



## A REVIEW: ON DIABETES MELLITUS (DM)

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### ABSTRACT

“Diabetes mellitus”, is the most common non-communicable diseases worldwide. Diabetes is one of the leading causes of mortality in the world with about 8.5% of the global population (422 million) are currently diagnosed. Diabetes mellitus (DM) is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced. India faces several challenges in diabetes management, including a rising prevalence in rural and urban areas, limited health care facilities, high cost of diagnosis, lack of disease awareness among the public, suboptimal glycaemic control and rising prevalence of diabetic complications. Conventionally, diabetes has been classified into three parts namely: Type 1 Diabetes Mellitus or insulin-dependent diabetes mellitus in which body fails to produce insulin, and presently requires the person to inject insulin. It is also known as "juvenile diabetes". Type 2 Diabetes Mellitus or non-insulin-dependent diabetes mellitus results from insulin resistance, a condition in which cells fail to use the properly insulin, with or without an absolute insulin deficiency, which accounts for more than 90% of all types diabetes cases. The third main type is gestational diabetes which occurs when women without a previous history of diabetes develop a high blood glucose level during her pregnancy. The pharmacotherapy is used for the treatment of diabetes mellitus includes insulin and oral hypoglycemic agents. Some drugs act by either increasing the secretion of insulin from pancreas or reducing plasma glucose concentrations by increasing glucose uptake and decreasing gluconeogenesis. The herbal drugs have been also provided effective due to their beneficial contents in treatment of diabetes. Insulin therapy for diabetes is most commonly delivered via subcutaneous injections, up to four times a day.

**Keywords:** Diabetes mellitus, diagnosis, classification, cause and treatment

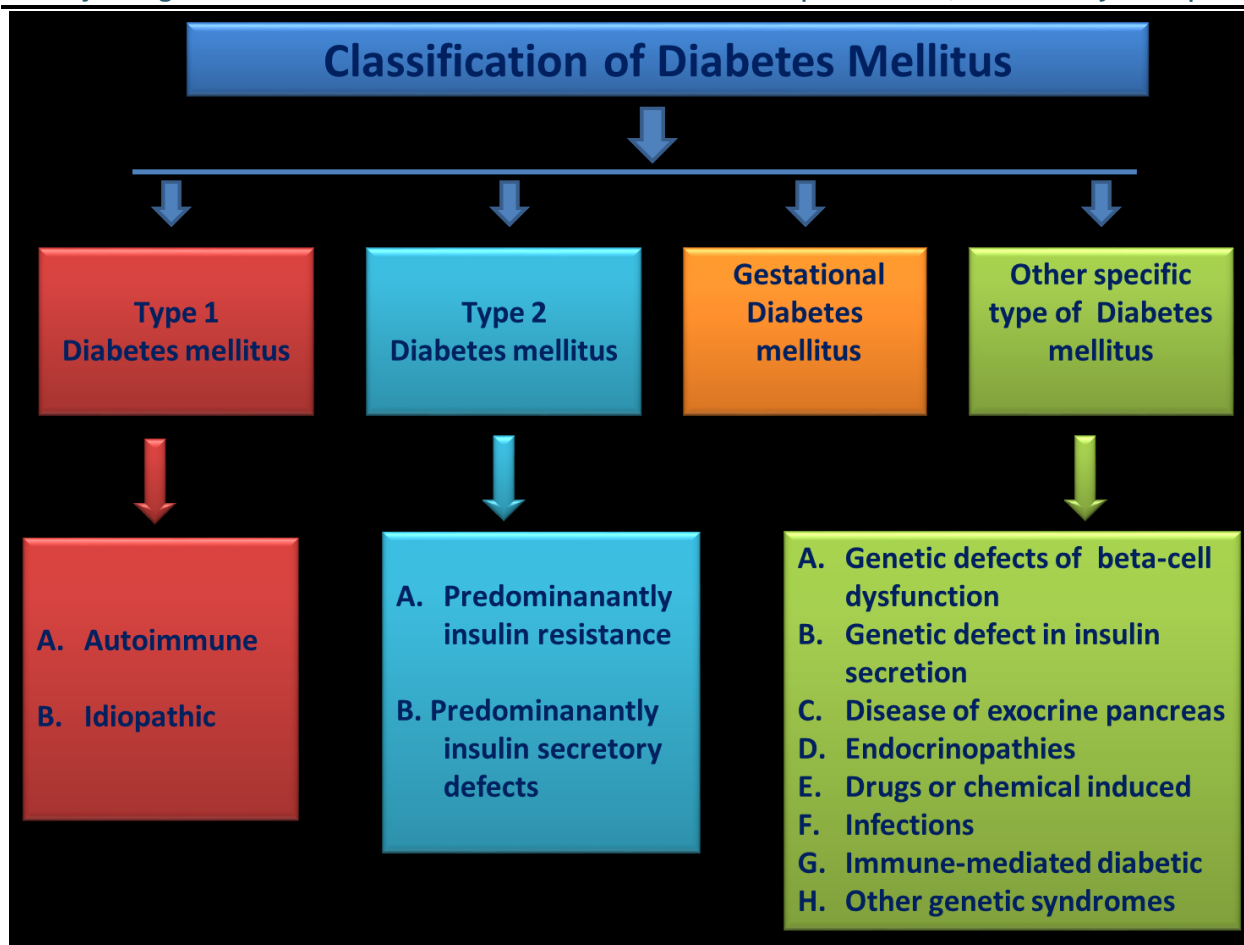
## Introduction-

Diabetes mellitus is characterized by derangements in carbohydrate, protein and fat metabolism caused by complete or relative insufficiency of insulin secretion or insulin action. Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia associated with several complications. Diabetes mellitus or simply 'diabetes' is a non-communicable chronic metabolic disorder characterized by hyperglycemia high level of sugar (glucose) in the blood, associated with disturbances of fat, carbohydrate and protein metabolism due to complete or relative deficiency in insulin secretion and action or both. 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. There are several forms of Diabetes mellitus which differ by pathogenic mechanisms by which hyperglycemia arises. Some forms of DM are characterized by an insulin deficiency or a genetic defect to defective insulin secretion, whereas other forms share insulin resistance as their underlying etiology. The long-term complications of diabetes mellitus include dysfunction and failure of various organs, particularly the eye (retinopathy), kidney (nephropathy), nerve (neuropathy), Heart (CAD) and blood vessels (PVD). Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the  $\beta$ -cells and glucagon is secreted by the  $\alpha$ -cells both are located in the islets of Langerhans's. The classical symptoms of diabetes are polyuria, polydipsia, polyphagia, blurring of vision and weight loss. Insulin replacement therapy is the mainstay for patients with type 1 Diabetes Mellitus while diet and lifestyle modifications are considered the cornerstone for the treatment and management of type 2 Diabetes Mellitus. The different types of hypoglycemic agents such as *biguanides* and *sulfonylureas* are also available for treatment of diabetes.

## Classification of Diabetes Mellitus-

The first mostly accepted classification of diabetes mellitus was published by World Health Organization (WHO) in the year 1980 and, it is modified in the year 1985. Diabetes mellitus is classified into three major types: type 1 Diabetes mellitus, type 2 Diabetes mellitus, and gestational diabetes mellitus (GDM).

World Health Organization in consultation with an expert committee of the American Diabetes Association (ADA) classified diabetes mellitus in four broad categories



**Fig. 01 Classification of diabetes mellitus**

**a) Type 1 Diabetes mellitus**

Type 1 Diabetes mellitus generally termed as Insulin Dependent Diabetes mellitus, accounts for 5 -10 % of those with Diabetes mellitus. This type of diabetes mellitus is also called autoimmunediabetes. Type I diabetes mellitus is also known as insulin- dependent diabetes mellitus. Type 1 diabetes usually affects children and people below thirty years of age, but can also affect older adults. Type 1 Diabetes mellitus is due to cell-mediated autoimmune destruction of  $\beta$ -cells of the pancreas. At a later stage of the disease, there is little or no insulin secretion, as manifested by low or undetectable levels of plasma C-peptide. Insulin- dependent diabetes mellitus (due to the destruction of  $\beta$ -cell which usually leading to absolute insulin deficiency) (American Diabetes Association, 2014). In the present modern world Type 1 Diabetes mellitus can occur at any stage of life. Treatment of this type of Diabetes mellitus is by insulin replacement therapy.

### **b) Type 2 Diabetes mellitus-**

Type 2 diabetes is the most common globally. Type 2 Diabetes mellitus accounts for 90-95% of those with Diabetes mellitus, it is also known as Non-Insulin Dependent Diabetes mellitus (NIDDM). Type 2 diabetes mellitus is also known as adult-onset diabetes. It predominantly affects adults above thirty years of age although many cases have recently been diagnosed amongst obese children. Non-Insulin Dependent Diabetes mellitus is due to insulin resistance and leads to insulin deficiency. This type of diabetes frequently is resistant to the action of insulin. The risk of developing Type 2 Diabetes mellitus increases with age, body fat and reduced physical activity. Non-Insulin Dependent Diabetic patients are treated with oral hypoglycemic drugs which increase insulin secretion and insulin action (American Diabetes Association, 2003). 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. Non-Insulin Dependent Diabetes mellitus (due to progressive insulin secretory defect in the background of insulin resistance).

### **c) Gestational Diabetes mellitus-**

Gestational Diabetes mellitus is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Women who develop Type 1 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). Treatment involves diet control, nutritional counseling by a dietitian and insulin as pharmacological therapy to reduce fetal morbidities (American Diabetes Association, 2003). Diabetes mellitus diagnosed in the second or third trimester of pregnancy that is not clearly overt Diabetes mellitus. The GDM may develop during pregnancy and may disappear after delivery. In the longer term, children born to mothers with gestational diabetes mellitus are at greater risk of obesity and Non-Insulin Dependent Diabetes mellitus in later life, a phenomenon attributed to the effects of intrauterine exposure to hyperglycaemia.

### **Other types of diabetes mellitus-**

#### **Monogenic diabetes-**

Monogenic diabetes is due to a genetic defect in single genes in pancreatic  $\beta$ -(beta) cells which results in disruption of  $\beta$ -(beta) cell function or a reduction in the number of  $\beta$ -(beta) cells. These types of diabetes is developed with mutations on chromosome twelve in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1a. It is classified according to the age of onset as neonatal diabetes before the age of 6 months or Maturity Onset Diabetes of the young before the age of 25 years. Mitochondrial diabetes is changing a point due to mutation in the mitochondrial DNA. They are less to 10 percentage of diabetes mellitus.

#### **Signs of Diabetes Mellitus -**

- ❖ High blood sugar (hyperglycemia)
- ❖ Increased ketones in your urine (diabetic ketoacidosis)
- ❖ Hyperglycemic hyperosmolar nonketotic syndrome

- ❖ Low blood sugar (hypoglycemia)

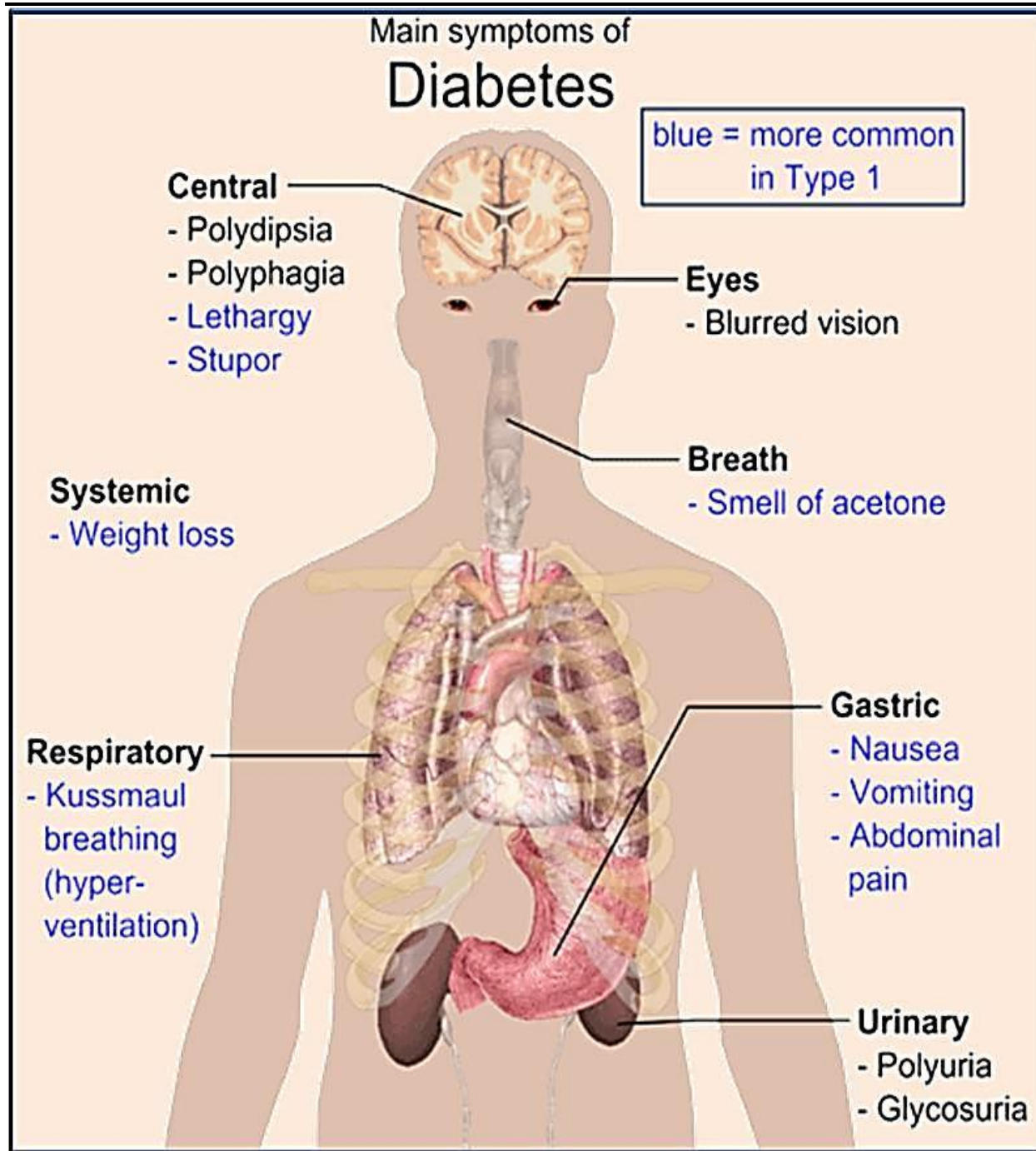
### Symptoms Diabetes Mellitus -

Diabetes mellitus symptoms vary depending on how much your blood sugar is elevated. Some people, especially those with pre-diabetes or Non-Insulin Dependent Diabetes mellitus, may sometimes not experience symptoms. In Insulin Dependent Diabetes mellitus, symptoms tend to come on quickly and be more severe.

The signs and symptoms of type 1 diabetes and type 2 diabetes are:

- ❖ Irritability
- ❖ Presence of ketones in the urine (ketones are a byproduct of the breakdown of muscle and fat that happens when there's not enough available insulin)
- ❖ Frequent infections, such as gums or skin infections and vaginal infections
- ❖ Frequent urination
- ❖ Unexplained weight loss
- ❖ Polyphagia (excessive hunger)





*Fig. 02 Symptom of Type 1 and Type 2 diabetes mellitus*

**Causes of Diabetes Mellitus**

Disturbances in gluco-receptor of beta cell so that they respond to higher glucose concentration or relative beta cell deficiency. The immune system mistakenly attacks and destroys insulin-producing beta cells in the pancreas. Type 1 diabetes is an immune system disease. Your body attacks and destroys insulin-producing cells in your pancreas. Without insulin to allow glucose to enter your cells, glucose builds up in your bloodstream. Genes may also play a role in some patients. Type 2 diabetes our body's cells don't allow insulin to work as it should to let glucose into its cells. The body's cells have become resistant to insulin. The pancreas cannot keep up and make enough insulin to overcome this resistance. Gestational diabetes hormones

produced by the placenta during your pregnancy make your body's cells more resistant to insulin. The pancreas cannot make enough insulin to overcome this resistance.

### **Risk factors of Diabetes mellitus-**

The several risk factors have been associated with the development of diabetes. The risk factors differ depending on the type of diabetes you ultimately develop.

#### **Risk factors for Type 1 diabetes-**

- ❖ Physical stress (such as surgery or illness).
- ❖ Injury to the pancreas (such as by infection, tumor, surgery or accident).
- ❖ Presence of autoantibodies (antibodies that mistakenly attack your own body's tissues or organs).

#### **Risk factors for Type 2 diabetes-**

- ❖ High blood pressure.
- ❖ Family history (parent or sibling) of type 2 diabetes.
- ❖ Overweight.
- ❖ Heart disease or stroke.
- ❖ Smoking
- ❖ Low HDL cholesterol (the "good" cholesterol) and high triglyceride level.

#### **Risk factors for gestational diabetes-**

- ❖ The overweight before the pregnancy.
- ❖ Family history (parent or sibling) of type 2 diabetes.
- ❖ Age above the 25 years.

### **Epidemiology of Diabetes-**

Epidemiology of diabetes deals to identify the actual and potential health problems in a population. Descriptive epidemiological methods of diabetes are used to locate the causes and risk factors of diabetes. It provides the basic driving forces for the diabetes control strategies and to understand the prevalence and spread of diabetes in particular locality. The global prevalence of diabetes among adults is currently estimated to be about 382 million; with 175 million undiagnosed and the greatest incident is between 40 years and 59 years of age by 2035, this number is expected to increase to over 592 million. In 2014, it is estimated that diabetes affects 422 million (8.5%) of the population in the world.

Non-Insulin Dependent Diabetes mellitus varies substantially from one geographical region to the other as a result of environmental and lifestyle risk factors.

Epidemiology of diabetes provides a systematic multidisciplinary assessment of all aspect of the geographical distribution, etiology, biology, screening, monitoring and evaluating programmed of diabetes. According to the World Health Organization report, it was estimated that the global diabetes occurrence would increase to about 4.4%, affecting more than 366,212million in2030 with a change of around 114% since 2000. Non-Insulin Dependent Diabetes mellitus varies substantially from one geographical region to the other as a result of environmental and lifestyle risk factors.

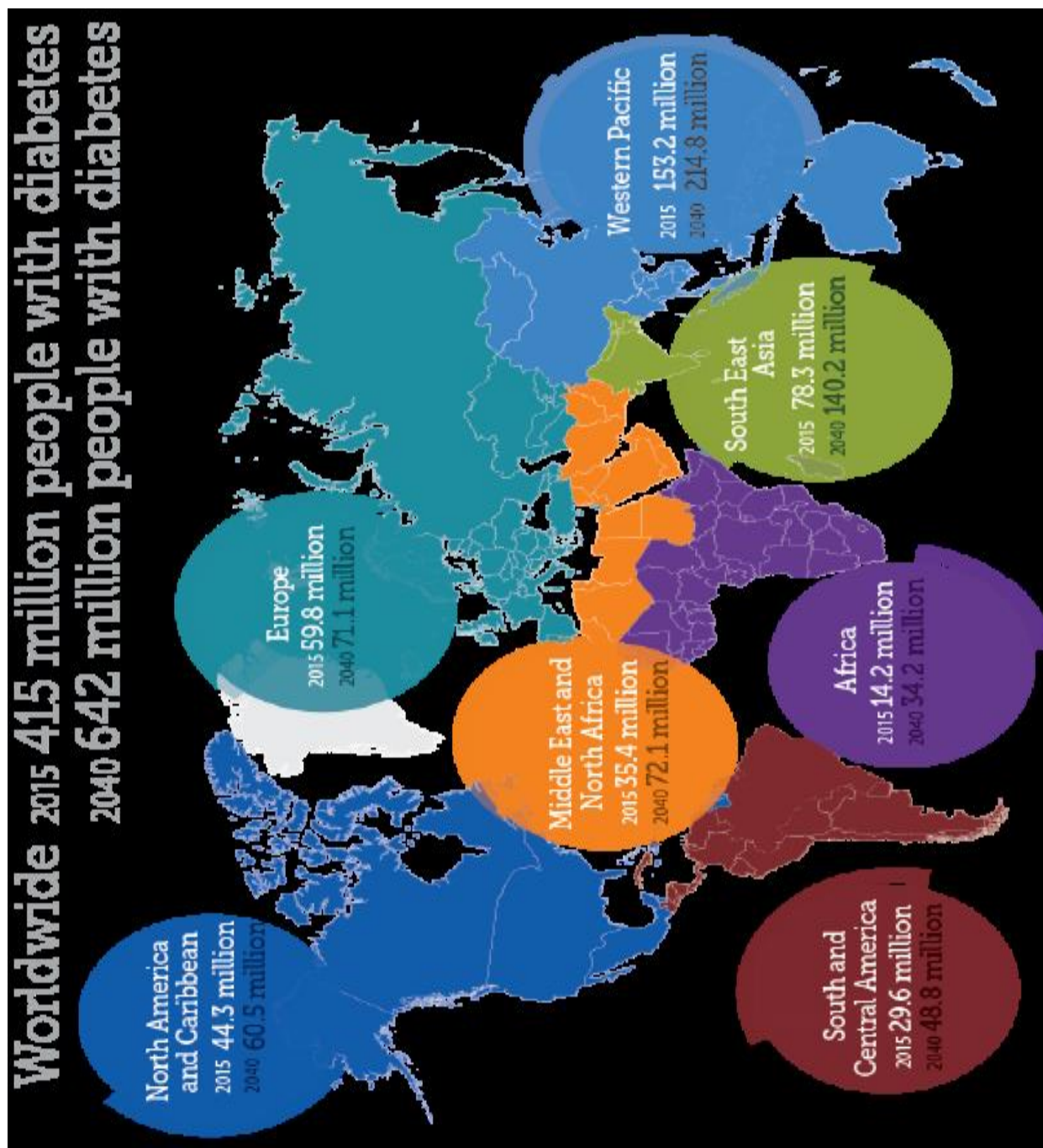


Fig. 03 The number of people with diabetes worldwide per region in 2015 and 2040 (20-75 yrs)



## Diagnosis of Diabetes Mellitus-

According to the *American Diabetes Association* (ADA), the fasting glucose concentration should be used in routine screening for diabetes; but postprandial blood sugar, random blood sugar and glucose tolerance test are also used for blood sugar determination. The ADA recommends that the following people be screened for diabetes:

- ❖ Women who have had gestational diabetes are advised to be screened for diabetes every three years.
- ❖ The any person who has been diagnosed with pre-diabetes is advised to be tested every year.
- ❖ The anyone with a body mass index higher than 25 (23 for Asian Americans), regardless of age, who has additional risk factors, such as high blood pressure, abnormal cholesterol levels, a sedentary lifestyle, a history of polycystic ovary syndrome or heart disease, and who has a close relative with diabetes.
- ❖ The any people older than age 45 is advised to receive an initial blood sugar screening, and then, if the results are normal, to be screened every three years thereafter.

The diagnosis of diabetes mellitus include, oral glucose tolerance test urine sugar,, glucose tolerance test, renal glycosuria, renal threshold of glucose, increased glucose tolerance, extended glucose tolerance curve, cortisonestressed glucose tolerance test, intravenous glucose tolerancetest, blood sugar, diminished glucose tolerance.

## Treatment of Diabetes Mellitus

The treatment for Diabetes mellitus to give high doses of regular insulin to patient. The goal of diabetes management is to keep blood glucose levels as close to normal as safely possible. People with diabetes must take responsibility for their day-to-day care. The diabetes patient monitoring blood glucose levels, dietary management, maintaining physical activity, keeping weight and stress under control, oral medications and, if required, insulin use via injections . To help patients achieve this, UCSF's Diabetes Teaching Center offers self-management educational programs that emphasize individualized diabetes care. The program enables patients to make more consistent and appropriate adjustments in their therapy and lifestyle. The aims of management of diabetes mellitus can be provide the patient with knowledge, motivation and Means to undertake this own enlightened care.

## Dietary Management and Physical Activity-

The Diabetes patient's changes the eating habits and increasing physical activity are typically the first steps toward reducing blood sugar levels. To provide patients with information on food nutrient content, healthy cooking and exercise and Food intake should be divided into regularly spaced meals of similar size. The diabetic patient balanced in regard to protein, carbohydrate and fats, in all cases it is necessary to restrict carbohydrate intake.

## Insulin Therapy-

The type 1 diabetes requires multiple insulin injections each day to maintain safe insulin levels. Insulin is often required to treat type 2 diabetes patients. These are insulin syringes, implantable pumps, pen devices, inhaled insulin, insulin pumps, and other routes of insulin delivery. The pump is about the size of a pager and is usually worn on your belt. Insulin is delivered through a small tube (catheter) that is placed under the skin (usually in the abdomen).

There are four major types of insulin:

- ❖ Rapid-acting
- ❖ Short-acting
- ❖ Intermediate-acting
- ❖ Long-acting

There is no standard insulin dose as it depends on factors such as your body weight, when you eat, how often you exercise and how much insulin your body produces.

## Oral Medications-

*Sulphonyl ureas* such as *glibenclamide, glipizide* and *biguanides* such as *metformin, phenformin* are oral hypoglycemic drugs. Newer approaches have constantly been explored and have lately yielded *thiazolidinediones, meglitinide analogues,  $\alpha$ -glucosidase inhibitors*, and the latest are *dipeptidyl peptidase-4 (DPP-4) inhibitors*. These include improve the effectiveness of the body's natural insulin, reduce blood sugar production, increase insulin production and inhibit blood sugar absorption. Oral Hypoglycaemic diabetes medications are sometimes taken in combination with insulin.

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