Journal of Research in Chemistry

E-ISSN: 2709-9423
P-ISSN: 2709-9415
JRC 2024; 5(1): 101-112

www.chemistryjournal.net
Received: 01-11-2023
Accepted: 06-12-2023

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Type 2 diabetes mellitus (T2DM) patients and correlation with adenosine deaminase (ADA)

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Abstract
The most common kind of diabetes mellitus is type 2 diabetes (T2DM). It is defined as a collection of genetically determined disorders that were linked to hyperglycemia symptoms resulting in increased free radical activity that can be managed with a combination of diet, hypoglycemic medications, and exogenous insulin**.** Chronic rise of blood glucose causes serious complications, such as failure and malfunction of the organs, especially the heart, blood vessels, kidneys, eyes, and nerves (neuropathy, retinopathy, and neuropathy). The primary isozymes of ADA are ADA1 and ADA2. ADA is broadly distributed in human tissues, with T-lymphocytes having the highest activity, it is thought to be an excellent indicator of a cell-mediated immune response, and many disorders have been linked to increased lymphocytic ADA activity, which is linked to changes in cell-mediated immune responses such as T2DM.

Keywords: Type 2 diabetes mellitus, adenosine deaminase, hyperglycemia

Introduction

Diabetes mellitus

A group of metabolic illnesses known as diabetes mellitus cause hyperglycemia in patients, with a form of type 1 diabetes (insufficient manufacturing of insulin) as well as type 2 diabetes (cells not reacting to insulin release) being the primary cause [1, 2]. The pancreatic beta cells produce the hormone insulin, which the body needs in order to use the carbohydrates from digested food as an energy source [3]. The most frequent endocrine condition and global health concern is diabetes mellitus (DM). In developing nations, DM is becoming more and more widespread, and when combined with poor control, significant complications lead to the most prevalent forms of morbidity and diabetes mortality [4, 5]. Wounds also take a while to heal, especially on the foot, Diabetes (DM) is a prevalent, rapidly spreading glucose homeostasis condition. According to the "World Health Organization" 80 million or more individuals worldwide have type 2 diabetes. It is projected that 592 million will be among them by 2035 [6]. Regardless of quality of life, this metabolic condition is high level and unexpectedly common in most tropical nations. Diabetes mellitus (DM) affects more than 217 million individuals globally now; by 2030, that figure is predicted to reach over 350 million. figure (1) [7, 8]. In 2015, 13.9% of Iraqis had diabetes, indicating an increasing incidence of the condition [9]. A notable factor contributing to the diabetes epidemic is the 30% to 80% of cases that go undiagnosed [10]. Diabetes may be divided into four categories: gestational diabetes, Type 2 diabetes (deficiency in relative insulin and insulin resistance), Type 1 autoimmune disorders (AUD) and absolute absence of insulin, and other forms of diabetes (e.g., pancreatic disease) [11].

Classification diabetes mellites

There are four primary forms of diabetes: type 1 diabetes, type 2 diabetes, Gestational diabetes, and additional types of diabetes. The other distinct forms are made up of a few hundred (personal causes). Diabetes mellitus is often referred to as "diabetes" without classification [13].

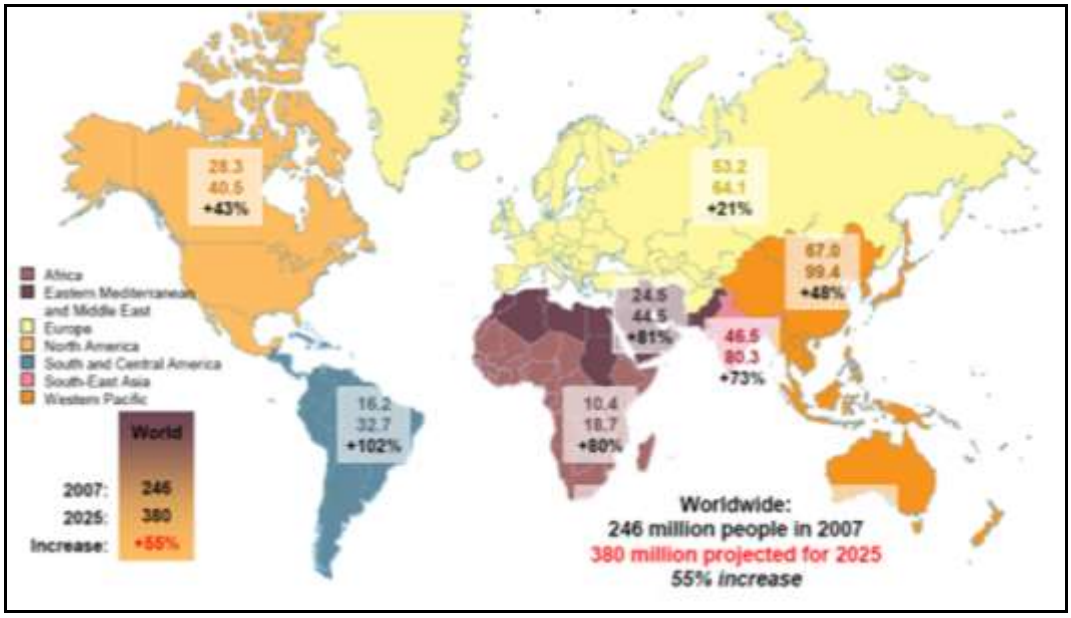


Fig 1: World expansion of diabetes mellitus, International Diabetes Federation [12].

Type 1 diabetes

Type 1 diabetes mellitus (T1DM) is characterized by an insulin deficit and is caused by the autoimmune destruction of pancreatic beta cells, which create insulin [14] Type 1 diabetes (T1DM) is characterized by an insulin shortage that results from the death of beta cells of the pancreatic located in the islets of Langerhans, which create insulin. Within this category, there are two subtypes: idiopathic and immune-mediated. The majority of T1DM cases are immune-related; an autoimmune assault driven by T cells damages beta cells, which results in insulin insufficiency [15]. Additionally, T1DM can result in unstable and occasional hyperglycemia, which is frequently followed by ketosis and, in rare circumstances, extremely low blood sugar. Additional dangers include endocrinopathy (like Addison's disease), gastroparesis, which results in uneven absorption of carbohydrates, and a slower counter-regulatory response to hypoglycemia. These events are estimated to affect 1% to 2% of T1D patients [16].

Type 2 diabetes mellitus(T2DM)

Type 2 diabetes mellitus is the most common form of the disease and is not insulin-dependent. Insulin resistance and/or decreased insulin production are indicators of it [17]. It is believed that the insulin receptor contributes to the body tissues' decreased resistance to insulin; nevertheless, particular vulnerabilities remain unidentified. Reduced insulin sensitivity is the most common abnormality in T2DM at this point. To treat hyperglycemia, a range of methods and drugs that either improve insulin sensitivity or lower the liver's gluconeogenic production will be used. The primary causes of type 2 diabetes are genetics and lifestyle choices. Stress, poor diet, inactivity, and obesity (measured as a body mass index) are recognized to have an impact on the infection of type 2 diabetes [18, 19]. Type 2 diabetes, or T2DM, is a major health issue that affects around 150 million people globally. This number is anticipated to triple in the first few decades of the third century [20]. Type 2 diabetes is one of the most common diseases in the modern period and is becoming more common. Globally, the prevalence of type 2 diabetes is increasing, with low- and middle-income countries housing 80% of all DM patients [21]. Therefore, it's critical to diagnose and treat DM in order to prevent the consequences linked to T2DM. According to the American Diabetes Association, glycemic control of <7.0% for HbA1C, <130 mg/dl for glucose concentration in fasting blood, and <180 mg/dl for glucose peak concentration after meals. Established risk factors for type 2 diabetes include hypertension, hyperglycemia, excess weight, elevated total and VLDL triglycerides (TG), low HDL cholesterol, and, less often, elevated levels of LDL and total cholesterol figure (2) [22].

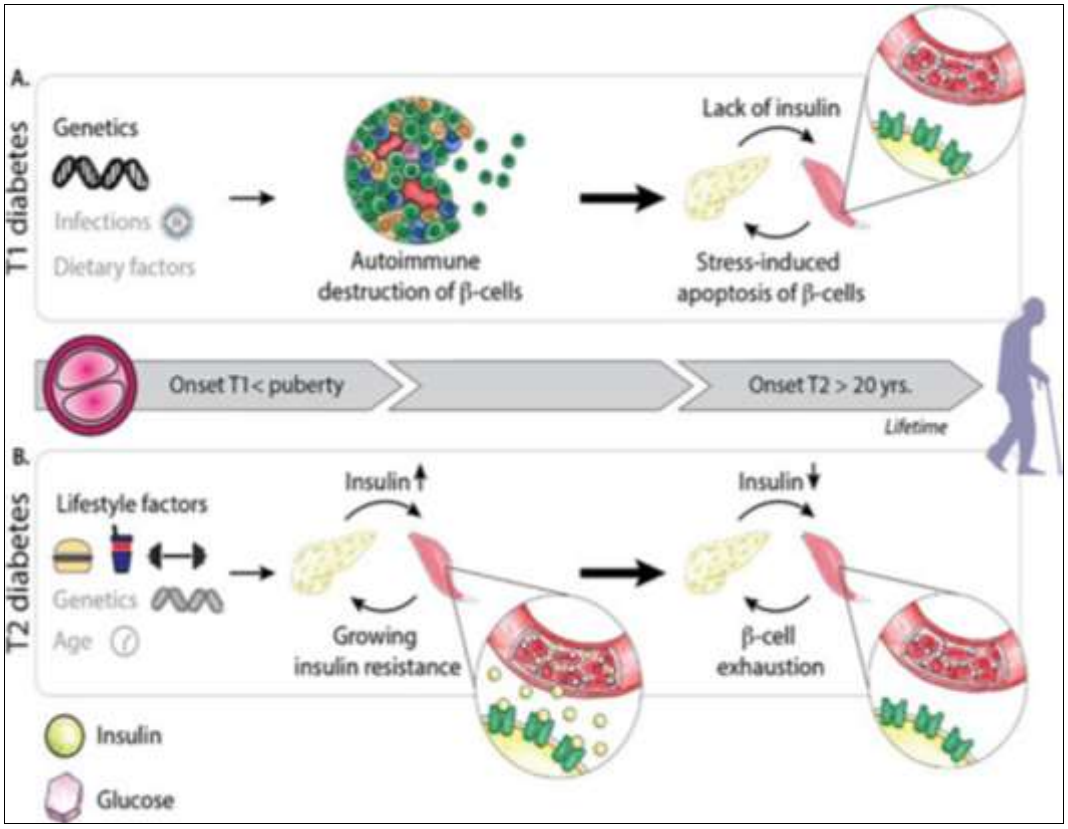


Fig 2: A comparison between the causes of T1DM and T2DM [23].

Gestational diabetes mellitus (GDM)

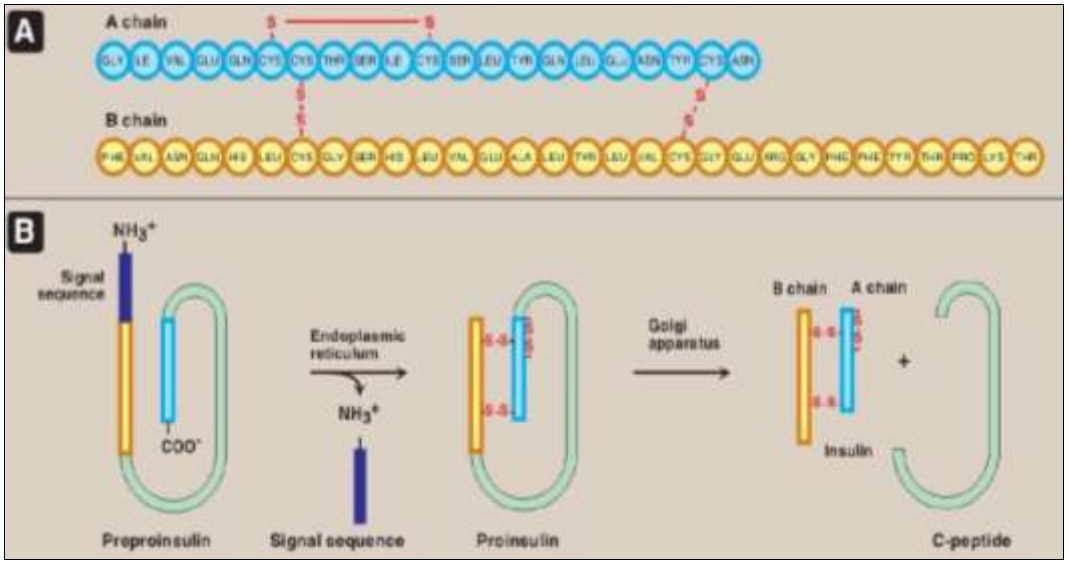
Resemble to T2DM, pregnant diabetes mellitus affects between two and ten percent of pregnancies along with is typified by multiple manifestations of comparatively poor insulin sensitivity and production. It can improve or go away after delivery. However, after giving birth, between five and ten of women with gestational diabetes eventually develop diabetes mellitus, with type 2 diabetes becoming the most common [24]. seen throughout the 2nd and third trimesters of pregnancy [25]. Although entirely curable, gestational diabetes does require constant medical supervision during pregnancy. Treatment options may include dietary adjustments, blood glucose monitoring, and, in certain situations, insulin. Even if it is just transient, untreated gestational diabetes can be harmful to the mother's or the embryo's health. The hazards for the embryo include increased weight, high birth weight, congenital heart problems, anomalies showing in the central nervous system (CNS) and deformities of the skeletal muscles [26].

Other types of diabetes Mellitus

The same factors that create type 1 diabetes in adults also induce a form of latent autoimmune diabetes of adults (LADA). Because of their age rather than the underlying reason, adults with LADA are frequently initially misdiagnosed as having T2DM [27]. Beta-cell dysfunction can be caused by autosomal or mitochondrial genetic mutations. In certain cases, insulin deficiency action may be determined by genetics[28]. Other forms of diabetes, such as thyroid disorders syndromes (including diabetes newborn babies and young-onset diabetes), Pancreatic exocrine cell infections (such pancreatitis and cystic fibrosis), as well as chemically or drug-induced diabetes (like that caused by HIV/AIDS medication, glucocorticoid usage, or following organ transplants) [29].

Insulin resistance (IR)

Insulin resistance refers to the decreased physiological response that results from stimulation by insulin in target tissues, including adipose, liver, and muscle tissue (IR). Insulin resistance (IR) and decreased muscle insulin sensitivity are two conditions that are exacerbated by elevated blood fatty acid concentrations. Because free fatty acids (FFAs) obstruct insulin's ability to transport glucose into tissues, blood glucose levels rise and more insulin is secreted, a condition known as hyperinsulinemia [30]. Hypertension, increased inflammatory markers, visceral obesity, diabetes mellitus, endothelial dysfunction, hyperuricemia, and prothrombic diseases are among the metabolic outcomes of insulin resistance. Insulin resistance can cause or aggravate type 2 diabetes (T2DM), nonalcoholic fatty liver disease (NAFLD), and metabolic syndrome [31]. Insulin resistance treatment should primarily focus on lifestyle modifications. The cornerstone of treatment is nutritional intervention, which entails calorie restriction and avoiding carbohydrates that increase insulin demand. Exercise can boost your body's ability to burn calories and enhance your muscles' sensitivity to insulin. Moreover, medications have the power to raise insulin sensitivity and lower insulin requirements [32].



Pathophysiology of hyperglycemia

T2DM is an age-related disease that is most prevalent among the elderly. Given that hyperglycemia is linked to diabetes-related issues at all ages, identifying diabetes early on is essential to reducing the risk of complications. As a result, the diabetes diagnostic standards apply to all age groups [33]. Owing to the combined effects of age, lifestyle, and environmental variables, the risk of type 2 diabetes is increased in older persons. These variables impact tissue insulin sensitivity as well as the capacity of β-cells to secrete insulin, which results in hyperglycemia. The emergence of type 2 diabetes in older adults is complicated by age-related physical limitations and comorbidities [34]. It also reduces protein production and gamma globulins, causing weakness and wasting of the body due to diabetes, polydipsia, and weak wound healing. Hyperglycemia outside the cell causes hyperglycemic coma and osmotic diuresis figure (3) [35]. Although glucose homeostasis is altered by resistance to peripheral insulin action, recent research indicates that aging directly affects the pathogenesis of diabetes by reducing insulin production through β-cell function impairment [35].

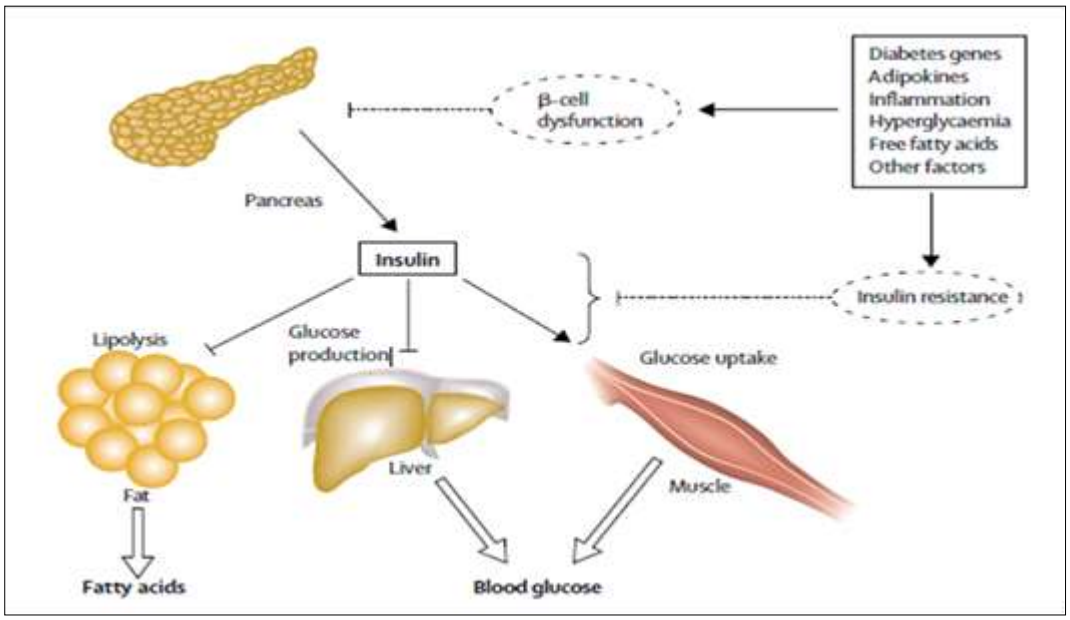


Fig 3: Hyperglycemia and increased circulating fatty acids in type 2 diabetes pathophysiology [36].

Etiology of Type 2 Diabetes

Genetic predispositions to insulin resistance and reduced insulin excretion combine with environmental factors including obesity, stress, aging, and lack of exercise to cause type 2 diabetes. Usually, there are multiple genetic and environmental factors involved, each contributing to the disease to differing degrees figure (4) [37].

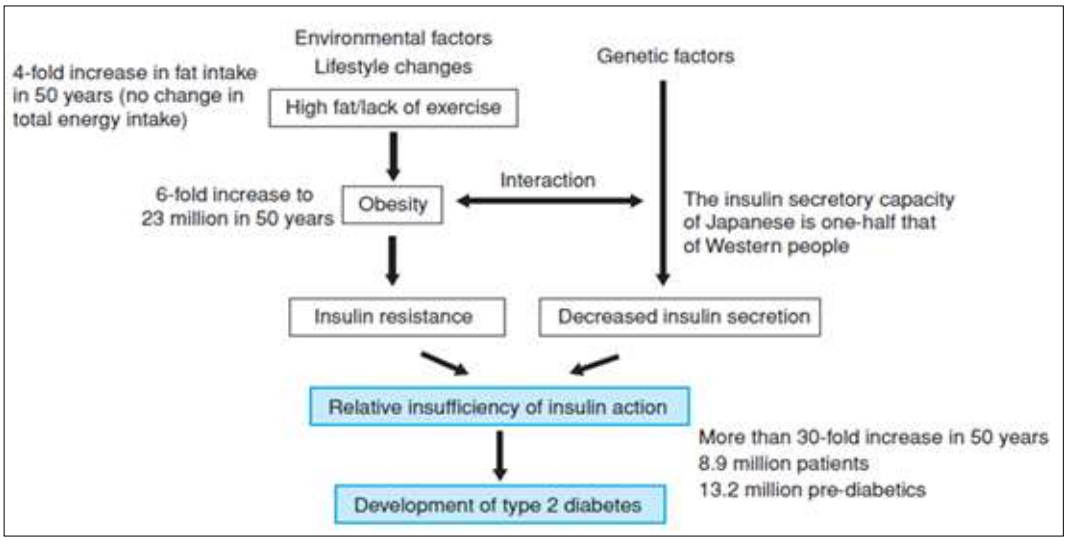


Fig 4: Etiology of T2DM [38].

Type 2 diabetes mellitus signs and symptoms

T2DM symptoms and signs typically appear gradually. In reality, one could have T2DM for months without realizing it. When there are early symptoms, they can include An increase in thirst and urine an increase in hunger, Unintentionally losing weight due to tiredness vision is hazy. sores that require a lengthy healing period, Consistent infections, darker skin patches, usually in the neck and armpits, and tingling or numbness in the hands and feet [39]. Extended periods of high level of glucose in the blood can lead to the absorption of glucose in the lens of the eye, changing its structure and ultimately affecting eyesight. One of the most frequent complaints that triggers a diabetes diagnosis is blurry vision. T1DM should still be suspected in situations of abrupt changes in vision, while T2DM changes are often more gradual but still need to be estimated [40].

Diagnosis of diabetes mellitus type 2

As stated by the WHO, diabetes mellitus can be identified using a variety of measures that can be used for each screening and diagnosis. Screening patients before the onset of signs and symptoms allows for earlier diagnosis and treatment, but it does not decrease end-organ injury rates [41]. There are numerous recommended tests for diabetes diagnosis and screening, ranging from history and questionnaires supporting to proteomics-based risk evaluation. Although some of these tests are useful, the current favorite tests are limited to two types: blood glucose tests and glycated hemoglobin tests [42]. The American Diabetes Association states that in order to diagnose diabetes mellitus (DM), The following criteria must be met by the patient: a HbA1C >6.5 percent, an FBS >126 mg/dl, or diabetic symptoms combined with spontaneous blood glucose >200 mg/dl or two-hour glucose concentration >200 mg/dl following a 75g oral glucose tolerance test (OGTT). If the individual's blood sugar levels exceed the specified ratios, and many analyses are performed to verify the accuracy of the results, this indicates a type 2 diabetes infection [43].

Fasting Plasma Glucose (FPG)

This analysis is based on the many glucose concentrations in plasma after a fast of at least 8 hours. As it is simple, inexpensive, and largely risk-free, it is a desirable option for diagnosis and screening. The typical blood sugar level in the morning is lower than 110 mg/dl (6.1 mmol/L). Blood sugar levels between 110 and 126 mg/dl (or 6.1 and 7 mmol/L) when fasting are considered to be in prediabetes. In cases of diabetes, it is equals of 126 mg/dl (7 mmol/L) or above [44].

Random Blood Glucose Test (RBG)

For the purpose of this test, a random blood sample from the subject must be taken. Regardless of when the previous meal was, Diabetes is indicated by a random blood glucose (RBS) level more than 200 mg/dl (11.1 mmol/L), whereas a level below this indicates normality [42].

Oral Glucose Tolerance Test (OGTT)

This test determines the patient's fasting blood sugar level if they will be fasting overnight. Following the administration of a glucose solution (75 mg/dl), the subject's blood and urine glucose levels are tracked for the following two hours (each test lasting 30 minutes). Blood sugar should not be more than 140 mg/dl (7.8 mmol/L). Prediabetes is defined as blood sugar levels between 140 and 199 mg/dl (7.8 and 11.0 mmol/L). After two hours, a blood sugar level of higher than 200 mg/dl (11.1 mmol/L) is indicative of diabetes [45].

Glycated Hemoglobin (HbA1c) Test

The HbA1c test was proposed in 1976 as a means of evaluating blood glucose control. Since then, it has developed into a commonly used standardized measure in both clinical and research contexts. One of its biggest functional benefits is that it may be utilized in situations where fasting is not required. Moreover, it is a three-month average of glucose regulation rather than a single point measurement. It determines how much glucose is bonded to hemoglobin. When blood sugar levels are high, some glucose is linked to hemoglobin. An HbA1c score of 6.5 percent or greater indicates the existence of diabetes. An HbA1c test of less than 6 percent indicates normal, whereas a level of 6 to 6.4 percent indicates pre-diabetes [44].

Obese

The primary causes are developing a well-developed sedentary lifestyle, giving up exercise, and becoming tired

of high-calorie or high-fat meals[46] As a result, since 1980, the prevalence of obesity has almost quadrupled worldwide. Among persons 18 years of age and older, over 39% were overweight in 2017; 13% were obese. World Health Organization (WHO) estimates that at least 41 million children under five are overweight or obese [47]. Obesity is recognized as a risk factor for several noncommunicable illnesses, including heart disease, hypertension, Type 2 diabetes mellitus, cardiovascular disease, and certain cancers. Beyond the physical disadvantages, it also triggers a number of psychological issues. According to WHO, those who are overweight or obese account for 44% of diabetes cases, 23% of cases of ischemic heart disease, and 7-41% of cases of cancer [48, 49].

Lifestyle

The higher risk of T2DM is related to a variety of unhealthy lifestyle factors, with obesity being the most powerful risk factor[50]. Smokers are at an increased risk, This rises in proportion to the amount of cigarettes smoked in a dose-response manner [51]. Aging, alcohol intake, and high-fat diets were also discovered to raise the risk of T2DM**,** By changing the fatty acid composition of cell membranes or by attaching to peroxisome proliferator-activated receptors, which modify gene expression, dietary fatty acids can impact insulin sensitivity [52]. In high-risk patients, lifestyle changes are more effective than drug therapy in reducing T2DM [53]. In high-risk people, exercise combined with a healthy diet will help them avoid developing T2DM [54].

Diabetes complications

Diabetes complications have the potential to considerably increase morbidity and death in individuals with both T1DM and T2DM. Diabetes can cause microvascular issues as well as macrovascular issues, with the former occurring far more frequently than the latter [55]. Neuropathy, nephropathy, and retinopathy are examples of microvascular effects; coronary artery disease, brain injury, and cardiovascular disease are examples of macrovascular problems figure (5). Diabetic foot syndrome, characterized by a foot ulcer, peripheral artery disease, neuropathy, and inflammation, is one of the primary reasons of lower limb amputation [56].

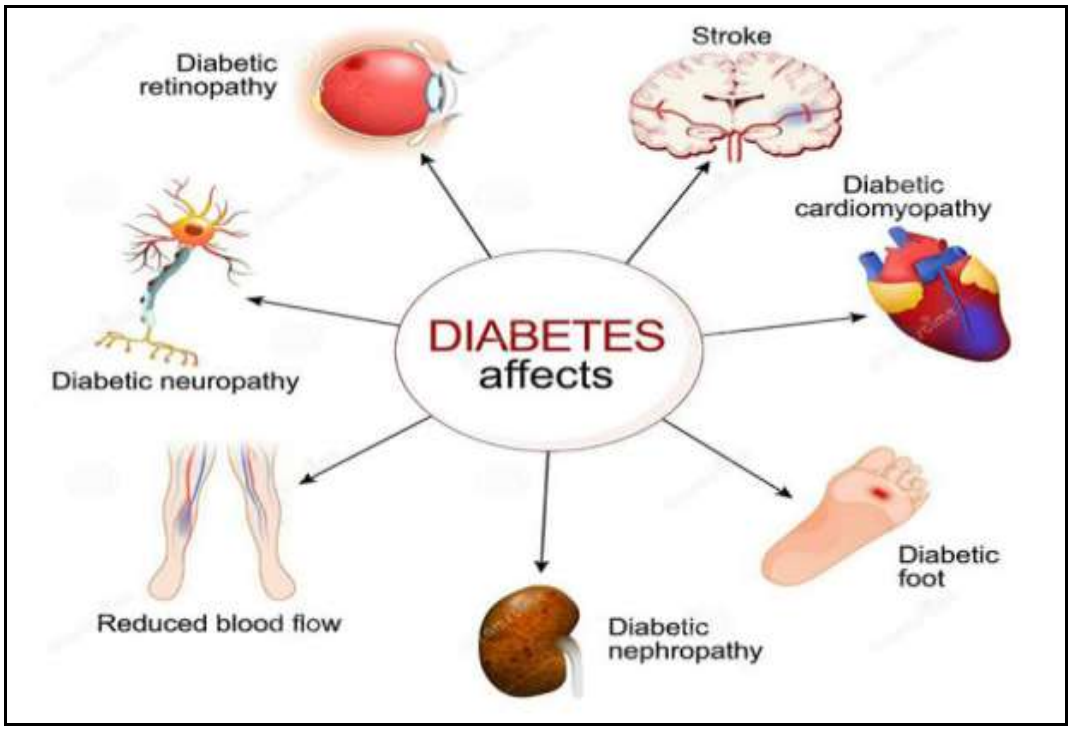


Fig 5: Diabetes complications [57].

Diabetes retinopathy

The most common cause of blindness among working-age individuals globally is diabetic retinopathy. Diabetic retinopathy affects nearly all people with T1DM and over 60% of T2DM patients after twenty years of diabetes [58]**.** Microaneurysms, lipid exudates, retinal hemorrhage, and vascular tortuosity emerge as symptoms of Type 1 non-proliferative diabetic retinopathy following years of clinically silent subretinal changes [59]. Some afflicted individuals develop type 2 proliferative diabetic retinopathy, also known as pathological retinal neovascularization. In patients with diabetic retinopathy, diabetic macula edema (DME) is the most common cause of visual loss, which is defined as liquid aggregation inside the central neuronal retina that manifests as uneven retinal thickness and cystoid development [60, 61].

Diabetes neuropathy (damage in nerves)

About half of people with diabetes develop diabetic neuropathy, a frequent consequence of both type 1 and type 2 diabetes [56]. Distal symmetric polyneuropathy, the most prevalent kind of peripheral nerve disease, affects nerves in the legs and feet in a bilateral, symmetric pattern that advances from the distal to the proximal regions. Diabetic neuropathy, often referred to as distal symmetric polyneuropathy, is a painful consequence that can result in the amputation of lower limbs and is associated with an increased risk of ulcers and infections [62].

Diabetes nephropathy (DN)

A diabetic patient with increased urine albumin excretion of 300 mg or more per day, proteinuria in their urine, and a progressive decline in their glomerular filtration rate (eGFR, 60 ml/min/1.73 m2) are all indicators of diabetic nephropathy [63]. Creatinine is the most widely utilized endogenous metric to evaluate glomerular function. Creatinine clearance, a GFR indicator, is computed and utilized. Since 24-hour samples are infamously unreliable, urine must be collected within 24 hours, or better yet, during a well planned period of 5 to 8 hours. The formula C = (U x V) / P may be used to determine creatinine clearance. In this calculation, U represents urine concentration, V denotes urine flow rate (volume/time, or ml/min), and P represents plasma concentration [64]. High blood sugar is the cause of DN because it destroys renal blood vessels and causes kidney dysfunction [65]. Renal function gradually declined as a result of hypertension and diabetic retinopathy, which were the normal sequelae to this clinical issue. Because their diabetes has been present for several years prior to the diagnosis, many individuals with type 2 diabetes develop microalbuminuria (MAU) and overt nephropathy shortly after receiving their diagnosis. Of T2DM patients with MAU, only approximately 20% result in overt [66]. There are distinct phases in the development of DN. early life with glomerular hyperfiltration, which was followed over a 15-20-year period by a progressive deterioration in renal function. Throughout the world, diabetes is the main cause of end-stage renal disease (ESRD) [67]. There are five recognized stages of diabetic nephropathy, and each one often results in a partial loss of kidney function; symptoms and deterioration do not show up until stage 4 figure (6), Diabetics should get a kidney function test at least once a year because the symptoms appear later in life. DN in stage 4 symptoms include blood in the urine, weakness brought on by low blood oxygen levels, swelling of the hands, thighs, and knees from water buildup, and nausea [68, 69].

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30-300 mg/g 3-30 mg/mmol	A3 Severely increased >300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Fig 6: Five stages of diabetic nephropathy [70].

Stage 5, or end-stage renal disease, may result from this (ESRD) figure (7), When the kidneys are unable to meet the demands of everyday life and the only options left are dialysis or kidney transplantation. Obesity, dyslipidemia, hypertension, and inadequate glycemic control are risk factors for diabetic ketoacidosis (DN). Since people with a family history of the condition are more likely to get it, smoking and a person's genetic composition are significant variables in the acquisition of DN [71].

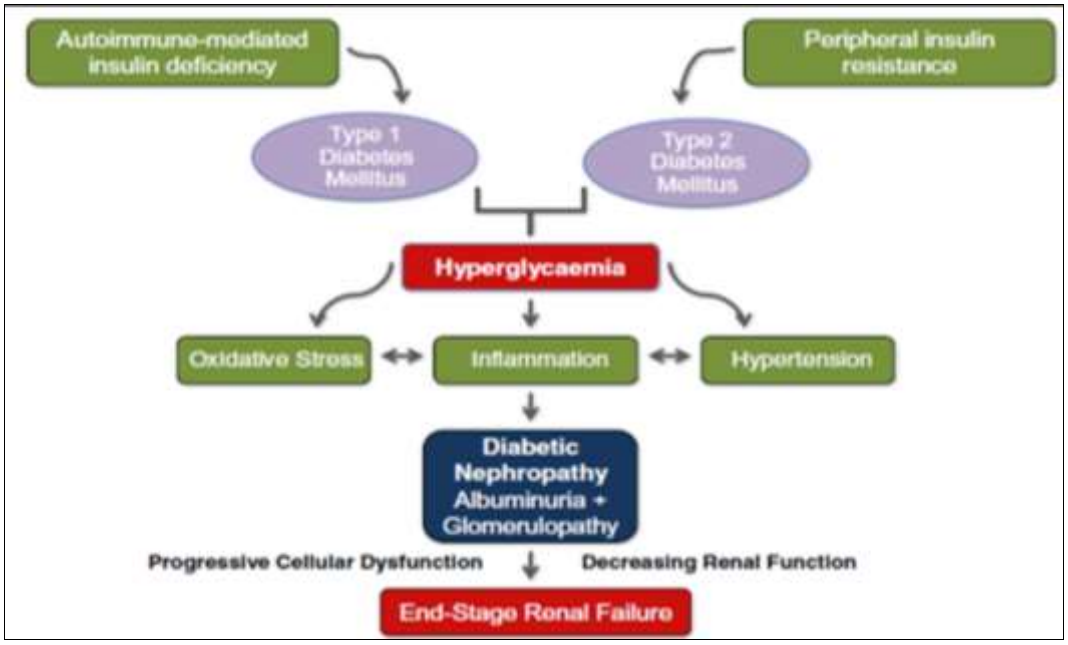


Fig 7: Development of diabetic nephropathy [72].

Adenosine deaminase

The purine metabolism enzyme adenosine deaminase (also known as adenosine amidohydrolase, Deoxyadenosine transforms into deoxy inosine by deamination, which is irreversibly catalyzed by EC 3.5.4.4, ADA [73]**.** Hypoxanthine is produced by the metabolism of these deaminated nucleosides, which is then transformed by xanthine oxidase into uric acid or by hypoxanthine-guanine phosphoribosyl-transferase into mononucleotides (Figure 7). The enzyme is present in all tissues of vertebrates and is crucial to several physiological processes [74]. Hazardous purine pathway products are recycled by ADA in lymphocytes and myeloid cells, where they are essential for DNA metabolism and cell survival [75]. Nearly every human tissue has ADA activity, but the lymphoid system—which mostly consists of monocytes and macrophages—including the spleen, thymus, and lymph nodes, has the greatest amounts [76]**.** ADA activity is present in many organs, even though the liver, skeletal muscle, heart, lymphoid, and adipose tissues have the highest concentrations of it [77]. Increased levels of ADA are observed in obesity, metabolic and physiological issues associated with the beginnings of type 2 diabetes and cardiovascular disease, liver cirrhosis and hepatoma, tuberculosis, brucellosis, typhoid fever, hypoxic settings, and cell-mediated immune responses [78]. Numerous studies have revealed that T2DM patients have greater levels of ADA activation [79-81]. It may be difficult to determine if changes in ADA activity are what leads to or causes real insulin resistance [82]. By increasing the rise in cyclic adenosine monophosphate (AMP) buildup brought on by norepinephrine, adenosine deaminase promotes lipolysis [83]. Type 2 diabetes is brought on by an increase in free fatty acids and a disruption in the metabolism of fat. Additionally, it has been shown that one of the factors causing a larger production of reactive oxygen species—which in turn results in oxidative stress—is raised ADA levels [74].

Isoenzyme

ADA exists in two main isoforms, each with a unique set of characteristics. The bulk of ADA activity is attributed to ADA1, It plays a crucial role in lymphocyte function, is found in all human tissues, and is mutated in hereditary instances of severe combined immunodeficiency [84] Conversely, the main ADA isoenzyme seen in serum is ADA2, which is mostly sourced from the monocyte-macrophage system [85, 86]. ADA1 and ADA2 are different proteins with varying molecular weights. As a monomer, ADA1 has a molecular weight of 30-40 kDa while as a dimer, it can reach up to 280 kDa [87]. Lowering intracellular amounts of adenosine, a signaling molecule that can be hazardous at high dosages, is the role of ADA1. Adenosine deaminaminase (ADGFs) is a unique family of growth factors that includes the recently discovered ADA2. ADGFs are crucial for the development of tissues [88]. On the other hand, ADA2 is found on the extracellular surface of a number of cells and has deaminase and cytokine-like growth factor activities. High levels of ADA2 are found in inflammatory disorders such diabetes, AIDS, rheumatoid arthritis, and TB [89, 90].

Relation between T2DM and Adenosine deaminase

One kind of purine nucleoside is adenosine. It is found in plasma and extracellular fluid, and it functions as a hormone in the physiology of smooth muscles, blood flow control, platelet aggregation, and nerve transmission. Adenosine has further impacts, such as affecting insulin activity. Because it converts adenosine to inosine, ADA, or adenosine deaminase, is essential in regulating the amount of adenosine in the body and its consequences. Glucose enters cells more easily with the help of adenosine. The quantity of adenosine and, hence, the amount of glucose that enters the cell are decreased when ADA activity is increased. This enzyme aids in the development and maturation of T lymphocytes [80]. The extra CAMP-adenosine cell route explains the higher etiology of ADA levels in type 2 diabetes. ADA promotes lipolysis and deactivates adenosine. Additionally, it promotes CAMP buildup [80]. When adenosine deaminase activity was investigated as a type 2 diabetes diagnostic marker, it was shown that diabetics had higher overall serum activity—particularly ADA2—than the control group. Consequently, they

discovered that the ADA may be a helpful test for identifying type 2 diabetes [81].

Several studies have shown that T2DM patients have higher levels of ADA activity than did healthy controls [73, 78]. Insulin effect and glycemic control may be significantly impacted by adenosine since it directly increases the action of insulin through a variety of pathways include leucine oxidation, lipogenesis, glucose transport, pyruvate dehydrogenase activity, and cyclic nucleotide phosphodiesterase activity [91]. Consequently, ADA activity predicts the prognosis of type 2 diabetes. Adenosine deaminase levels have been found to be higher in those with type 2 diabetes in several investigations. Insulin treatment has been demonstrated to lower type 2 diabetics' high ADA activity [92] Cells absorb glucose more easily when adenosine is present. Thus, increased ADA activity in insulin-sensitive tissue lowers adenosine levels, which lowers glucose uptake by cells [107]. Additionally crucial for the development and proliferation of lymphocytes, ADA is especially active in T-lymphocytes [93].

Conclusion

In most of the research mentioned in the study, higher serum ADA and its isoenzyme activities have a higher glycemic index in T2DM,

We conclude from this review that obesity, the nature of the diet, exposure to high temperatures, and lack of exercise lead to type 2 diabetes.

High blood sugar for long periods and lack of proper control of blood sugar levels lead to serious complications.

There is a relationship between higher type 2 diabetes and the enzyme TADA and isoenzyme ADA2, and high adenosine is considered a dangerous indicator that warns of the occurrence of diabetes complications.

Recommendations

It is recommended to conduct a study on the relationship between MDA and the adenosine enzyme and its analogues in patients with type 1 diabetes.

Also, increasing the size of the study regarding type 2 diabetes, as well as studying the effect of fats and oxidative stress on diabetes in pregnant women with gestational diabetes.

Conducting research on increasing adenosine in the blood from external sources or treatment that stimulates the production of adenosine because it is important in reducing insulin resistance and has been proven in several studies.

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