and protein. Most people are not aware of their blood glucose levels, which can lead to life-threatening situations. If left untreated, diabetes mellitus can cause serious side effects like retinopathy, neuropathy, nephropathy, and cardiovascular diseases. Improving patient outcomes and minimizing complications need early diagnosis, lifestyle changes, and proper medical management. This review focuses on diabetes melilotus's pathophysiology, etiology, risk factors, symptoms, complications, and management techniques.

Graphical Abstract
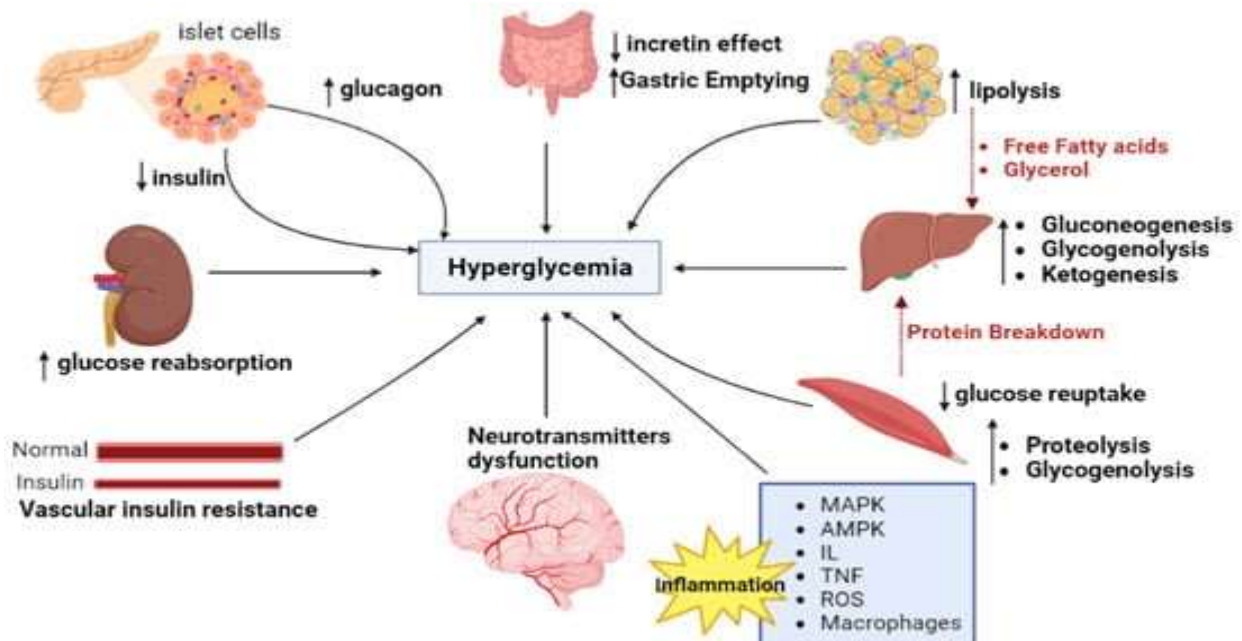
History of Diabetes mellitus:

Diabetes mellitus has a long history that dates back to antiquity. Charaka, Samhita, and Sushruta Samhita are among the ancient Sanskrit literature that describe the ailment known as "Madhumeha." Madhumeha means "honey urine," and the ants are drawn to the honey's taste. It is thought to be among the first documented cases of diabetes mellitus.[1]

Epidemiology: -

Diabetes mellitus, a chronic metabolic disease, is a rapidly expanding global issue with significant social and health ramifications. It is estimated that 285 million people worldwide (about 6.4% of the adult population) suffered from this illness in 2010. Without better management or treatment, this number is predicted to rise to 430 million. Two primary causes of the rise are obesity and an aging population. Additionally, it has been demonstrated that nearly half of those suspected of having diabetes do not receive a diagnosis until ten years after the disease first manifests; therefore, the true prevalence of diabetes must be extremely high worldwide.[2] Diabetes mellitus affected around 415 million persons aged 20 to 79 in 2015, according to the International Diabetes Federation (IDF). This number is predicted to increase to an additional 200 million by 2040, demonstrating that diabetes is a global public health concern.[3]

Introduction

Diabetes mellitus is defined as a metabolic disorder in which the level of the blood glucose is elevated. It is termed an endocrine disorder because it mainly affects the normal functioning of the pancreas, a gland that is responsible for the production of insulin. Insulin is a hormone that is responsible for the regulation of blood sugar levels. Diabetes mellitus is of several types, including type 1 diabetes, type 2 diabetes, gestational diabetes mellitus, or prediabetes [4] Retinopathy, neuropathy, nephropathy, and cardiovascular difficulties are among the serious consequences of diabetes that are guaranteed to rise as the disease progresses due to tissue or vascular damage. Diabetes mellitus is of several types, including type 1 diabetes, type 2 diabetes, gestational diabetes mellitus, or prediabetes [2]
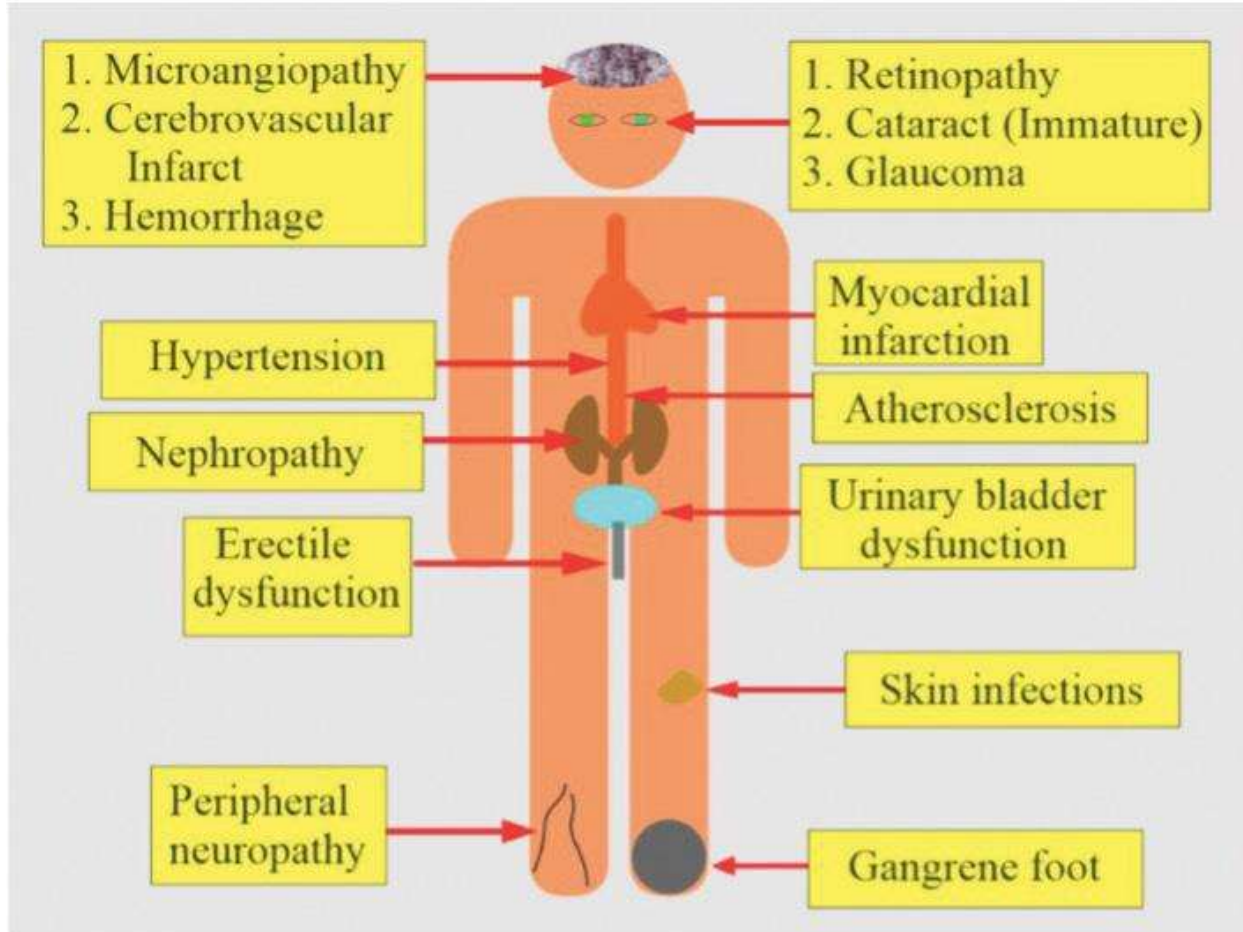
Figure1.: Diabetes a silent killer

Type1 diabetes mellitus: - It is also known as insulin-dependent diabetes mellitus or juvenile diabetes mellitus. It is an autoimmune disease in which the insulin-producing beta cells of the pancreas are destroyed. The beta cells of the pancreas are responsible for the insulin production that maintains the level of glucose. It is rapidly developing, and this type of diabetes accounts for 10% of people. It is most commonly present in children and adolescents. However, the causes are unknown, but it may be due to genetics.[5][6]

Type2 diabetes mellitus: -It is one of the most prevalent metabolic diseases; type two diabetes mellitus is brought on by a combination of two main factors: the pancreatic beta cells, impaired ability to secrete insulin and the tissues incapacity to react to insulin as they should since insulin activity and release are necessary for maintaining glucose homeostasis. It is becoming more prevalent in kids and young adults.[7]

Gestational diabetes: -gestational diabetes (i.e. diabetes during pregnancy) was originally mentioned by Bennewitz in 1823. He believed that the diabetes is a temporary pregnancy symptom after two pregnancies, all the symptoms and glycosuria vanished this is confirmed by

his theory.[1] It is a metabolic disorder that occurs during pregnancy that causes an increase in blood glucose level due to the hormones produced by the placenta, causing difficulty in the metabolism of sugar.[8]

Prediabetes: -a fasting glucose level of 100-125mg/dl is indicative of pre-diabetes, a condition that lies between the normal glucose management and diabetes [9] This condition is characterized by beta cell malfunction and insulin resistance. Most people with prediabetes are not aware that they have a condition; consequently, it is crucial to identify the related diseases, especially when mild hyperglycemia is present; therefore, early treatments may be beneficial to them.[10] People with prediabetes might delay or avoid type 2 diabetes by following evidence-based lifestyle regimens that promote dietary modifications and modest weight loss. In order to stop the disease from getting worse, anyone exhibiting signs and symptoms of prediabetes should have their type 2 diabetes evaluated.[11]

Etiology: -

A group of illnesses known as diabetes mellitus causes abnormalities in the metabolism of carbohydrates, which leads to unwarranted hyperglycemia. Depending on their insulin needs, the majority of people with this illness can be divided into one or two groups. Insulin-dependent diabetes mellitus is the most recent diagnosis for people who need insulin therapy to stay alive, whereas non-insulin-dependent diabetes mellitus is the diagnosis for people who can live without insulin treatment.[12]

Type1 Diabetes mellitus

The pancreatic islets of Langerhans include two primary subclasses of endocrine cells. Beta cells that produce insulin and glucagon Alpha cells that secrete hormones and alpha and beta cells continuously adjust their levels according to their glucose levels. become unnecessarily biased; hyperglycemia results from diabetes mellitus when insulin is either absent or acts poorly (insulin resistance) [4]

Genetics association of type1 Diabetes mellitus: -

Type 1 diabetes mellitus has an unclear origin; however, some human leukocyte antigens, including the HLA alleles DR and DQ, are closely linked to hereditary susceptibility. About 40% of the familial aggregation of type 1 diabetes mellitus has been attributed to HLA genes. In type 1 diabetes mellitus, the HLA class 2 DRB1-DQA1-DQB1 genotype confers the high genetic risk factors.[13]

Autoimmunity: -

Pancreatic beta cells autoantigens are the target of several T1D-related autoantibodies, which course immune mediated beta cell death. Antigens in the cytoplasm of islets (ICA), insulin (IAA), glutamic acid decarboxylase isoform 65 (GAD65), insulinoma antigen 2/islets tyrosine

phosphate 2 (IA-2), and zinc transporter isoform 8 (ZnT8) are among the targets of autoantibodies. The majority of IAAS are found in youngsters. The most prevalent antibody seen in adults is GAD65. It is crucial to test for autoantibodies to pancreatic beta cell autoantigen in order to confirm the diagnosis and differentiate type 1 diabetes from other types of diabetes, primarily type 2 diabetes. An increased risk of type 1 diabetes is associated with both the quantity of detectable antibodies and their titers.[13]

Environmental factors: -

Numerous illnesses during pregnancy and after delivery, such as rubella, shingles, and chickenpox. It raises the risk of diabetes mellitus and some pollutants such as POPs and DDT. Perhaps somewhat to blame for diabetes.[14]

Type2 Diabetes mellitus: -

Beta cells in the pancreas are the cause of impaired insulin creation in type 1. Diabetes is operating because of resistance to intestinal hormones that promote insulin's secretion, lipotoxicity, and glucotoxicity. Insulin-resistant peripheral organs such as the kidney and the liver muscles decrease blood glucose absorption. Excessive renal glucose absorption raises gluconeogenesis, which in turn causes hyperglycemia. Lipid buildup, endoplasmic reticulum stress, dysfunction of mitochondria, inflammation, and genetic abnormalities are the reasons behind the resistance of insulin or impaired insulin action.[15]

Contributing factors are: -Genetic predisposition: -

More than 20 years ago, a well-known study of identical twins in the United Kingdom demonstrated the genetic connection. It discovered that there was nearly a 100% concordance rate for this condition, meaning that if one twin developed type 2 diabetes mellitus, the other twin would also develop it.[7][16]

Insulin resistance: -

Muscles, liver, and adipose tissues are examples of peripheral tissues that lose their sensitivity to insulin. Result in increased hepatic glucose synthesis and decreased glucose absorption. Strongly linked to physical inactivity and obesity.[16]

Beta-cell dysfunction: -

Insulin secretion decreases as pancreatic beta cell activity gradually declines. Main result from inflammation, lipotoxicity (high free fatty acids), and glucotoxicity (chronic elevated blood sugar).[17]

Obesity and lifestyle factors: -

Increasing the release of inflammatory cytokines and free fatty acids is one way that central (visceral) obesity leads to insulin resistance. Muscles that lead sedentary lives absorb less glucose. Insulin resistance is caused by an unhealthy diet that includes processed meals, high-calorie food, and sugary drinks.[18]

Gestational diabetes

Significant insulin resistance is brought on by the release of placental hormones. The main hormone linked to elevated insulin resistance is human placental lactogen, which also promotes insulin secretion and beta cell proliferation to control maternal hyperglycemia in healthy pregnancy. On the other hand, maternal pancreatic beta cell malfunction or delayed beta-cell response occurs in individuals with gestational diabetes mellitus due to certain diseases or events that lower insulin's secretion and eventually cause maternal hyperglycemia. Maternal obesity in the early stages of pregnancy is another factor that contributes to unusually elevated insulin resistance because it raises free fatty acid levels, which prevents the mother from absorbing glucose and enhances hepatic gluconeogenesis.Some research on gestational diabetes mellitus also identified evidence of a genetic cause. A few comparable genetic effects have also been linked to gestational diabetes mellitus, although the main focus has been on the link between type 2 diabetes and genetic mutations. MTNR1B, TCF7L2, HKDC1, GCKR, PPP1R3B, and IRS1 are among the genetic variants linked to insulin secretion, glucose metabolism, and insulin resistance that have been discovered in patients with type 2 diabetes and linked to gestational diabetes mellitus in a number of studies. These result in a similar underlying cause.[19]

Prediabetes: -The condition is characterized by beta cell malfunction and insulin resistance. Pre-diabetes is linked to related conditions that are usually only taken into account when diabetes is already present. Include cancer, fatty liver disease, metabolic syndrome, low testosterone, obstructive sleep apnea, cognitive dysfunction, microvascular disease, cardiovascular diseases, periodontal disease, and metabolic syndrome.

The following factor put the patient at greater risk:

Overweight and obesity (especially a body mass index greater than 25 kg/m²)

Lack of physical activity

Increased blood pressure

-Gestational diabetes (diabetes during pregnancy)

- PCOS (polycystic ovarian syndrome)

Hyperlipidemia [20]
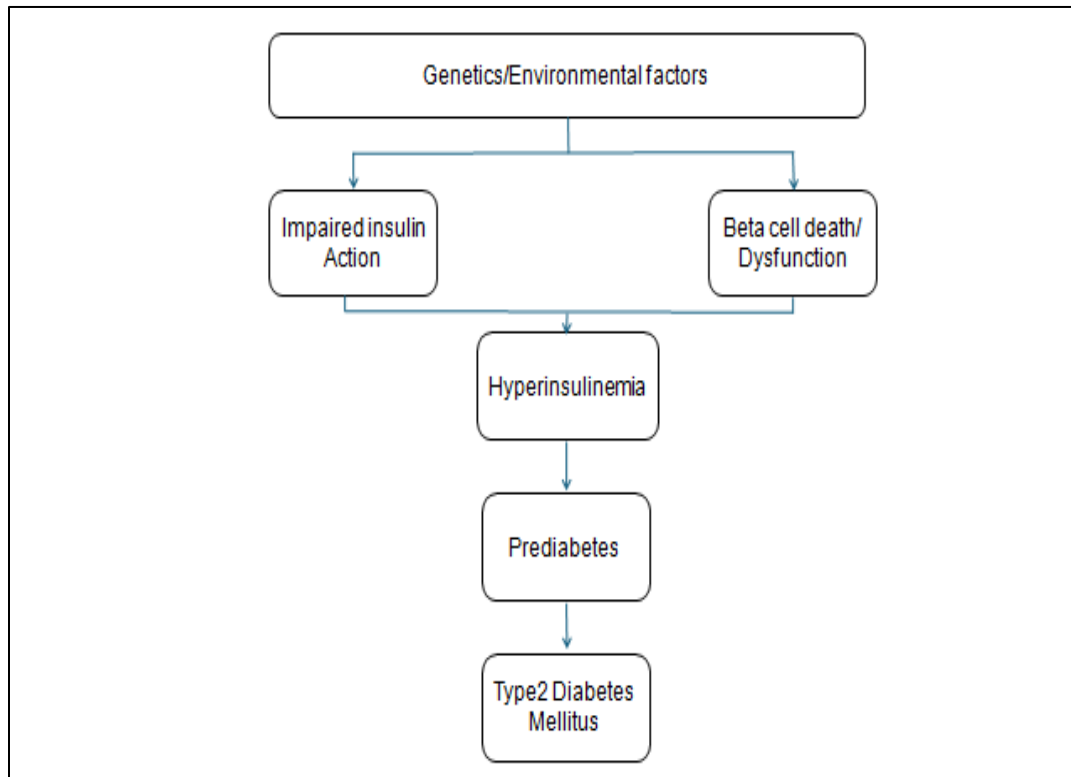
Pathogenesis of diabetes mellitus: -

Depending on the type, diabetes has different pathophysiology. Insulin production is reduced or nonexistent in Type 1 Diabetes Mellitus (T1DM) due to the destruction of pancreatic beta cells by an autoimmune reaction. The cells in the body do not react to insulin as well in Type 2 Diabetes Mellitus (T2DM). At first, this results in more insulin being produced, but eventually, the beta cells of the pancreas malfunction, which leaves the secretion of insulin insufficient.

**Figure no.2: Pathogenesis of type1 Diabetes mellitus [21]**
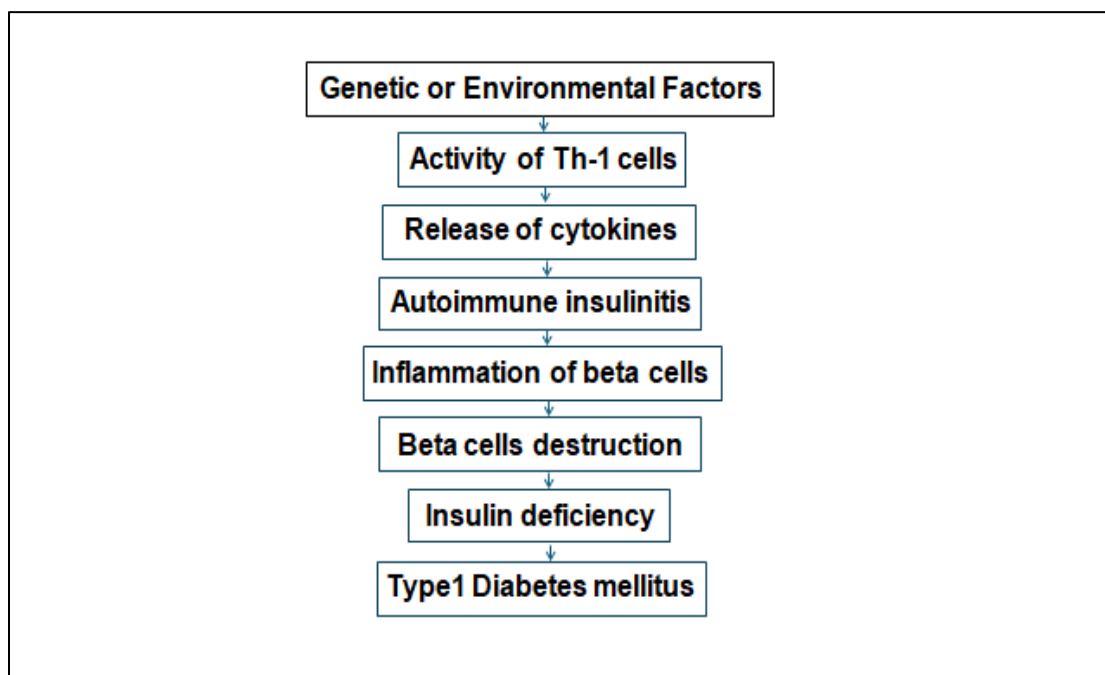
pathogenesis of type2 diabetes mellitus and prediabetes[21]

Pathogenesis of gestational diabetes mellitus

Insulin resistance and insufficient insulin production during pregnancy or give factor in pathophysiology of gestational diabetes mellitus hormonal changes during the pregnancy such as elevated level of hormones interfere with the insulin signaling.[19]
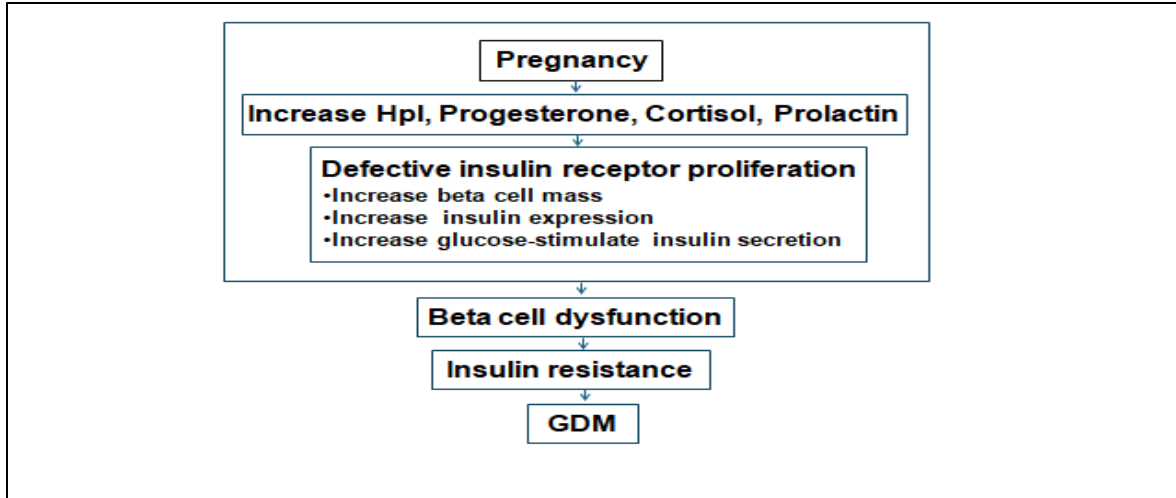
Signs and symptoms of Diabetes mellitus: -

The type 1 diabetes mellitus and type 2 diabetes mellitus contributed to the similar warning indicators. While the symptoms in type 1 diabetes mellitus come quickly as compared to type 2 diabetes mellitus. The signs and symptoms are as follows: **Tiredness and fatigue:You may also feel more exhausted than normal if you're not getting enough insulin and glucose.**

Polyurea: The normal individual needs to urinate 4-7 times in a 24-hour period, but diabetics need to urinate much more frequently. Because normal glucose reabsorption occurs when it moves through the kidney. Your kidney might not be able to replenish blood sugar when diabetes raises it. The body needs for you to produce more urine as a result of this. This means you need to go more frequently.

Weight loss: You may become extremely thirsty as a result of your frequent urination. Depending on whether a person has type 1 or type 2 diabetes, there are a number of reasons why they may lose weight. (a) Insulin-producing cells are attacked by the immune system in type 1 diabetes, which results in little or no insulin in the body. Rapid weight loss results from the body breaking down muscle and fat for energy when insulin is not present, but she cannot observe glucose for energy. Weight loss is further exacerbated by frequent urination and dehydration brought on by excess glucose leaking into the urine.

(b) The body perceives starvation because insulin resistance stops glucose from entering the cell. Weight loss occurs gradually as a result of increased fat and muscle breakdown for energy. in a 24-hour period, but diabetics need to urinate much more frequently. Because normal glucose reabsorption occurs when it moves through the kidney. Your kidney might not be able to replenish blood sugar when diabetes raises it. The body needs for you to produce

Mood fluctuation: Diabetic patients frequently experience more swings as a result of hormonal imbalance, emotional stress, and variation in blood sugar levels. Mood control can also be affected by hormonal changes, such as those in insulin and cortisol, and neurotransmitters like dopamine and serotonin. Moreover, mood swings are exacerbated by sleep problems brought on by variable glucose level.

Blurred vision: Variation in blood sugar level impacts the eyes, causing blurred vision in diabetics. When blood sugar levels are excessively high, too much glucose gets into the lens of the eyes, attracting water and making it swell. This modifies the curvature of the lens, making it harder to focus and produce blurriness. diabetes over time can cause diabetic retinopathy. Which damages the blood vessel in the retina and causes vision loss.

Slow wound healing: High blood sugar levels in diabetes caused damage to blood vessels and hindered circulation. Which is the primary cause of slow wound healing. The healing process is slowed down by poor circulation, which lowers the wound's availability of oxygen and nutrients.[22][23]

Gestational diabetes mellitus signs and symptoms: -Gestational diabetes typically shows no overt symptoms. However, some women make experience is some symptoms such as
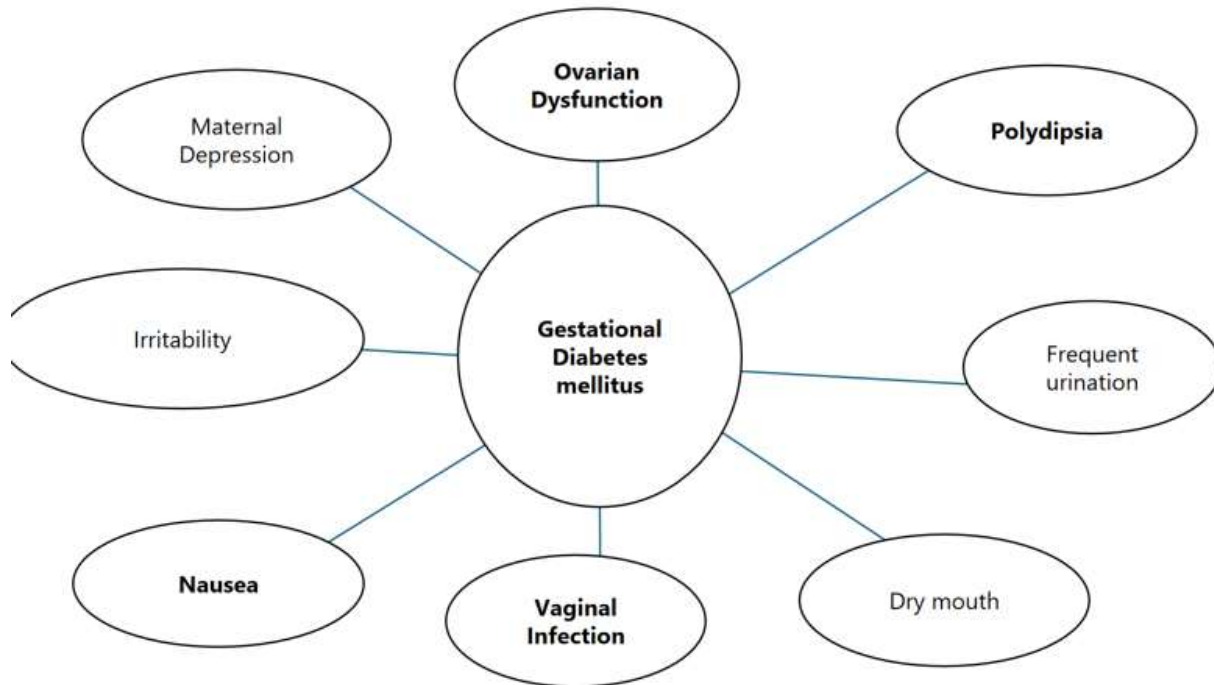
Figure no.3: Risk factors of Diabetes mellitus: -

Type1 Diabetes mellitus

The etiology is believed to be type 1 diabetes mellitus by autoimmune response (an unintentional attack on the body). The prevention of type 1 diabetes is unknown; there are established risk factors that reduce the likelihood of developing type 1 diabetes.

Genetics: The condition type one diabetes is inherited. Individuals who carry a specific gene are more likely to acquire type 1 diabetes. The risk of acquiring type 1 diabetes is 30-70% for identical twins if one twin has it. Diseases of the pancreas: Diseases include chronic pancreatitis, cystic fibrosis, and many more. Environment: Diet, vitamin D exposure, obesity, viral exposure, and a decrease in the richness of gut microbiome are among environmental factors that contribute to developing type 1 diabetes.Age: all Though it can appear at any age, children, teenagers, and young adults are most likely to have it.[24][25]

Prediabetes & type2 Diabetes mellitus: -

Diabetes type 2 and pre diabetes nearly every risk factor is the same. You are at an increased risk of developing type2 diabetes if you already have Prediabetes.

Factors that increasing the risk of developing pre diabetes and type two diabetes includes: -

(a)Environmental factors

(b)Obesity

(c)genetics

(d)gestational diabetes (i.e diabetes in pregnancy)

(e) Hyperlipidemia

(f) Hypertension [26]

Gestational diabetes

Risk factors for gestational diabetes mellitus include:

(a) Overweight: A person who has a body mass index (BMI) over 25 is considered obese, which gives rise to various diseases, including diabetes.

(b) Family history of type 2 diabetes: - It can pass from one generation to another if the individual carries certain genes.

(C) Age: Age more than 25 is considered to be a risk factor for developing diabetes.

(d) Birth weight: The risk is increased when a baby weighs more than 9 pounds.

(e) PCOS: PCOS is defined as polycystic ovarian syndrome. It is a hormonal disorder that is considered to be your risk factor for diabetes.[8]

Diagnosis of Diabetes mellitus [27] Blood test: -

Test name	Description	Range
Fasting plasma glucose test	After atleast eight hours of fasting,your blood sugar levels is measured.	Less than 100mg/dl
Random plasma glucose test	Calculate your body's sugar content at any time of the day	125mg/dl or less
Oral glucose tolerance test	Evaluate the efficiency of your body's sugar processing.it can assist the diagnosis of Diabetes and GDM.	less than (140mg/dl)

Treatment of Diabetes mellitus

Insulin therapy: -insulin and oral hypoglycemic medications because nature is so effective at preventing hypoglycemia in between meals and reducing hyperglycemia therapy should try to emulate it. Insulin injections can be administered intramuscularly or intravenously, and the site of delivery is equally crucial for better and safer effects. There are various forms of insulin, including human and cow insulin. There are also current side effects associated with insulin therapy. When an incorrect insulin dosage is administered and meals and insulin injections are not coordinated, the most significant side effects include weight gain and hypoglycemia. After beginning insulin therapy for uncontrolled diabetes, weight gain is an expected side effect that results from increased muscle mass and truncal fat. This is also because there is less energy loss from glycosuria.[28]

Oral hypoglycemic agent: - [29]

S.no	Class	Drugs	Action
1	Secretagogues		
	Sulfonylurea	Glyburides Glipizide Glimepiride	Stimulate sustained insulin release
	Meglitinide	Repaglinide	Stimulate insulin brust
	D-phenylalamine	Nateglinide	Stimulate rapid insulin burst
2	Biguanides	Metformin	Decrease hepatic glucose output
3	Thiazolidinediones	Pioglitazone Rosiglitazone	increase insulin sensitivity
4	Glucosidase inhibitors	Acarbose Miglitol	Delay carbs absorption

150 mg/dl

Advances in technology: -

Technology advancements Continuous glucose monitoring of intestinal glucose and automated insulin delivery devices are now widely used; results indicate improvement in diabetes control with continuous glucose monitoring, with the greatest benefits observed with near-continuous use. Sensor-augmented pumps incorporate alarms to alert the user to actual or credit hypoglycemia, with some devices ceasing insulin administration at certain thresholds. Hybrid closed loop devices are now available, these systems use and open loop for patient initiated premeal bolus but a computer controlled closed loop for basil period between meals and overnight including hyperglycemia-initiated insulin dolls increase, embedded bolus calculator help patient manage their insulin requirement during meals, overall result from community-based study of hybrid devices indicate equal or improve it glycemic control.[30][31]

Conclusion:- this is special issue's research and review pieces all demonstrate how the fields's understanding of diabetes complication is developing.Thus, lowering blood sugar to a safe, patient centred range, using glucose lowering medication that have a solid evidence base for reducing diabetes complications and access and depository in addition to lowering HbA1c, minimising treatment burden and enhancing quality of life, and putting in place care delivery models that sport high quality efficient safe care are all necessary for high quality evidence based management of diabetes.

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