



## Review on: Diabetes Mellitus is a Disease

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### ABSTRACT

In this review article, an attempt was made to present an overview of diabetes mellitus. Diabetes mellitus (DM) is a group of insulin resistance syndrome characterized by a high blood sugar level over a prolonged period of time. Diabetes is not a contagious disease. We can say Insulin dependent disorder. Nowadays, Diabetes Mellitus detect in many more peoples all over the World. In this report, we all know about Diabetes Mellitus. In that, we include its classification, sign & symptoms, etiology, pathogenesis, diagnosis, treatment etc. It's had Four types, namely type 1, type 2, gestational Diabetes Mellitus & Other specific types such as, lada, mody. Fatigue Polyphagia, Polydipsia, polyuria, vomiting, dehydration etc., are common signs & symptoms are observed in Diabetes Mellitus. Diabetes Mellitus is mainly caused by the destruction of beta cells in the pancreas. Its cause's autoimmune disorders such as Addison's Disease, Hashimoto's Thyroiditis & Graves' disease. Some genetic factors, prior family history, environmental factors, autoimmune destruction, high insulin resistance these factors increase the risk of the development of diabetes mellitus. Most of the diabetic patients are older adults. Blood Glucose tests are used to detect diabetes mellitus. Insulin therapy is helpful to prevent or treat diabetes mellitus. For some patients, we used Islet replacement therapy and stem cell therapy used. In diabetes mellitus treatment, some drugs are used, such as miglitol, metformin, nateglinide, pioglitazone, glipizide, dapagliflozin, colestimide, bromocriptine etc. it's known as anti-diabetic drugs. Diabetics patients are more fastly rise in World.

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a group of insulin resistance syndrome characterized by a high blood sugar level over a prolonged period of time. It was explained by ancient Egyptians 3000years ago [2]. In the local area is commonly known as diabetes/ sugar disease. It is a non-communicable disease [3]. Serious long-run complications such as cardiovascular disease, stroke, chronic nephropathy and foot ulcers etc. It has nothing to do with "Diabetes Insipidus", which is kidney-related fluid retention problems. Diabetes mellitus has four types. T1DM, T2DM, GDM & Other specific types [4].

### INTRODUCTION

The word "Diabetes" & "Mellitus" come from the Greek language. "Diabetes" means "passer-by: a siphon" & "mellitus" means "sweet" [1]. (DM) is

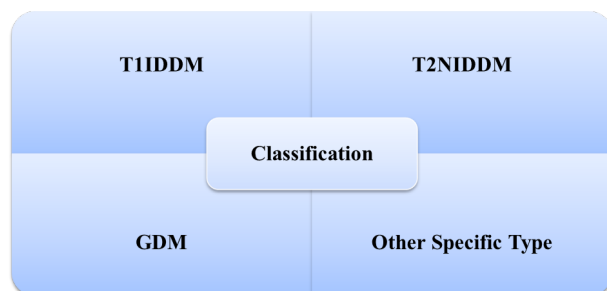
As of 2019, Approximately 463 Million people have diabetes over the World. About 8.8% of adults are affected by diabetes mellitus; T2DM contains about 90% of the cases. In 2019, diabetes mellitus caused an estimated 4.2 Million Deaths. In the US, the cost

of diabetes mellitus in 2017 was about 327 billion US\$. The global economic cost of diabetes mellitus related health expenditure in 2017 was estimated at 727 billion US\$. Normal diabetics make up 25-30% of the population. About 1 in 90 North Americans has diabetes each year. Develops proliferative Retinopathy & 1 in 80 macular edema [5].

Average medical expenditures among people with DM are about two times higher. Diabetes mellitus increase the risk of early death up to double. Trends suggest that rates will constantly or frequently increase. T1DM results in pancreatic cells being unable to produce enough Insulin. T2DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. GDM occurs when pregnant women without previous diabetes mellitus develop high blood sugar levels. T1DM can be managed by insulin injections. Treating T2DM involves maintaining a healthy diet, maintaining weight and physical exercise [6].

90% of diabetes mellitus people suffer or fight with T2D. High blood pressure, a condition often present in people with T2DM, that together with diabetes greatly increases the risk of cardiovascular disease. Control BP, Proper foot & eye care are important for people with the disease. Weight loss or reduced surgery is an effective measure in obese or fatty people. GDM usually resolves after a newborn baby or fetus [7].

Diabetic patients are more rapidly or constantly rising all over the World, which poses a great challenge to the current therapeutic approach. Other than insulin therapy here, we will develop a new one is islet transplantation & stem cell transplantation. Islet transplantation therapy is a low success rate as well as it has some challenges like limited donors, proper long-term functioning etc., So, it's rarely used in the treatment of diabetes mellitus disease. In the treatment of diabetes, use a group of insulin drugs that include insulin secretagogues (Sulphonylureas, Meglinides); Insulin sensitizers (Biguanides, Thiazolidinediones); Alpha-glucosidase Inhibitor; Sodium-glucose co-transporter 2 inhibitors [8].



**Figure 1: Classification of Diabetes Mellitus**

### **Insulin Dependent Diabetes Mellitus (T1IDDM)**

This type of diabetes mellitus is also known as Auto-immune Diabetes and it's previously known as Juvenile onset diabetes [9]. It is also known as a ketosis-prone polygenic disease [10]. This occurs mainly in children, and Adults & it develops before the age of 40, the disease occurs suddenly in teenagers & it can also be life-threatening. T1DM can be handled or treated with Insulin, but there is no cure. This form was previously known as "Insulin-Dependent Diabetes Mellitus" [9]. The exact causes of T1DM are unknown [6]. People who have T1DM require Insulin. T1DM results from the pancreas's failure to produce an adequate amount of Insulin due to loss of beta-cells, destruction of Beta-cells [11].

A large amount of sugar in the blood can lead to short-term and long-term problems. T1DM is a chronic metabolic syndrome defined by the inability of insulin production. Glucose from your food can't enter cells resulting in increased concentration in the bloodstream. About 10% of people suffer from type 1 DM [12]. The pathogenesis of T1DM is shown in Figure 1.

### **Non-Insulin Dependent Diabetes Mellitus (T2NIDDM)**

T2NIDDM is also known as Adult onset Diabetes Insulin secretion defects identified in T2DM contribute to Insulin Resistance (IR). This form was previously known as "non-insulin-dependent diabetes mellitus" [9]. It causes by insulin resistance and defects in beta cells due to glucose built in the bloodstream [13]. It is a progressive disease that develops in stages. A condition in which cells fail to respond to Insulin properly or reduced insulin level develops hyperglycemia and FFA [3]. The stages of T2DM are shown in Figure 1. In T2DM, we will observe Blood vessels, heart and it also causes illness and death of the patient. The most common cause is a combination of overweight and lack of exercise. Firstly it's developed pre-diabetes. In T2DM occur long term complications in the kidney [10].

### **Gestational Diabetes Mellitus (GDM)**

Those pregnant with this Diabetes are divided into GDM. It is the most common type of heritable kind of Monogenic disease women's who have suffered from ClassA2 need Insulin or other Medications. Gestational diabetes is the 3rd main type, and it occurs in pregnant women without a previous history of diabetes mellitus. GDM usually is detected in the later stages of pregnancy and often occurs in women who have no previous history of diabetes mellitus [9]. A fetus born with diabetes mellitus is the high risk of obesity & T2DM in future. GDM have

two classes - Class A1 & Class A2. It occurs in about 4% of all pregnancies [14]. Class A1 are handled by Diet and Exercise. Gestational diabetes is projected to increase by approximately 18% globally [15].

### Other Specific Type of Diabetes Mellitus (Monogenic Types)

It's into MODY, LADA & Endocrinopathies. It's also caused by genetic abnormalities in the internal secretion of insulin hormone. 1 to 5% of people who have suffered from it develop by mutations. This includes diseases of the pancreas, certain Surgeries, Genetic defects in beta cells, Cancer Therapies, medications & Infections etc. Some medicines are utilized or mixed with the treatment of HIV /AIDS or organ transplantation [16]. It's had sub-types MOODY, LADA & Endocrinopathies.

#### MODY

They may or may not be required Insulin. MODY stands for maturity onset diabetes of young [9]. MODY is inherited diabetes mellitus by a genetic mutation in an autosomal dominant gene that affects the secretion of insulin secretion or production & it's not an insulin dependant diabetes. Individual diagnosis is generally in children less than age 25 with genetic factors. HNF1-Alpha (Hepatocyte Nuclear Factor) gene causes about 70% of cases of MODY [17]. It associates with a genetic defect of the  $\beta$ - cells. In this type occurs hyperglycemia at an early age. They are clinically closer to T2DM.

#### LADA

LADA stands for latent autoimmune diabetes in adults. After Diagnosis, it's not required for Insulin for months to a year. They do not produce any insulin and it's clinically similar to T1DM, LADA occurs because pancreatic cells stop insulin production. LADA is present in young adults in their twenties & can be confused with type 2 diabetes mellitus because of age [18]. Type 1DM are different from LADA (Table 1).

#### Endocrinopathies

Several hormones play activity on insulin action or inhibit insulin action. Impaired fasting blood glucose presents as an FBG higher than 100mg/dl but less than 126 mg/dl [18]. It may include polycystic ovarian syndrome, pancreatic cancer or tumours & other hormonal Disruptions in insulin production.

#### Etiology of Diabetes Mellitus

Sometimes chemicals & drugs are causes T1DM. Its cause's autoimmune disorders such as Graves' Disease, Hashimoto's Thyroiditis & Addison's disease [9]. Which can seriously causes that type of diabetes mellitus. In about 70 – 80% of cases, beta-cells

are destroyed the immune system. In T1DM, the beta cells fail to produce Insulin. T1DM is commonly caused by the destruction of beta-cells. The cause of this autoimmune response is unknown T1DM characterized by Anti-Glutamic acid decarboxylase [19].

Due to improper use of insulin, the glucose level decreased in the body, the leading cause of Type 2DM. It's also caused by Overeating, smoking, alcoholism, dysfunction of the endocrine & nervous system [20]. 33% of American adults have higher kidney disease. African Americans, Latinos, Native Americans, Asian Americans, & Pacific Islanders all have a high risk of kidney disease [21]. In T2DM, the body fails to utilize Insulin. Some traditional groups have a higher inherited incidence of it. The body produces a hormone called Insulin that maintains normal blood sugar levels. During pregnancy, the placenta produces higher pregnancy hormones that can interfere with Insulin. The body can make more insulin during pregnancy to keep blood glucose levels normal. Still, in some women, the body cannot make sufficient insulin during pregnancy and blood sugar levels grow up & its causing GDM. The main cause of diabetes Retinopathy is blindness & it causes 2.6% of global blindness [22].

#### Pathophysiology of DM

Figure 2, Shows Pathophysiology of Type 1 & Type 2 Diabetes Mellitus.

#### Sign and Symptoms of DM

Table 2 contains some signs & symptoms are seen in Diabetes Mellitus.

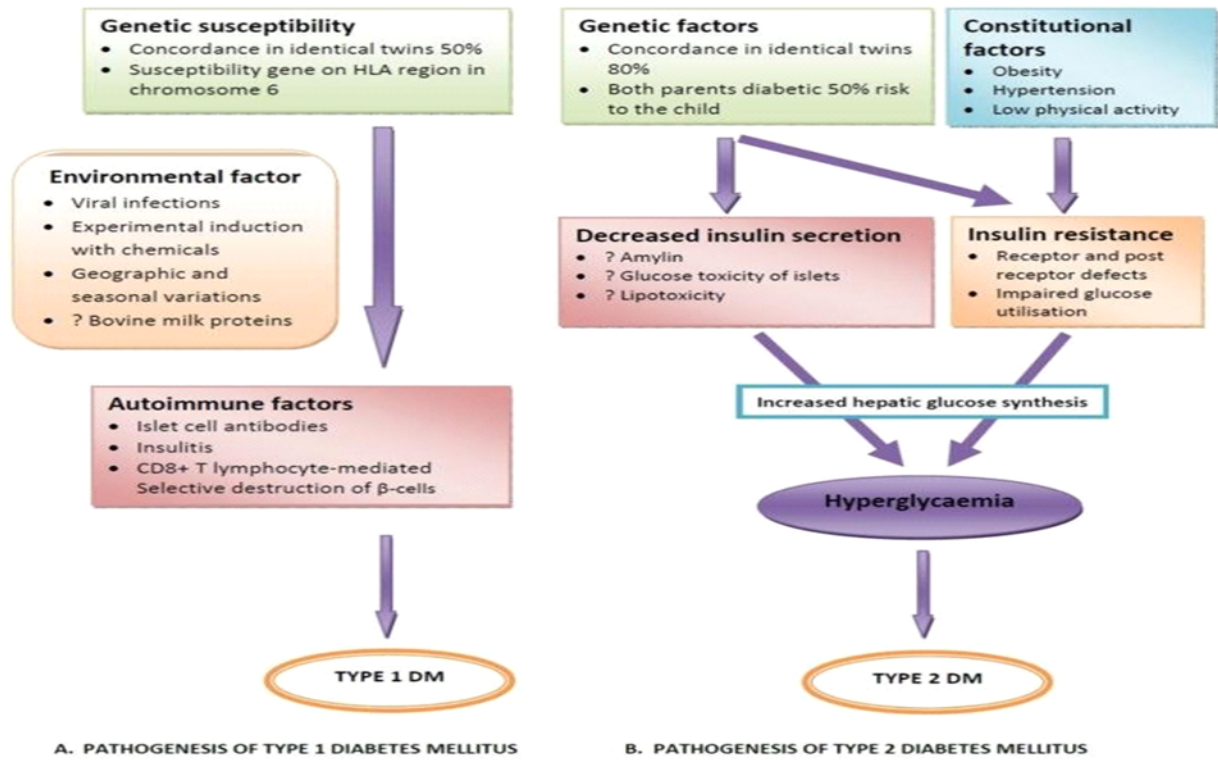
#### Test For Diagnosis Diabetes Mellitus

Diabetes is diagnosed by testing the blood glucose/sugar levels. Blood is tested before eating some food. Mostly it performs in the morning time before breakfast (Table 3). If a blood sugar level after fasting blood sugar level will be increased above 125 mg/dL, hence diabetes mellitus is diagnosed. Your doctor will examine blood pressure, weight & feet.

1. Obesity - A condition that greatly raises a person's risk for T2DM.
2. High BP - A condition often present in people with T2DM, that together with diabetes, will increase the risk of cardiovascular diseases.
3. Weak pulses in the feet - A condition that can prevent or reduce foot sore healing & possibly amputation. To decrease the risk of ulceration or re-ulceration by using specialized footwear's [7].

**Table 1: Difference parameters of Diabetes Mellitus**

	T1DM	T2DM	MODY	LADA
Typical Age of Onset	Youth	Adult	Youth	Adult
Presence of Autoantibodies	Yes	No	No	Yes
Insulin Dependence	Yes	No	Not Always	Yes, within years
Insulin Resistance	No	Yes	Yes	No
Progression to Insulin Dependence	Rapid	Slow	Slow	Month/Year



**Figure 2: Pathophysiology of T1DM & T2DM**

**Table 2: Sign and Symptoms of Diabetes Mellitus**

Sign	Symptoms
Extreme Hunger (Polyphagia)	Dry Skin & Mouth
Excessive Thirst ( Polydipsia )	Foot Pain
Frequent Urination ( Polyuria )	Yeast Infection
Slow Wound Healing	Genital & Skin Infection
Acanthosis Nigricans	Fatigue
Weight Loss	Nausea
Dehydration	Pain in Stomach
Headache	Vomiting
Flushed Face	Blurry Vision

**Table 3: Laboratory Tests**

Test	Normal ( mg/dL )	Pre-Diabetes ( mg/dL )	Diabetes ( mg/dL )	Ref
Fasting Plasma Glucose Test	<100 mg/dL	100 – 125 mg/dL	>126 mg/dL	[23]
Oral Glucose Tolerance Test	<140 mg/dL	140 – 199 mg/dL	>200 mg/dL	
Random Blood Glucose Test	NA	NA	>200	
Hemoglobin A1C Test	<5.7 %	5.7 – 6.4 %	>6.5 %	

**Table 4: Types of Insulin**

	Rapid Acting	Short/ Regular Acting	Intermediate Acting	Long Acting	Act- not peak	Ultra-long Action	Ref
Onset	15 min	30 min	2 – 4 hours	2 hours		6 hours	[24]
Peak Time	1 – 2 hours	2 – 3 hours	4 – 12 hours	Dose not peak		Dose not peak	
Duration	2 – 4 hours	3 – 6 hours	12 – 18 hours	24 hours or long		36 hours or long	
Example	Humulin R, Velosulin R	Humulin N, Novolin N	Degludec, Glargine	Glargine, Detemir, Degludec		Glargine U-300	

**Tests For Diagnosis GDM****O'Sullivan Test**

This test is used to examine GDM. A fasting patient is given 50g of glucose. Blood is drawn at every hour. GDM is indicated by plasma levels above 1500mg/dL [18].

**Treatment of Diabetes Mellitus**

T1DM is unavoidable because it's caused by a problem with the immune system. Most diabetes prevention or treatment strategies involve making simple changes to your diet and fitness routine. Some causes of T2DM, such as your genes or age, are out of your control. Yet many other diabetes mellitus risk factors are manageable. These aren't the only ways to prevent diabetes mellitus. Diabetes Mellitus is a chronic disease with an unknown cure [7]. Here are some things you can do to delay or prevent T2DM,

1. Get at least 20 min/day of aerobic exercises.
2. If you are overweight, try to lose 7% as a reliable source.
3. The diet excludes refined carbohydrates from your diet.
4. Eat many more fruits, vegetables and whole grains daily.

It may be possible to manage by eating healthy foods, exercising, and maintaining healthy body weight.

The goal of treatment is to maintain healthy blood glucose levels and to prevent diabetes mellitus related complications,

**Diet**

A high fiber & low-fat diet based on fruits, vegetables, and whole grains are suggested by doctors. Avoid clarified sugar containing foods.

Alcohol contains a lot of sugar, so consumption of alcohol (Alcoholism) should be reduced [26].

**Exercise**

Exercise effect on Physical, Mental & Social health. Exercise helps to lower blood glucose levels. Regular exercise also helps maintain healthy body weight and control high blood pressure and high blood cholesterol levels [27].

This, in turn, helps to reduce the risk of related health conditions such as cardiovascular diseases. Sitting still (i.e. being sedentary) for long periods is a risk factor for T2DM. You should aim to get up regularly and move around for a few minutes [26].

**Weight**

Overweight is high risk [22]. People with T2DM and overweight (BMI > 35) may be able for weight-loss surgery (bariatric surgery) [26].

**Skin**

DM causes some skin related complications such as Bacterial & Fungal Infections, Itching and some Allergic reactions etc., [28].

**Table 5: Anti-Diabetic Drugs and their action with Generic Name**

Types of Drug	Action of Drug	Adverse Effects	Generic Name	Reference
Alpha Glucosidase inhibitors	Inhibitor slow break-down of oligosaccharides and disaccharides into monosaccharides & also prevents its absorption.	Flatulence & Diarrhea	Acarbose, Miglitol	[25]
Biguanides	Lowers the hepatic glucose output and increase uptake of glucose by the periphery, including skeletal muscle.	modest weight loss	Metformin	
Meglitinides	Its trigger the beta-cells of the pancreas to increase the secretion of Insulin.	Hypoglycemia	Repaglinide, Netaglinide	
Thiazolidinediones	It improves insulin sensitivity in adipose tissue and skeletal muscle for good work.	Skin allergies, Chest pain, heart failure.	Pioglitazone, Rosiglitazone	
Sulfonylureas	Increase insulin secretion by stimulating Beta pancreatic cells.	Hypoglycemia, Cardiovascular Diseases	Glimepiride; Glibenclamide; Glipizide	
Sodium-glucose co-transporter 2 inhibitors	lower blood glucose levels by blocking the re-absorption of glucose in the kidney and improve glucose excretion.	Vaginal yeast infections, Urinary tract infections	Empagliflozin, Canagliflozin, Dapagliflozin, Ipragliflozin.	
Bile Acid Sequestrants	Developed glucose-lowering effect and improved tolerance.	Constipation, Heart Burn, Bloating	Colesevelam, Colestimide	
Dopamine D2 Receptor Agonist	improves insulin sensitivity and lower insulin resistance.	Cardiac Arrhythmia, Hypotension	Bromocriptine	

**Family History**

The high risk of T2DM due to family history [22].

**Age**

Risk of diabetes increases as you get younger, especially after 45 years old [22].

**Blood glucose monitoring**

Depending on a person's treatment plan, their blood glucose levels may require to be checked and noted from time to time or, if treated with Insulin, several times a day. Many factors can interfere with blood glucose levels, so careful measure is the way to ensure that blood sugar levels remain within their normal range [26].

Two blood glucose level problems requiring immediate attention are,

**High blood glucose (hyperglycemia)**

Eating too much food or not taking enough diabetes

medication can result in a blood glucose level that is too high. Hyperglycemia is a life-threatening condition that requires immediate hospitalization to prevent complications & death of the patient [29].

**Low blood glucose (Hypoglycemia)**

It defines a blood sugar level <70 mg/dL. Blood glucose levels can drop for many reasons, e.g., skipping, taking diabetes medication, or exercising more than usual. Hypoglycemia is most likely when taking insulin or diabetes medications that promote the secretion of Insulin. Drinking or eating something sweet will correct a low blood glucose level [26].

**Insulin Therapy**

People with T1DM need insulin therapy [30]. The goal of insulin therapy is to maintain or control blood sugar level. It's administrated subcutaneously using a syringe, insulin pen or insulin pump (Table 4). Insulin therapy is the most important part of T1DM & sometimes for T2DM [31].

When your doctor talks about Insulin, they'll mention three main things,

1. Onset
2. Peak time
3. Duration

### Islet Replacement Therapy

Insulin injections are traditional in vitro therapy that cannot correctly cure diabetes mellitus. Islet replacement therapy is an alternative treatment for diabetic patients. In this therapy, insulin producing beta-cells are replaced with pancreas or islet-cell transplants [32]. It's used sometimes because low success rate.

Instead, this major transition from conventional/traditional Insulin to islet transplants has some challenges such as limited donors, proper functioning of islet grafts, long term survival etc., [33].

### Stem cell therapy

Stem cells are responsible for the development of the whole human body. Stem cell therapy is used to treat T1DM. To cure T1DM, replacing stem cells must be more than just a case of alternate Insulin generating cells from the pancreas those diminished by diabetes in diabetic patients [32]. This property of stem cell is help to the proper functioning of pancreatic beta cells that are production a sufficient amount of insulin to maintain blood glucose level (Table 5).

### Common Diabetes Medications for Diabetes Mellitus

If some lifestyle changes are inadequate or unable to control its blood glucose level, maybe need some medications are required.

### CONCLUSIONS

The above review has given information about Diabetes Mellitus, Types, Signs & Symptoms, Causes, Diagnosis, and Treatment. Diabetes Mellitus become a common disease among children and more severe if no initiative is taken to control it. Diabetes Mellitus is a Non-Curable (Incurable) Disease, but it can handle or Prevent by Insulin Therapy & Anti-Diabetic medicines for a while. Proper diet and exercise for diabetic's patients is a must. 80-90% of Diabetic Patients suffer from T2DM in India & US. If not appropriately treated, The disease will affect 90 - 95% of the World's population & it will generally appear in people of all age's in the future.

### Abbreviation

Type1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), Gestational Diabetes Mellitus (GDM), Type 1 Insulin Dependent Diabetes Mellitus (T1IDDM), Type2 Non-Insulin Dependent Diabetes Mellitus, (T2NIDDM), Low density Lipoprotein (LDL), Diabetes mellitus (DM), High Density Lipoprotein (HDL), Low Density Lipoprotein Cholesterol (LDL-C).

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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