

## Diabetes Mellitus-Types and Prevalence: A Mini Review

Amjid Ahad\*

Department of Biochemistry, Lipid Metabolism laboratory, Faculty of Science, Jamia Hamdard, Hamdard Nagar, New Delhi 110062, India

### Abstract

Diabetes Mellitus (DM) is a condition in which a person has a high blood sugar level over a prolonged period. DM arises as a result of complete or relative insufficiency of insulin secretion and/or insulin action. There are three main forms of diabetes, type 1 (insulin-dependent DM), type 2 (non-insulin-dependent DM) and gestational DM. The incidence of Diabetes Mellitus (DM) has substantially increased worldwide. It is estimated that around 382 million people were affected with diabetes in 2013, and the number is expected to rise to 592 million by 2035. All major types of DM are characterized by hyperglycemia, dyslipidemia, abnormal protein metabolism and oxidative stress. People with DM have an increased risk of developing micro vascular and macrovascular complications later in life. This review focuses on the types of DM and its relative prevalence across the different countries of world. The present review not only updates our knowledge about the DM and its associated secondary complications, but also provides statistics of diabetes prevalence around the world.

**Abbreviations:** CVD: Cardio Vascular Disease; DM: Diabetes Mellitus; DN: Diabetic Nephropathy; FBG: Fasting Blood Glucose; GAD: Glutamic Acid Decarboxylase; GFR: Glomerular Filtration Rate; GLUT4: GLUcose Transporter-4; IRS: Insulin Receptor Substrate; PI-3-K: Phosphatidyl Inositide 3-Kinase; LPO: Lipid Peroxidation; TGF- $\beta$ , Transforming Growth Factor-beta; TNF- $\alpha$ : Tumor Necrosis Factor-alpha; T2DM: Type-2 Diabetes Mellitus; WHO: World Health Organization

**Keywords:** Diabetes Mellitus; Diabetic Complications; Dyslipidemia; Hyperglycemia

**\*Corresponding Author:** Amjid Ahad, Department of Biochemistry, Lipid Metabolism laboratory, Faculty of Science, Jamia Hamdard, Hamdard Nagar, New Delhi 110062, India; Tel: +91 9643163303; E-mail: amjidpar12@gmail.com

### Introduction

Diabetes Mellitus (DM), which literally means "sweet excessive urine," is a diverse group of diseases that occurs as a result of body either not producing enough insulin or because body cells do not use insulin effectively, and is characterized by altered carbohydrate, lipid and protein metabolism [7]. DM is clinically manifested by increased blood glucose level (a condition called as hyperglycemia). The characteristic symptoms of DM include polydipsia (excessive thirst), polyuria (excessive urine), blurring of vision and loss of weight. Persistent hyperglycemia can damage body tissues, affecting mainly optic, renal and neural cells. Diabetic patients are also at increased risk of developing cardiovascular diseases [11]. DM is broadly classified into three major types: a) type 1 diabetes, b) type 2 diabetes, and c) gestational diabetes.

### Type 1 Diabetes Mellitus

Type 1 DM develops as a result of an autoimmune reaction in which the body's immune system destroys the insulin-producing beta islets of Langerhans (also called  $\beta$ -cells)

in the pancreas. This condition leads to the deficiency of insulin in the body, as a result of which glucose is not utilized by the body cells, thus causing hyperglycemia. The exact mechanism behind the development of autoimmunity is not fully understood. Type 1 DM predominantly occurs in children and young adults; however, the disease can affect people of all age groups [4]. Type 1 diabetic patients need exogenous insulin every day so as to maintain the glycemic control. The symptoms of type 1 DM include dry mouth and excessive thirst, Polyuria (frequent urination), fatigue, polyphagia (increased appetite), continuous weight loss, slow wound repair, repeated infections and blurred vision. Type 1 DM accounts for 5 to 10% of all diabetics [18]. Type 1 DM can further be divided into two types: autoimmune diabetes (Type 1A), and idiopathic diabetes (Type 1B).

#### Autoimmune Diabetes Mellitus (Type 1A)

This form of diabetes results from autoimmune mediated destruction of the beta cells of the pancreas. The rate of destruction is quite variable, being rapid in children [9]. Patients with Type 1A diabetes often depend on insulin for survival and are at higher risk of ketoacidosis [19]. The markers of immune destruction, including auto antibodies to insulin,  $\beta$ -cell auto antibodies, and auto antibodies against Glutamic Acid Decarboxylase (GAD) are found in the individuals with Type 1A DM. This form of type 1 diabetes accounts for 90-95% of type 1 diabetic patients [16]. The risk factors for this type of DM include genetic predisposition to autoimmune destruction of beta cells and environmental factors, both of which are poorly understood. Other risk factors include autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease [1].

#### 1) Idiopathic diabetes mellitus (Type 1B)

It is a form of Type 1 diabetes which has no known aetiology. Such patients have permanent insulin deficiency and are at higher risk of ketoacidosis, but have no indication of autoimmunity [13]. Type 1B diabetes is mostly found in individuals of African and Asian subcontinents.

#### a) Type 2 diabetes mellitus

Type 2 diabetes is the most common form of DM. It mainly affects adults, but is increasingly found in children and teenagers as well. In this form of DM, the pancreas is normal and able to produce insulin but the body does not respond to the insulin (also known as insulin resistance), leading to an increased level of blood glucose. Most of the patients with type 2 DM remain undiagnosed for a long time because of the absence of symptoms at earlier stage, during which time the body is being damaged by hyperglycemia. Type 2 DM often leads to various organ specific complications and is the leading cause of nephropathy, neuropathy and cardiovascular dysfunction. This type of diabetes accounts for 90 to 95% of all diabetic patients [6]. The risk factors for type 2 DM include obesity, unhealthy diet, physical inactivity, ageing, family history of diabetes, ethnicity, and hyperglycemia during pregnancy. Unlike type 1 diabetics, the majority of type 2 diabetic patients are not dependent on exogenous insulin, but may require it for the control of blood glucose levels along with other oral hypoglycemic agents. The incidence of type 2 DM is growing rapidly worldwide because of economic development, increasing urbanisation, changed dietary habits, physical inactivity, and changes in lifestyle patterns [18]. Insulin resistance is an important feature of type 2 DM. In obese type 2 diabetic patients, the insulin resistance develops due to defect at many levels, with decreases in receptor concentration and kinase activity, the concentration and phosphorylation of Insulin Receptor Substrate-1 (IRS-1) and IRS-2, Phosphatidyl Inositide 3-Kinase (PI-3-K) activity, GLUCOSE Transporter-4 (GLUT4) translocation, and the activity of intracellular enzymes [12]. Insulin binds to its receptors on adipocyte and skeletal muscle cells and increases the uptake of glucose from bloodstream by stimulating the translocation of the GLUT4 from intracellular vesicles to the plasma membrane [14]. Circulating Free Fatty Acids (FFAs) derived from adipocytes are elevated in type 2 diabetic patients and have been suggested to play a key role in the development of insulin resistance by inhibiting glucose uptake, glycogen synthesis, and by increasing hepatic gluconeogenesis. Elevated serum lipid levels are also implicated

in the reduction of IRS-1 phosphorylation and PI-3-K activity. The link between increased circulating lipids and insulin resistance might involve accumulation of triglycerides and fatty acid-derived metabolites (diacylglycerol, fatty acyl-CoA, and ceramides) in muscle and liver. Expression of pro-inflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is increased in the various animal and human subjects of type 2 diabetes and have been shown to cause phosphorylation of IRS-1, leading to reduced insulin receptor kinase activity and insulin resistance [8].

#### b) Gestational Diabetes Mellitus

Gestational Diabetes (also known as gestational diabetes mellitus or GDM) occurs in women who develop insulin resistance and subsequent hyperglycemia during pregnancy. It arises around the 24th week of pregnancy, probably due to the blockage of insulin action by placental hormones. The baby is not usually at immediate risk as gestational diabetes normally develops later in pregnancy, at the time when baby is already well-formed. However, uncontrolled hyperglycemia in GDM can be lethal for both the mother and her baby and can lead to a quite larger baby (a condition referred to as foetal macrosomia), which makes a normal birth unmanageable and risky. High blood glucose level can also lead to hypertension thus increasing the risk of preeclampsia (a condition where sudden high blood pressure threatens the health or life) of the mother and her baby. Gestational diabetes normally disappears in mothers after birth. However, both mothers and their babies are at a higher risk of developing type 2 diabetes later in life. Pregnant women with GDM should continuously monitor and control blood glucose levels as well as take up a healthy diet and moderate exercise.

#### The global burden of DM

DM is regarded as the fourth leading cause of death in developed countries and is becoming an epidemic in many developing countries. Diabetes is doubtlessly one of the most challenging health problems of the 21st century. The present data confirms that low and middle income countries face the greatest burden of diabetes. A number of studies consistently

reveal that substantial proportion of people with diabetes is unaware and never being previously diagnosed, the main reason of which is the non-occurrence of symptoms mainly in type 2 diabetes. Furthermore, complications due to diabetes are a major cause of morbidity and mortality [3]. Diabetes is found in almost every country. Type 2 diabetes accounts for 85% to 95% of all diabetes in high-income countries and may account for an even higher percentage in low- and middle income countries [17]. Type 1 diabetes, although less common than type 2 diabetes, is increasing each year in both rich and poor countries. In most high-income countries, the majority of diabetes in children and adolescents is type 1 diabetes. Gestational diabetes is common and, like obesity and type 2 diabetes, is increasing throughout the world. The risk of developing type 2 diabetes is high in women who have had gestational diabetes.

#### Prevalence

According to a recent report by International Diabetes Federation, Approximately 382 million people (8.3% of adults) worldwide were affected by diabetes in 2013 and the number is expected to increase to 592 million by 2035, or, in other words one adult in 10, will have diabetes (Table 1). This equates to approximately three new cases every 10 seconds, or almost 10 million per year (Table 2) [11].

**Table 1:** Estimated increase in number of diabetic patients in 2013 and 2035

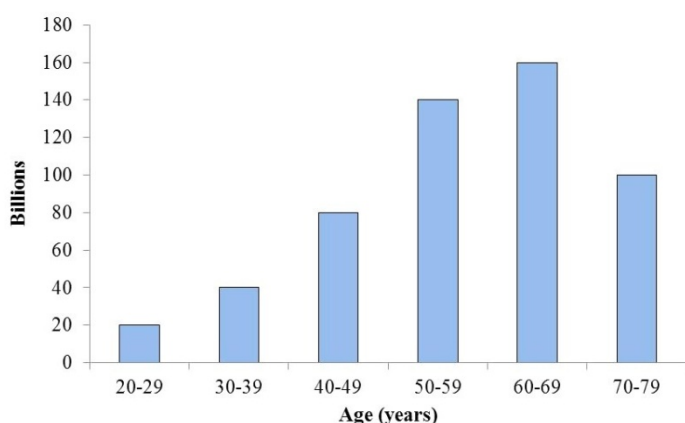
| At a glance                               | 2013 | 2035 |
|-------------------------------------------|------|------|
| Total world population (billions)         | 7.2  | 8.7  |
| Adult population (20-79 years, billions)  | 4.6  | 5.9  |
| Diabetes (20-79 years)                    |      |      |
| Global prevalence (%)                     | 8.3  | 10.1 |
| Comparative prevalence (%)                | 8.3  | 8.8  |
| Number of people with diabetes (millions) | 382  | 592  |

**Table 2:** Top 10 countries/territories for number of people with diabetes, 2013 and 2035

| Country/Territory        | 2013<br>(Millions) | 2035<br>(Millions) |
|--------------------------|--------------------|--------------------|
| China                    | 98.4               | 142.7              |
| India                    | 65.1               | 109.0              |
| United States of America | 24.4               | 29.7               |
| Brazil                   | 11.4               | 19.2               |
| Russian Federation       | 10.9               | 11.2               |
| Mexico                   | 8.7                | 15.7               |
| Indonesia                | 8.5                | 14.1               |
| Germany                  | 7.6                | 7.5                |
| Egypt                    | 7.5                | 13.1               |
| Pakistan                 | 5.2                | 12.8               |

### Health expenditure

Diabetes imposes a large economic burden on individuals and families, national health systems, and countries. In 2013, health spending on diabetes accounted for 10.8% of total health expenditure worldwide (Figure 1). Global health spending to treat diabetes and manage complications totalled at least USD 548 billion in 2013. By 2035, this number is projected to exceed USD 627 billion. The estimates show that 76% of global health expenditure on diabetes in 2013 was for people between the ages of 50 and 79 years [11].

**Figure 1:** Health expenditure due to diabetes by age (USD)

### Diabetic burden on India

India is regarded as the diabetic capital of world. It is currently estimated that approximately 8.2% of the adult population worldwide (72.1 million people) have diabetes, out of which 65.1 million live in India. The number is expected to increase to 123 million by 2035 – 10.1% of the adult population. Almost half of people with diabetes in India are undiagnosed [3]. India leads in having the maximum number of children with type 1 diabetes. Around 1.1 million deaths were attributed to diabetes in 2013, thus making India the largest contributor to diabetic mortality. More than half (55%) of these deaths occurred in people under 60 years of age and over one-quarter (27%) in people under 50 years of age [11].

### Diabetes Complications

Long-term diabetes leads to a number of organ specific complications and life-threatening health problems. These diabetic complications are broadly classified into two groups, micro vascular and macrovascular complications. Micro vascular complications of diabetes mainly affect retina, renal glomerulus and peripheral nerve and for this reason, diabetes is considered as the leading cause of blindness, end-stage renal disease and various enfeebling neuropathies. Macrovascular complications affect arteries that supply the heart, brain and lower extremities. As a result, patients with diabetes have a much higher risk of myocardial infarction, stroke and limb amputation [5, 15]. Maintaining glycemic control, normal blood pressure and cholesterol levels can help delay or prevent diabetes complications.

#### 1) Cardio Vascular Disease

Cardio Vascular Disease (CVD) is the most common cause of morbidity and mortality in diabetic patients. Angina, stroke, myocardial infarction, peripheral artery disease, and congestive heart failure are various cardiovascular diseases that accompany diabetes. Hyperglycemia, dyslipidaemia, hypertension and other risk factors contribute to the increased risk of cardiovascular diseases in diabetic patients [11].

## 2) Diabetic Nephropathy

Diabetic Nephropathy (DN) is one of the most serious secondary complications of diabetes mellitus, and is the leading cause of ESRD. DN is characterized by macro albuminuria (urinary albumin excretion > 300mg/24hrs) and abnormal renal function as represented by a disturbed Glomerular Filtration Rate (GFR). The disease arises as a result of damage to small blood vessels that supply the nephrons that in turn lead to renal cell damage [11].

## 3) Retinopathy

Patients with long-term diabetes are at higher risk of developing eye disease (retinopathy) later in life that often leads to blurred vision or blindness. Persistent hyperglycemia along with hyperlipidemia and hypertension are the main causes of retinopathy. The disease arises as a result of damage to blood vessels that supply the retina.

## 4) Nerve Damage

Persistent hyperglycemia and hypertension can provoke damage to nerves throughout the body (neuropathy). Nerve damage can lead to various problems including indigestion and frequent urination, erectile dysfunction, numbness and a number of other defects. Neuropathy particularly affects lower limb extremities, especially the feet. Nerve damage in these parts is called peripheral neuropathy, and can lead to tingling, pain and loss of feeling. If untreated, it can lead to serious infections and ulceration, diabetic foot disease, and major amputations [11]. The pathophysiological features of diabetic micro vascular diseases in retina, glomerulus and neurons are same. At earlier stages, intracellular hyperglycaemia causes abnormalities in blood flow and increased vascular permeability represented by increased activity of vasoconstrictors such as angiotensin II and endothelin-1, and elaboration of permeability factors such as Vascular Endothelial Growth Factor (VEGF). The downstream effect of these changes causes extracellular matrix accumulation and an irreversible increase in vascular permeability. As the disease progresses, micro vascular cell loss occurs as a result of apoptosis. Together, these changes lead to ischaemia, oedema and neo vascularization in the retina, proteinuria, mesangial

matrix expansion and glomerulosclerosis in the kidney, and multifocal axonal degeneration in peripheral nerves [2].

## 5) Diabetic Foot

People with diabetes are at a higher risk of developing foot problems. The main cause of diabetic foot is the hyperglycemia-induced damage to nerves and blood vessels. These factors, often associated with infection and ulceration, lead to an increased risk of lower limb amputation [10]. However, proper management of glycemic control and normal blood pressure can prevent a large proportion of amputations.

## 6) Pregnancy Complications

Pregnant women are at increased risk of developing any type of diabetic complications if blood glucose is not monitored regularly and managed at normal levels. Hyperglycemia can cause the foetus to gain excess size and weight, and overproduce insulin. These can create problems at delivery, and can put both mother and baby into risk. Babies exposed for longer times to high blood glucose in the mother's womb are at higher risk of developing type 2 diabetes later in life [11].

## 7) Oral Health

Patients with diabetes are an increased risk of developing gingivitis (inflammation of gums), which in turn is the most serious cause of tooth loss.

## Future Perspectives

Glycemic control and antihypertensive drugs are two widely used strategies for the treatment of diabetes and its associated secondary tissue derangements. Despite a tremendous increase in our understanding of the intricate pathways involved in the pathophysiology of metabolic disorders, diabetes mellitus continues to remain a huge clinical problem. The challenge for future research will be to unravel the complex interactions between high blood glucose levels, dyslipidemia, hypertension, hemodynamic factors, micro inflammation and growth factors, which may lead to a better understanding of the pathogenesis of diabetic complications. Accordingly, there is an ongoing need for development of new therapeutic strategies in the treatment of diabetes and its associated complications, which may involve



the combined intervention against various pathways critically important in the development of diabetic complications.

### Conflicts of interest

The author declares that there is no conflict of interest.

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