DIABETES MILLUTUS AN OVERVIEW

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ABSTRACT

Many of people worldwide suffer from diabetes mellitus, a complicated metabolic disease marked by disrupted glucose homeostasis. This review summarizes the results of current research, illuminating the complex nature of DM. Environmental variables and genetic predisposition play a role in the development of diabetes mellitus. Our knowledge of the genetic basis of type 1 and type 2 diabetes is strengthened by the discovery of novel genetic loci linked to the disease by recent research, such as that conducted by the DIAGRAM collaboration. In order to effectively control diabetes, technological advancements are essential. Insulin pumps, artificial pancreas devices, and continuous glucose monitoring systems are transforming patient treatment, optimizing glycemic management, and boosting quality of life. Furthermore, studies on cutting-edge drugs, such as SGLT2 inhibitors and GLP-1 receptor agonists, point to promising directions for more efficient and customized care.

Keyword: *Diabetes mellitus, diagnosis, cause and treatment.*

1.INTRODUCTION:

Diabetes mellitus is a condition of macromolecule metabolism marked by a decreased body's capacity to respond to hormones and maintain appropriate blood sugar (glucose) levels.[1] The endocrine system transports blood sugar into your cells so that it can be stored or utilized as fuel. When you have polygenic disease, your body either produces insufficient amounts of hormones or uses the ones it does produce efficiently. Untreated hyperglycaemia caused by polygenic Disease can harm your kidneys, eyes, nerves, and other organs (2).

- A heart-breaking example of diabetes mellitus-related death was reported to the globe in 2023, highlighting the widespread effects of this chronic metabolic illness. The person, whose identity is being withheld, passed away due to difficulties brought on by unmanaged blood sugar levels. Diabetes Mellitus, with its far-reaching repercussions, continues to represent a daunting global health burden despite advances in medical knowledge, affecting millions of people. This regrettable event is a sobering reminder of how vital diabetes treatment is and how quickly more awareness, early detection, and proactive action are needed. In the larger framework of public health and personal wellbeing, the consequences of Diabetes Mellitus continue to be a poignant narrative as researchers work toward breakthroughs and healthcare systems tackle the complex aspects of this condition.
- Diabetes mellitus (DM) is a very common disease worldwide and affects human society at all stages, although its prevalence varies from region to region. According to the International Diabetes Federation, 382 million people were diagnosed with DM in 2013 and this number is likely to increase by 55% to 592 million by 2035 . These statistics show that diabetes is a huge and growing problem with a huge impact on society. According to the National Diabetes diabetic Retinopathy Survey report published by the Ministry of Health and Family Welfare, the prevalence of diabetes in India has increased to 11.8% in the last four years. The World Health Organization (WHO) estimated that in 2014, the global prevalence of diabetes among people under the age of 18 was 8.5%. There are about 72.96 million cases of diabetes in the Indian adult population. Prevalence in urban areas varies between 10.9% and 14.2%, and prevalence in rural India was 3.0-7.8% among people aged 20 and over and much more common among people aged 50 and over (INDIAB study). Diabetes and

diabetic retinopathy have emerged as a major non-communicable disease-causing eye disease. Diabetic retinopathy was estimated to account for 1.06% of blindness and 1.16% of visual impairment worldwide in 2015. There are no recent studies on the prevalence of diabetic retinopathy in different parts of India. As a result, it is difficult to identify the areas where diabetic retinopathy screening and treatment programs are most needed, the government said (5).

2.TYPES OF DIABETES MILLUTUS:

Diabetes is a group of metabolic disorders characterized by elevated blood sugar levels due to defects in insulin secretion, insulin action, or both. There are several types of diabetes, each with its own characteristics.

1.Type 1 diabetes (T1D): This autoimmune disease occurs when the immune system mistakenly attacks and destroys insulin-producing beta cells in the pancreas. As a result,

the body cannot produce insulin. T1D usually appears in childhood or adolescence and requires lifelong insulin therapy.

2. Type 2 diabetes (T2D): This form is characterized by insulin resistance, in which the body's cells do not respond effectively to insulin. At first, the pancreas compensates by producing more insulin, but over time it may not keep up with demand. T2D is often related to lifestyle factors such as obesity, sedentary behaviour and genetic predisposition.

Gestational diabetes (GDM): GDM during pregnancy causes high blood sugar levels. Although it usually resolves after delivery, women with GDM are at increased risk of developing T2D later in life. Appropriate treatment, including diet, exercise and sometimes medication, is critical during pregnancy.

Monogenic diabetes syndromes: These rare forms are caused by mutations in a single gene that affect insulin production and secretion. Examples include diabetes of the young (MODY), diabetes of the new-born, and mitochondrial diabetes. Secondary diabetes: Certain diseases, such as certain hormonal disorders, pancreatic diseases, or the effects of medications, can cause secondary diseases. Diabetes Treatment of the underlying cause is essential in this type of treatment. These classifications help tailor treatments, emphasizing lifestyle changes, oral medications or insulin therapy, according to the type and characteristics of diabetes. (15,16)

GESTATIONAL DIABETES :

- The intolerance to aldohexose, which is mainly diagnosed during pregnancy ,Appears as physiological diabetes (GDM).Women's World Health The organization develops type 1 diabetes during pregnancy and in girls with\diagnosed asymptomatic diabetes. Observed during pregnancy is Classified as a physiological state. Diabetes mellitus (GDM) ; in the long term, young people born to GDM mothers have a higher risk of obesity and multigene disorder later in life. This development is due to the consequences of in utero exposure to hyperglycaemia(17,18)

3.PATHOPHYSIOLOGY :

Diabetes Mellitus (DM) is a complex metabolic disorder characterized by chronic hyperglycaemia resulting from defects in insulin secretion, action, or both. The pathophysiology involves multiple steps.

Beta-cell Dysfunction: In Type 2 Diabetes, there's an initial impairment in insulin secretion from pancreatic beta cells due to genetic and environmental factors, leading to elevated blood glucose levels.

Insulin Resistance: Peripheral tissues become resistant to insulin action, particularly in muscle, liver, and adipose tissue. This reduces glucose uptake, exacerbating hyperglycaemia.

Hepatic Glucose Overproduction: The liver compensates by increasing gluconeogenesis, releasing more glucose into the bloodstream, further contributing to elevated blood glucose levels.

Incretin Effect: Impaired incretin hormone action, responsible for enhancing insulin secretion and reducing glucagon release, is observed, worsening glucose homeostasis.

Adipose Tissue Dysfunction: Dysregulation of adipokines, such as adiponectin and leptin, contributes to insulin resistance and inflammation, creating a pro-diabetic environment. Inflammation and Oxidative Stress: Chronic low-grade inflammation and increased oxidative stress play pivotal roles in the progression of diabetes, damaging pancreatic beta cells and impairing insulin signaling.(50,51)

Amylin Dysfunction: In Type 1 Diabetes, the absence of insulin is accompanied by a lack of amylin, leading to uncontrolled glucagon secretion, delayed gastric emptying, and postprandial hyperglycaemia.

Understanding these steps is crucial for developing targeted therapies. References include research by Kahn, Shulman, and Defronzo, among others, providing insights into the molecular and cellular mechanisms underlying the pathophysiology of Diabetes Mellitus.(66)

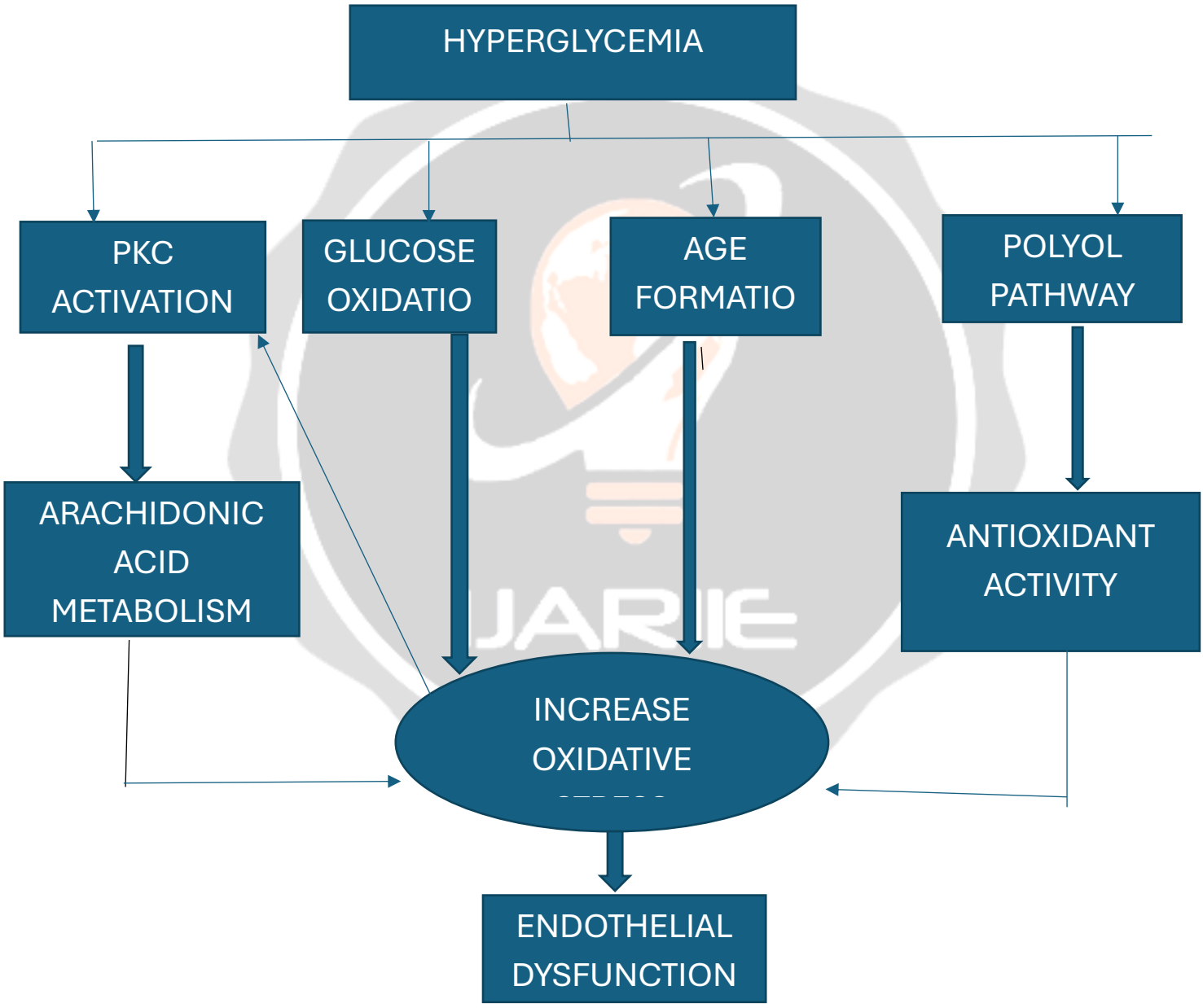

FIGURE 2.

4.CAUSES OF DIABETES MILLUTUS:

Diabetes is a complex metabolic disorder characterized by elevated blood sugar levels. The two main types are type 1 and type 2 diabetes, each with its own causes.

TYPE 1 DIABETES: Autoimmune Destruction

1. Stage: genetic predisposition affects certain types of human leukocyte antigens (HLA), which increase susceptibility.
2. Stage: environmental factors such as viral infections can trigger an autoimmune response.
3. Stage: the immune system targets and destroys the insulin-producing beta cells in the pancreas. (19,20)

TYPE 2:

1 diabetes: insulin resistance and beta cell dysfunction

1: genetic factors play a role and family history affects susceptibility.

2. stage: lifestyle factors, including obesity and a sedentary lifestyle, increase risk.

4. Stage: insulin resistance develops, causing cells to respond poorly to insulin signals.
5. : Pancreatic beta cells have difficulty producing sufficient insulin, which results in a relative insulin deficiency.(21,22)

Common mechanisms:

1. Step: inflammation: chronic inflammation promotes insulin resistance.
2. Step: genetics: polymorphisms in different genes affect the risk of diabetes.
3. Step: Lifestyle: An unhealthy diet and lack of exercise are common risk factors(23,24)

5.SIGN AND SYMPTOMS:

Excessive thirst (polydipsia): People may experience constant and increased thirst, often accompanied by dry mouth.

Frequent urination (polyuria): Frequent urination, especially at night, is a common symptom that reflects the body's attempt to get rid of excess. Glucose

Weight Loss: Despite regular eating habits, unexplained weight loss can occur because the body destroys muscle and fat for energy when cell lack glucose

Fatigue: General weakness and fatigue can be caused by (12)

6.TREATMENT AND MANAGEMENT OF DIABETES MILLUTUS:

Diabetes is a chronic metabolic disorder characterized by elevated blood sugar levels due to insufficient insulin production or ineffective use of insulin. The main goal of diabetes treatment is to keep blood sugar in the target range to prevent complications.

Lifestyle modifications are the foundation of diabetes treatment, emphasizing a balanced diet, regular physical activity, and weight control. Medications, including oral hypoglycemic agents and insulin, are prescribed according to individual needs. Continuous glucose monitoring helps patients monitor their blood sugar levels, allowing timely changes to the treatment plan. Regular monitoring of blood pressure, cholesterol and kidney function is critical because diabetes increases the risk of cardiovascular disease and kidney complications. An annual eye exam is essential to detect and treat diabetic retinopathy, a common eye disease associated with diabetes.Patient education is key to self-care. Healthcare providers educate patients about proper nutrition, medication adherence and lifestyle choices. Diabetes education programs empower people to make informed decisions about their health.(13,14)

CLASSIFICATION OF DIABETES:

1) Metformin (Biguanide) Example: Metformin

2).Sulfonylureas Examples: Glipizide, Glyburide, Glimepiride

3).Incretin-Based Therapies (DPP-4 Inhibitors) Examples: Sitagliptin, Saxagliptin, Linagliptin

4).SGLT2 Inhibitors Examples: Canagliflozin, Dapagliflozin, Empagliflozin

5).Insulin and Injectable Medications (GLP-1 Receptor Agonists) Examples: Insulin, Exenatide, Liraglutide(6)

MOA OF METFORMIN HYDROCHLORIDE:

Metformin hydrochloride's mechanism of action (MOA) involves multiple steps:

- Inhibition of Gluconeogenesis: Metformin suppresses hepatic glucose production by inhibiting gluconeogenesis, the process by which the liver produces glucose.
- Activation of AMP-activated Protein Kinase (AMPK): Metformin activates AMPK, a cellular energy sensor. This enzyme helps regulate glucose and lipid metabolism, leading to improved insulin sensitivity.
- Enhancement of Glucose Uptake: Metformin increases glucose uptake in peripheral tissues, particularly skeletal muscles, by enhancing insulin-mediated glucose transport.
- Reduced Intestinal Glucose Absorption: Metformin may decrease glucose absorption in the intestines, contributing to lower postprandial glucose levels.

The United Nations agency published the first generally accepted classification of diabetes 1980. in and that changed during 1985.The most common and Ecessary primary or disordered diabetes. Is the focus of our discussion.(7) This should range from Secondary diabetes, which includes a variety of symptoms associated with identifiable causes, \in which exocrine islets are destroyed, to inflammatory exocrine gland diseases, surgery, tumours, certain medications, iron overload (hemochromatosis) and certain diseases. Acquired \genetic endocrinopathies.The classification includes all clinical stages and Etiological types of diabetes and various classes of hyperglycaemia. Assigning a Polygenic disorder to a person usually depends on the circumstances of the gift (8,9). Recognition time and diabetics simply do not fit into one category .Primary .Diabetes probably represents a heterogeneous group of diseases with Typical symptoms .The new classification of diabetes includes stages that reflect the different severity of Symptoms. Individual patients have one of the disease processes that can cause diabetes . The recent and new terms insulin-dependent (IDDM) or non-insulin-dependent (NIDDM) developed by the United Nations in 1980 and 1985 have disappeared, and the terms of the most a new classification system also recognizes four types of polygenic disorders Mellitus: type 1 (IDDM), type 2 (NIDDM), "other specified types" and polygenic Pregnancy disease (WHO Professional Committee 1999). These were reflected in the following International Terminology of Diseases (IND) in 1991 and the tenth version of the International Classification of Diseases (ICD-10) in 1992.(10,11)

7.ROLE OF INSULIN :

- Insulin the main hormone produced by pancreatic beta cells, plays a key role in regulating glucose homeostasis in the human body. Its main function is to facilitate the consumption of glucose by cells and ensure a balanced energy supply.(14) When carbohydrates are consumed, insulin secretion is triggered, which signals tissues such as muscle and fat cells to absorb glucose from the blood. This process is essential to maintain blood glucose levels within a narrow range and prevent hyperglycaemia. (25,26,27)
- The effects of Insulin go beyond the regulation of glucose and affect various metabolic processes.(28))It promotes glycogen synthesis in the liver and muscles and acts as a glucose reserve for future energy needs. In addition, insulin inhibits gluconeogenesis, the production of glucose from sources other than carbohydrates, which further promotes blood sugar control. (29,30)
- In addition to metabolism, insulin affects fat metabolism. It promotes the deposition of triglycerides in adipose tissue and prevents lipolysis, reducing the release of fatty acids into the bloodstream.(19) This dual role of insulin in carbohydrate and lipid metabolism emphasizes its importance in general energy balance.

- In addition, insulin affects protein metabolism by facilitating the uptake of amino acids into cells, supporting protein synthesis, and preventing protein breakdown. This anabolic action promotes tissue growth, repair and maintenance.(31,32)
- Dysregulation of insulin action leads to diseases such as diabetes mellitus. In type 1 diabetes, the pancreas cannot produce insulin, in type 2 diabetes the cells become resistant to its effects. Both diseases lead to impaired absorption of glucose, leading to elevated blood sugar levels and various metabolic disorders.(33,34)
- Understanding the complex role of insulin in metabolism is essential for the management and prevention of metabolic disorders. Ongoing studies continue to unravel the molecular mechanisms that regulate insulin action and provide insight into potential therapeutic interventions for diabetes and related diseases.(35,36)

8.COMPLICATION :

Diabetes causes countless complications that affect various organ systems. Chronic hyperglycaemia can lead to microvascular complications such as cardiovascular disease and microvascular complications including nephropathy, retinopathy, and neuropathy.(23)Cardiovascular complications increase the risk of heart attack and stroke. Nephropathy manifests as kidney damage that can lead to kidney failure. Retinopathy affects the eyes, which can lead to blindness, while neuropathy causes nerve damage, leading to sensory and motor deficits. In addition, diabetes increases susceptibility to infections and slows wound healing. These complications significantly reduce the patient's quality of life and represent a significant health burden.(24) Early detection, blood sugar control, and lifestyle changes are critical to preventing and managing these complications.(37,38)

MICROVASCULAR:

Microvascular complications are common in diabetes mellitus (DM) and significantly increase disease-related morbidity. (39))The microvasculature, consisting of small blood vessels such as arteries, capillaries and veins, is particularly susceptible to the adverse effects of chronic hyperglycaemia in diabetics.

One of the most important microvascular complications is diabetic retinopathy, which is the main cause of; blindness in the whole world. . Long-term exposure to high glucose levels damages the small blood vessels in the retina, leading to vision loss. Another major complication is diabetic nephropathy, which affects the kidneys. Inflammation and oxidative stress caused by hyperglycaemia contribute to kidney failure, which eventually leads to kidney failure.(40,41)

In addition, diabetic neuropathy damages nerves in various organs, leading to sensory and autonomic dysfunction. (37)It can manifest as peripheral neuropathy, which affects the limbs, and autonomic neuropathy, which affects organs such as the heart and digestive systs.(42,43,44)

MACROVASCULAR:

Macrovascular complications in diabetes refer to conditions that affect larger blood vessels and contribute to cardiovascular disease. The progression of these complications involves several steps, each of which increases the risk of serious outcomes.(45,46)

Endothelial dysfunction: Diabetes causes endothelial dysfunction, in which the lining of blood vessels weakens. This dysfunction impairs the regulation of blood vessel tone and inflammation.(47)Atherosclerosis: Increased blood sugar levels promote the formation of atherosclerotic plaques. The chronic inflammation and oxidative stress associated with diabetes promotes the accumulation of fatty deposits, which leads to narrowing and hardening of the arteries

Development of high blood pressure: Diabetes often occurs with hypertension. The combination of endothelial dysfunction and atherosclerosis further increases blood pressure and places an additional burden on the cardiovascular system.(48)

Thrombosis and occlusion: Atherosclerotic plaques are prone to rupture, exposing the blood to prothrombotic factors. This increases the risk of thrombus formation, leading to vessel valve failure and possible ischemic events such as myocardial infarction or stroke.(49,50)

These Macrovascular complications significantly increase the morbidity and mortality associated with diabetes. Treatment strategies include glycemic control, blood pressure, and lipid-lowering therapy. Lifestyle changes, such as a healthy diet and regular exercise, are also crucial in preventing and mitigating these complications..(51,52)

9.PREVENTION:

Preventing diabetes involves a holistic approach that focuses on lifestyle changes and managing risk factors.(53,54) Regular physical activity, maintaining a healthy weight through a balanced diet and avoiding excessive consumption of refined sugars can significantly reduce the risk of developing type 2 diabetes .Several studies emphasize the importance of the plant. A diet high in fruits, vegetables, whole grains and lean proteins to prevent diabetes(55,56,57) . In addition, minimizing the consumption of processed foods and saturated fats promotes overall metabolism. Regular blood sugar level monitoring is critical for early detection and intervention. In addition, maintaining optimal mental health and managing stress are central to diabetes prevention(58,59) Chronic stress can negatively affect insulin sensitivity and glucose metabolism. Adequate sleep is another critical factor, as poor sleep has been linked to an increased risk of diabetes.(60,61)

Finally, preventing diabetes requires a multifaceted approach that includes food choices, physical activity and stress. For treatment and regular health checks..(62,63)

10.RISK FACTOR:

Diabetes mellitus (DM) is a complex metabolic disorder characterized by elevated blood sugar and several risk factors contribute to its development. Genetics play an important role and family history is a determining factor. Certain gene variants, such as those associated with insulin resistance and beta cell function, increase susceptibility. (64)

Lifestyle factors such as an unhealthy diet and sedentary behavior greatly in crease the risk of developing DM. A diet high in refined sugar, saturated fat and low in fibre is associated with insulin resistance and obesity, which are key factors in type 2 diabetes (T2DM). Physical inactivity increases these risks.(65)

Obesity is an important independent risk factor for T2DM. Adipose tissue, especially visceral fat, releases inflammatory substances that affect insulin sensitivity. Central obesity, often measured by waist circumference, is strongly associated with increased risk.

Age is another nonmodifiable risk factor, with the prevalence of both type 1 diabetes (T1DM) and T2DM increasing with age. Ethnicity also plays a role, with certain populations such as African Americans, Hispanics, and Native Americans more prone.

Gestational diabetes (GDM) during pregnancy increases the risk of T2DM later in life. Other diseases, such as hypertension and polycystic ovary syndrome, are associated with a higher risk of Diabetes Mellitus.

11.CONCLUSION:

The term diabetes encompasses a number of different metabolic disorders, all of which, if left untreated, lead to abnormally high levels of blood sugar, called glucose. Type 1 diabetes occurs when the pancreas no longer produces significant amounts of the hormone insulin, usually due to autoimmune damage to the insulin-producing beta cells in the pancreas. Instead, type 2 diabetes is now thought to be caused by autoimmune attacks on the pancreas and/or insulin resistance. The pancreas of a person with type 2 diabetes can produce normal or even abnormally high amounts of insulin. Other goals of diabetes care are to prevent or treat the many complications that can arise from the disease itself and its treatment. By keeping blood sugar under control, diabetes can become a patient’s companion and he can enjoy life.(67)

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