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# Diabetes Mellitus : A Review of Current Trends

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## Introduction

Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretary response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemias

[1] Diabetes mellitus (DM) is commonly referred to as a "sugar" and it is the most common endocrine disorder and usually occurs when there is deficiency or absence of insulin or rarely, impairment of insulin activity (insulin resistance) [2]. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 [3].

Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the beta (ß) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan's. Insulin decreases the blood glucose level by the disorders, and malignancy in future life of fetus after delivery [6]. Type II diabetes mellitus comprises 80% to 90% of all cases of diabetes mellitus. Geographical variation can contribute in the magnitude of the problems and to overall morbidity and mortality [7, 8]. Moreover, people with diabetes who undertake moderate amounts of physical activity are at inappreciably lower risk of death than inactive persons [24] It is now well established that a specific genetic constitution is required for such an event to cause [9] The growing burden of diabetes and other non- communicable diseases is one of the major health challenges to economic developments bedeviling WHO African Region states [10]. See figure (1 and 2).In diabetes, there is an aberration either in the synthesis or secretion of insulin as seen in Type 1 diabetes mellitus (T1DM) and stenosis in the pancreatic duct, or the development of resistance to insulin or its subnormal production as in the case of Type 2 diabetes (T2DM) andcertain secondary diabetes.

## Classification of Diabetes Mellitus

The first mostly accepted classification of diabetes mellitus was published by WHO in the year 1980 [11] and, it is modified in the year 1985 [12]. The most common and important form of Primary or idiopathic diabetes mellitus, which is focus of our discussion. It must be different from secondary diabetes mellitus which includes forms of hyperglycemia associated with glycogenesis and transport glucose into the muscles, liver and adipose tissue. Neural tissue and erythrocytes do not required insulin for glucose utilization whereas alpha (α) cells plays an important role in controlling blood glucose by producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis [4, 5].

In addition to increased risk of obesity, metabolic and cardiovascular identifiable causes in which destruction of pancreatic islets is induced by inflammatory Pancreatic diseases, surgery, tumors, certain drugs, iron overloaded (Hemochromatosis) and certain acquired or genetic endocrinopathies [1].The classification encompasses both clinical stages and aetiological types of diabetes mellitus and other categories of hyperglycemia [13].Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, and many diabetic individuals do not easily fit into a single class [14] Primary diabetes mellitus probably represents a heterogeneousgroup of disorders that have hyperglycemia as a commonfeature [1].

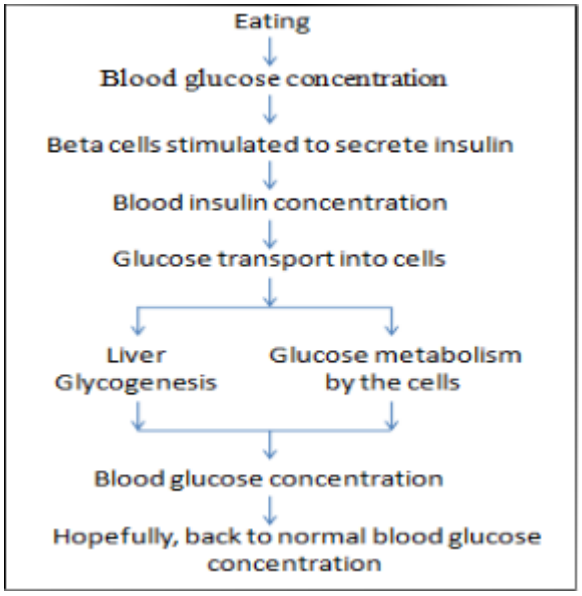


**Fig 1:** Glucose Metabolism

The new classification of diabetes mellitus contains stages which reflect the various degrees of hyperglycemia in individual subjects with any of the disease processes which may lead to diabetes mellitus [15, 16]

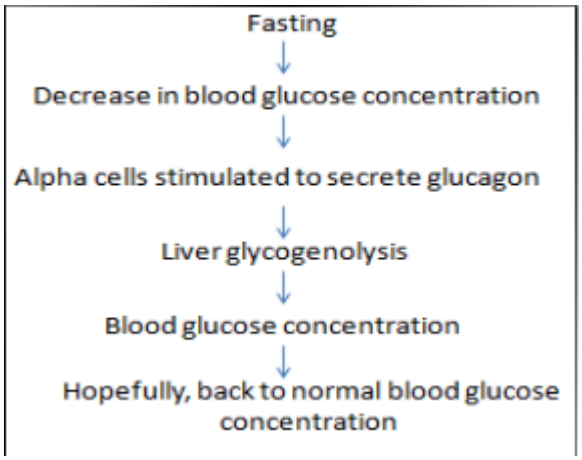


**Fig 2:** Normal response to fasting [10, 11]

The old and new terms of insulin-dependent(IDDM) or non- insulin-dependent (NIDDM) which were proposed by WHO in1980 and 1985 have disappeared and the terms of new classification system identifies four types of diabetes mellitus: type 1(IDDM), type 2(NIDDM),"other specific types" and
gestational diabetes (WHO Expert Committee 1999). These were reflected in the subsequent International Nomenclature of Diseases (IND) in1991and the tenth revision of the International Classification of Diseases (ICD-10) in 1992 [13]. Hence, classification of diabetes mellitus is described as below:

**1.** Insulin Dependent Diabetes Mellitus (Type1 IDDM) This type of diabetes mellitus is also called autoimmune diabetes and previously known as juvenile-onset or ketosis- prone diabetes. The individual may also seek with other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease [17]. Type I diabetes mellitus is also known as insulin- dependent diabetes mellitus (IDDM), this occurs mainly in children and young adults; the onset is usually sudden and can be life threatenin [4]. Type 1 is usually characterized by the presence of anti–glutamic acid decarboxylase, islet cell or insulin antibodies which identify the autoimmune processes which leads to beta-cell destruction [34]. Type 1 diabetes (due to the destruction of b-cell which is usually leading to absolute insulin deficiency) (American Diabetes Association, 2014). The rate of destruction of beta- cell is quite variable; it can be occur rapidly in some individuals and slow in others [18]. There is a severe deficiency or absence of insulin secretion due to destruction of ß-islets cells of the pancreas. Treatment with injections of insulin is required [4]. Markers of immune destruction, including islet cell auto-antibodies, and/or auto antibodies to insulin, and auto antibodies to glutamic acid decarboxylase (GAD) are present in 85-90 % of individuals with Type 1 diabetes mellitus when fasting diabetic hyperglycemia is initially detected [19]. The exact cause of diabetes mellitus is remain unknown, although, in most people, there is evidence of an autoimmune mechanism involving auto-antibodies that destroy the beta-

islet cells [4].

**2.** Non-Insulin Dependent Diabetes Mellitus(Type2 Niddm) Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretary defect on the background of insulin resistance (American Diabetes Association, 2014) [20]. People with this type of diabetes frequently are resistant to the action of insulin [21]. The long-term complications in blood vessels, kidneys, eyes and nerves occur in both types and are the major causes of morbidity and death from diabetes [1]. The causes are multifunctional and predisposing factor includes: Obesity, Sedentary lifestyle, increasing age (affecting middle- aged and older people), Genetic factor (Ross and Wilson 2010), such patients are at increased risk of developing macrovascular and micro vascular complications [22, 23].

**3.** Gestational Diabetes Mellitus

The glucose intolerance occurring for the first time or diagnosed during pregnancy is referred to as gestational diabetes mellitus (GDM) [2]. Women who develop Type1 diabetes mellitus during pregnancy and women with undiagnosed asymptomatic Type 2 diabetes mellitus that is discovered during pregnancy are classified with Gestational Diabetes Mellitus (GDM) [16]. Gestational diabetes mellitus (GDM) (diabetes diagnosed during pregnancy that is not clearly over diabetes) [17]. The gestational diabetes mellitus may develops during pregnancy and may disappear after delivery; In the longer term, children born to mothers with GDM are at greater risk of obesity and type 2 diabetes in later life, a phenomenon attributed to the effects of intrauterine exposure to hyperglycaemia.

**4.** Other Specific Type (Monogenic Types)

The most common form of monogenic types of diabetes is developed with mutations on chromosome 12 in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1a.They also referred to as genetic defects of beta cells. These forms of diabetes are frequently characterized by onset of hyperglycemia at an early age (generally before age of 25 years). They are also referred to as maturity onset diabetes of the young (MODY)[12] or maturity-onset diabetes in youth or with defects of insulin action; persons with diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; persons with dysfunction associated with other endocrinopathies (e.g. acromegaly); and persons with pancreatic dysfunction caused by drugs, chemicals or infections[16]. Some drugs also used in the combination with the treatment of HIV/ AIDS or after organ transplantation. Genetic abnormalities that result in the inability to convert proinsulin to insulin have been identified in a few families, and such traits are inherited in an autosomal dominant pattern. They comprise less than 10% of DM cases [11].

**Some Common Sign and Symptoms**

In diabetes mellitus, cells fails to metabolized glucose in the normal manner, effectively become starved [2]. The long term effect of diabetes mellitus which includes progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, and neuropathy with risk of foot ulcer, Charcot joint and features of autonomic dysfunctions and sexual dysfunction [24] People with diabetes are at increases risk of diseases. See table(1).

Other, various symptoms are observed due to-

i. Gluconeogenesis from amino acids and body protein, causing muscle wasting, tissue breakdown and furtherincreases the blood glucose level.
ii. Catabolism of body fat, releasing some of its energy and excess production of ketone bodies [2]

## Etiology of Diabetes Mellitus

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

1. It is currently believed that the juvenile-onset (insulindependent) form has an auto immune etiology.
2. Viruses may also play a role in the etiology of diabetes like coxsackieB.
3. Mumps and rubella viruses all have been shown to produce morphologic changes in the islet-cell structure.
4. The genetic role in the etiology of diabetes is controversial. Possibly a genetic trait makes an = individual's pancreas more susceptible to one of the aboveviruses [45].

**Causes of Diabetes Milliteus**

Disturbances or abnormality in gluco-receptor of ß cell so that they respond to higher glucose concentration or relative ß cell deficiency. In either way, insulin secretion is impaired; may progress to ß cell failure [25]. The theory of principal in micro vascular disease leading to neural hypoxia, and the directeffects of hyperglycaemia on neuronal metabolism [26].

1. Reduced sensitivity of peripheral tissues to insulin: reduction in number of insulin receptors, 'down regulation' of insulin receptors. Many hypersensitive

and hyperinsulinaemic, but normal glycaemic; and have

associated dyslipideaemic, hyperuriaemiac, abdominal obesity. Thus there is relative insulin resistance, particularly at the level of liver, muscle and fat. Hyperinsulinaemic has been implicated in causing angiopathy [24].

2. Excess of hyperglycaemia hormone (glucagon) etc.
/obesity; causes relative insulin deficiency –the ß cells lag behind. Two theories have demonstrated abnormalities in nitric oxide metabolism, resulting in altered perineural blood flow and nerve damage [25].
3. Other rare forms of diabetes mellitus are those due to specific genetic defects (type 3) like "maturity onset diabetes of young" (MODY) other endocrine disorders, pancreatectomy and gestational diabetes mellitus (GDM).
[24].
4. Due to imbalance of specific receptor can cause diabetes mellitus. Some specific receptors are Glucagon-like peptide-1(GLP-1) receptor, peroxisomes proliferator- activated (γ) receptor (PPARγ), beta3 (ß3) ardent-receptor some enzymes like α glycosidase, dipeptidyl peptidase IV enzyme etc [24].
5. Current research on diabetic neuropathy is focused on oxidative stress, advanced glycation-end products, protein kinase C and the polyol pathway [26].

**Diagnosis of Diabetes Mellitus**

The diagnosis of diabetes in an asymptomatic subject should neverbe made on the basis of a single abnormal blood glucose value. If a diagnosis of diabetes is made, the clinician must feel confident that the diagnosis is fully established since the consequences for the individual are considerable and lifelong [27]. The diagnosis of diabetes mllitus include, urine sugar, blood sugar, glucose tolerance test, renal threshold of glucose, diminished glucose tolerance, increased glucose tolerance, renal glycosuria, extended glucose tolerance curve, cortisone stressed glucose tolerance test, intravenous glucose tolerance test, oral glucose tolerance test.

**Treatment of Diabetes Mellitus**

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

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

## A. Types of Therapy Involved In Diabetes Mellitus

### 1. Stem cell therapy

Researchers have shown that monocytes/ macrophages may be main players which contribute to these chronic inflammations and insulin resistance in T2DM patients [28]. Stem cell educator therapy, a novel technology, is designed to control or reverse immune dysfunctions [29]. The procedure includes: collection of patients' blood circulating through a closed-loop system, purification of lymphocytes from the whole blood, co-culture of them with adherent cord blood-derived multi-potent stem cells (CB-SCs) *in vitro* and administration of the educated lymphocytes (but not the CB-SCs) to the patient's circulation

### 1 Antioxidant therapy

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

Anti-inflammatory treatment

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

**B. Dietary Management**

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

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

**C. Newer Insulin Delivery Devices**

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

**D Oral Hypoglycaemic or Antidiabetic Agents**

Clinically useful biguanide phenformin was produced parallel to sulfonylurea's in 1957. Newer approaches have constantly been explored and have lately yielded thiazolidinediones, meglitinide analogues, α-glucosidase inhibitors, and the latest are dipeptidyl peptidase-4(DPP-4) inhibitors [24].

**Important Features of Oral Hypoglycaemic Agents**

Diabetes mellitus can be considered a disease of the modern world with a great impact of morbidity, morality and the quality of type of the affected individual. Diabetes mellitus is a frequent complication of cushing syndrome which is caused by chronic exposure to Glucocorticoids by several clinical symptoms such as central obesity, proximal muscles weakness, hirsutism and neurophysiological disturbance, macro-vascular complication autonomic neuropathy, digestiveproblems, dental problems etc. [24].

## Conclusion

Diabetes mellitus is a serious complication in today life. The lifestyle and day today circumstances are play major role in occurring this type of serious complications. In this review weget some idea regarding diabetes mellitus.

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