Basic Concepts of Diabetics Mellitus for the Welfare of General Patients

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Abstract

Diabetes mellitus is a chronic but non-contagious metabolic disease that is characterized by elevated levels of blood sugar (glucose), causes absolute or relative insulin deficiency or both, which is produced by the beta cells of the Islets of Langerhans within the pancreas. For the run- short of insulin the body loses its ability to properly oxidize carbohydrates and to make balance of sugar in blood during energy production. Diabetes reduces life expectancy and increases significant morbidity related to microvascular complications, and diminished quality of life. If the disease is left undiagnosed or poorly controlled for the long-time, it may damage heart, vasculature, eyes, kidneys, and nerves. This study aims to give an insight at various aspects of diabetes mellitus including risk factors, prevention, and treatment of the disease to improve the physical and psychological problems of the diabetic patients.

Keywords: diabetics, insulin, diagnosis, β-cell, risk factors, prevention, treatment

1. Introduction

Diabetes mellitus (DM) is a group of metabolic disorders in which there are high levels of sugar (glucose) in the blood (hyperglycemia), either for inadequate insulin production, or for the body cells do not respond properly to insulin, or both (García et al., 2017). Glucose is a main source of energy and comes mostly from the foods we eat, such as carbohydrate and fat. It is stored in the liver, in the form of glycogen, and released into the bloodstream when the level of glucose in the circulating blood decreases. Insulin is a hormone that helps our body cells to absorb the glucose from the blood and use it or store it for energy (Ambler et al., 2021).

Diabetes mellitus (DM) is not a pathogenic entity but a group of aetiologically different metabolic defects. The effects of DM are long-term damage, dysfunction and failure of various organs (WHO, 2002). The pancreas contains β-cells that release a hormone called insulin, which helps to move the glucose from the blood into the cells (Goodpaster, 2010). DM is caused by a deficiency in the production of insulin in the β-cells of the Islets of Langerhans within the pancreas. The prevalence of DM has been increasing steadily all over the world (Schwartz et al., 2016).

In 2017, about 425 million people are infected by diabetes mellitus (DM) worldwide, and total global health expenditure is about \$727 billion (International Diabetes Federation, 2017). About 80% of people with type 2 diabetes (T2D) living in low- and middle- income countries. It is expected that total DM people would have risen to 552 million by 2030, among them 439 million people would have T2D (Olokoba et al., 2012). International Diabetes Federation (IDF) shows that in 2019, diabetes caused 4.2 million deaths, and 463 million adults aged between 20 and 79 years old are living with diabetes that costs \$720 billion. It is expected that

diabetes patients may rise up to 700 million by 2045 (Galicia-Garcia et al., 2020).

2. Literature Review

Literature review is an important item for a researcher. In any research, it is a starting section, where works of previous researchers are emphasized (Polit & Hungler, 2013). It helps the new researchers to understand the subject area for performing their research efficiently (Creswell, 2007). Pouya Saeedi and her coauthors have tried to provide global estimates of diabetes prevalence for 2019, and projections for 2030 and 2045. In their study they have obtained that just fewer than half a billion people are living with diabetes worldwide and the number is projected to increase by 25% in 2030 and 51% in 2045 (Saeedi et al., 2019). Alfonso Barquilla García has realized that chronic hyperglycemia is associated with serious long-term complications in several organs, especially in the eyes, kidneys, nerves, heart, and blood vessels. He has reviewed the diagnostic process, screening recommendations, prevention strategies, initial assessment upon diagnosis; therapeutic targets regarding both blood glucose levels and the other vascular risk factors (García et al., 2017).

Vanesa Bellou and her coworkers have realized that T2D is a global epidemic associated with increased health expenditure, and low quality of life. In their study they have obtained that 415 million people are living with T2D in 2015, and by 2040 the number will be almost 642 million (Bellou et al., 2018). Kohei Kaku studies that both impaired insulin secretion and increased insulin resistance are the two main pathophysiological features of type 2 diabetes (T2D). He has emphasized that earlier intervention and continued treatment are the keys to achieve the treatment goals (Kaku, 2010). Abdulfatai B. Olokoba and his coauthors observed that T2D is a metabolic disease that can be prevented through lifestyle modification, diet control, and control of overweight and obesity. Novel drugs are being developed, yet no cure is available in sight for the disease, despite new insight into the pathophysiology of the disease (Olokoba et al., 2012).

Christina Rariden warns that pre-diabetes is a national and worldwide health concern, and early identification and intervention have been successful in delaying and/or preventing the progression to T2D (Rariden, 2019). Unai Galicia-Garcia and his coworkers have analyzed the key aspects of T2D, as well as the molecular mechanisms and pathways implicated in insulin metabolism leading to T2D and insulin resistance to identify cardiovascular risk (Galicia-Garcia et al., 2020).

3. Research Methodology of the Study

To lead in the academic world an academician takes the research as an essential and influential work to improve his/her carrier and welfare of the institution (Pandey & Pandey, 2015). The research design is a plan of the researchers to develop research area that is reinforced by philosophy (Tie et al., 2019). Methodology is the guideline to perform any kind of research in any kind of field, where scientific methods are followed precisely and efficiently (Kothari, 2008). Therefore, research methodology is a strategy for planning, arranging, designing and conducting a fruitful research confidently to obtain a successful result (Legesse, 2014).

We have started our research work with classification of diabetes mellitus, and then we briefly discuss historical background of the disease. Then we have highlighted the symptoms, causes, prevention of diabetes. We have also tried to consult on risk factors, complications, and treatments of diabetes. To prepare this article we have taken help from the secondary data sources. We have consulted the books, handbooks, and theses of famous authors. We have also collected valuable information and necessary materials from websites and internets to enrich the paper.

4. Objective of the Study

The main objective of this study is to discuss the aspects of diabetes mellitus. Other trivial objectives of the study are as follows:

- to provide the symptoms and causes of diabetes,
- to highlight the prevention and risk factors of diabetes, and
- to show the complications and treatments of diabetes.

5. Classification of Diabetes

Classification of diabetes mellitus is necessary to understand the etiology of the disease and study its natural history to identify and differentiate between its various forms and places them into a rational etiopathologic framework (Harris & Zimmet, 1997). The classification of diabetes and other categories of glucose intolerance were developed in 1979 by the National Diabetes Data Group (NDDG) (Berggren et al., 2011). The first widely accepted classification of DM was published by WHO in 1980, and in modified form in 1985 (WHO, 1980, 1985).

Diabetes is among the top ten causes of death in adults, and is estimated to have caused four million deaths globally in 2017 (Saeedi et al., 2019). It can be classified into four types: i) type 1 diabetes (T1D), ii) type 2

diabetes (T2D), iii) pre-diabetes, and iv) gestational diabetes mellitus (GDM). Other specific types of DM due to other causes are; monogenic DM (neonatal diabetes), MODY DM (maturity-onset diabetes of the young), diseases of the exocrine pancreas (cystic fibrosis and pancreatitis), LADA DM (latent autoimmune diabetes of the adult), drug-induced diabetes (glucocorticoids, antiretrovirals, in the treatment of HIV/AIDS, or after organ transplantation), etc. (International Diabetes Federation, 2017).

5.1 Type 1 Diabetes (T1D)

Type 1 diabetes (T1D) usually occurs in children; before the age of 30, but it can also develop among older adults or at any age, and is characterized by low serum insulin levels at the young adults (Diamond Project Group, 2006). It is also called insulin dependent diabetes because it is characterized by an absolute deficiency of insulin (Daneman, 2006). When β-cells in the pancreas are destructed due to invasion by virus, action of chemical toxins, action of autoimmune antibodies, etc. causes insulin deficiency; and consequently, T1D is visible in the body (Wang et al., 2011). It is abruptly begins with severe symptoms, and dependent on exogenous insulin to sustain life. The body of the patient makes little or no insulin due to an immune system response that destroys insulin-producing β-cells. Consequently, T1D is also called insulin-dependent diabetes, juvenile diabetes, or early-onset diabetes (Harris & Zimmet, 1997).

Some people carry genes that make them more likely to develop T1D damaging cells in the pancreas through the process "autoimmune". In T1D when glucose and ketone levels become very high in the blood and there is severe dehydration and loss of salts from the body. In this situation it is called diabetic ketoacidosis, and is life-threatening and requires urgent hospital treatment (Ambler et al., 2021). About 5-10% of all diabetes cases are T1D, and patients will need to take insulin injections for the rest of their life to prevent the development of ketoacidosis, coma, and even death; following a special diet recommended by doctors, dieticians, and nutritionists. These patients need to take insulin every day to stay alive and fit (WHO, 1999; Diamond Project Group, 2006,). The pancreatic β-cells are damaged that is caused by various viruses, such as the mumps virus and coxsackie virus β-4, through the release of chemical agents, or by destructive cytotoxins and antibodies released from sensitized immunocytes (Nolte & Karam, 2001).

5.2 Type 2 Diabetes (T2D)

Type 2 diabetes (T2D) is also called non-insulin dependent diabetes, and is usually detected after the age of 40. It is also known as "*adult-onset diabetes mellitus*" (AODM). It is developed when the body does not produce enough insulin for proper function (Chatterjee et al., 2017). It is caused by a combination of two primary factors: i) defective insulin secretion by pancreatic β-cells, and ii) the inability of insulin-sensitive tissues to respond appropriately to insulin (Galicia-Garcia et al., 2020). About 90% of all cases of diabetes worldwide is T2D, and patients control the disease by losing weight, following a healthy diet, doing plenty of exercise, monitoring their blood glucose levels, and through the use of oral hypoglycemic medications, such as metformin, if necessary. Sometimes, eventually may require insulin for control T2D (Chatterjee et al., 2017).

Risk factors of T2D are a complex combination of genetic, metabolic, and environmental factors that interact with one another contributing to its prevalence (Goodpaster, 2010). Some risk factors are older age, being overweight or obese, genetic predisposition, family history, gut dysbiosis, epigenetics and mitochondrial deregulation, and having certain ethnic backgrounds (Schellenberg et al., 2013). For example, higher incidence rates of T2D in Asians compared with a White American population, and white population in the UK (Sattar & Gill, 2015). Overweight and obese people who are physically inactive and eating the wrong foods have a higher risk of developing T2D (Lynch et al., 1996). People in certain ethnic groups, such as African Americans, native Hawaiians, Hispanic/Latino Americans, Mexican Americans, American Indians, Alaska Natives, and Asian Americans seem to be more likely to develop T2D (Harris, 1991; WHO, 1999).

5.3 Pre-Diabetes

Pre-diabetes is a condition that comes before diabetes, in which blood sugar levels remain greater than "normal", but is not high enough to be called diabetes. It is also known as impaired glucose tolerance (IGT). Pre-diabetes means the insulin is not working properly. If it is not managed appropriately for a long time, it can quickly evolve to T2D (American Diabetes Association, 2019). It is a progressive condition, and it can take a few years for patients to become diabetic from a pre-diabetes state. There is a strong association between obesity and pre-diabetes. Some other risk factors to convert pre-diabetes to diabetic are physical inactivity, hypertension, dyslipidemia, family history of diabetes, and smoking (Alomari & Al Hisnah, 2022).

Living a healthier lifestyle can prevent or delay the onset of T2D if anybody has been diagnosed with pre-diabetes (Rariden, 2019). Unfortunately, more than 84% patients do not know they have it (Bennasar-Veny et al., 2020). Fasting blood sugar (glucose) level of pre-diabetes is in the range 110 to 125 mg/dl (6.1 mmol/l to 6.9 mmol/l) and A1C is in the range 5.7% to 6.4% (WHO, 1999).

5.4 Gestational Diabetes

Gestational diabetes mellitus (GDM) affects 4-5% females in the second or third trimester of pregnancy (beyond 24 to 28 weeks of gestation) due to uncontrolled blood glucose levels and its consequences, although previously they have not diabetes. It usually disappears after the baby is born, but has a risk of developing T2D later on (White, 1949). It occurs because the body cannot produce enough insulin to meet the extra needs of pregnancy (WHO, 1999).

The majority of gestational diabetes patients can control their diabetes with exercise and diet; about 20% of the patients need blood-glucose controlling medications (Ross, 2006). Uncontrolled GDM can raise the risk of complications during childbirth; both the mother and the kid may experience various problems for this (Yuen et al., 2019). GDM can damage the health of the fetus, and can create various complications, such as growth abnormalities, pre-eclampsia, placental abruption, miscarriage, intrapartal hypoxia, accelerated growth, low blood calcium (hypocalcemia) and magnesium (hypomagnesemia), jaundice, high red blood cell mass (polycythemia), etc. (WHO, 2002; García, 2017; Tarvonen et al., 2021).

GDM imposes two main risks on the baby: growth abnormalities and chemical imbalances after birth that may require admission to a neonatal intensive care unit (Metzger et al., 2008). Untreated GDM results either large or small for gestational age, and increased the susceptibility of the fetus to intrapartum hypoxia (Setji et al., 2005). It also interferes with maturation, causing dysmature babies prone to respiratory distress syndrome due to incomplete lung maturation and impaired surfactant synthesis (Jones, 2001).

6. Historical Background

Diabetes has been recognized for about 4,000 years from the ancient literature of Egypt, India and China! We have found various descriptions in ancient history about diabetes, such as in the Egyptian papyri, in ancient Indian and Chinese medical literature, as well as in the work of ancient Greek and Arab physicians (Ghalioungui, 1987). The word "diabetes" comes from Greek word that means a "siphon". Greek physician Aretaeus of Cappadocia in Asia Minor during the second century AD, named the condition diabainein, for the patients who passing too much urine like a siphon. He spoke of diabetes as "*the mysterious sickness*". Aretaeus and other physician of ancient Greek were unable to treat it effectively (Laios et al., 2012). In ancient China, people observed that ants were attracted to some people's urine and called the disease "*sweet urine disease*" (McGrew, 1985).

In 1675, Thomas Willis, a personal physician to King Charles II of England, added mellitus means "honey" to the term diabetes that means "*siphoning off sweet water*". He could determine whether his patients had diabetes or not by sampling their urine. This method of monitoring blood sugars goes on largely unchanged until the 20th century. In 1796, John Rollo, Surgeon General to the Royal Artillery, started treatment of polyuria for the first time through the dietary restrictions. In 1857, French physiologist Claude Bernard (1813-1878) has established the role of the liver in glycogenesis, and the concept that diabetes is due to excess glucose production (Ahmed, 2002).

In 1889, German physician and physiologist Oskar Minkowski (1858-1931) and German physician Joseph von Mering (1849-1908) performed their famous experiment of removing the pancreas from a dog and producing severe and fatal diabetes. Before the discovery of the insulin little could be done for patients suffering from diabetes. Low calorie diets prolonged their lives but left them weak and near starvation (Karamanou et al., 2016).

In 1921, Canadian medical scientist, physician, and painter Frederick Grant Banting (1891-1941) and his student and assistant American-Canadian medical scientist Charles Herbert Best (1899-1978) have discovered insulin, which is used for the treatment of diabetes (Pyke, 1997). They have isolated insulin from pancreatic islets and administrated to patients suffering from T1D, and save lives of millions diabetes patients and have commenced a new era in diabetes treatment (von Engelhardt, 1989). In the 1950s, it is discovered that there are two types of diabetes: "*insulin sensitive*" (T1D) and "*insulin insensitive*" (T2D) (WHO, 2002).

7. Symptoms of Diabetes

Diabetes patients with high blood sugar (hyperglycaemia) will experience some common symptoms, such as polyuria (increased urination), polydipsia (increased thirst), unusual weight loss, sometimes weight gain, blurry vision, male sexual dysfunction, fatigue, cuts and bruises that do not heal, polyphagia (increased hunger), numbness and tingling in hands and feet, etc. Severe hyperglycaemia may lead to hyperosmolar syndrome and insulin deficiency to life-threatening ketoacidosis (WHO, 2002). Often symptoms of DM are not severe, or may be absent. Consequently, many patients cannot detect that they are DM infected for a long-time, and they face major organ problems before the diagnosis is made (WHO, 1999).

8. Causes of Diabetes

The causes of diabetes are complex and not fully understood. The cause of all types of diabetes is having high

amounts of glucose in the blood. It is estimated that immune system attacks the cells that produce insulin in the pancreas and destroys them. Recently, it has estimated that the functional pancreatic β-cell mass decreases and T2D progresses over time (Kaku, 2010). The pancreas has many β-cells to spare, so symptoms of DM do not appear until more than 90% of the β-cells have been destroyed. Yet there is no treatment proven to stop diabetes developing in the body (Ambler et al., 2021). During pregnancy placenta makes more hormones that may be insulin resistance, and lead to high blood sugar, and cause pre-diabetes (WHO, 1999).

Genetics and environmental factors may have a role that a viral infection can develop diabetes. Type 2 diabetes is caused by a combination of i) genetic factors, which is related to impaired insulin secretion and insulin resistance, and ii) environmental factors, such as obesity, sequence overeating, alcohol drinking, smoking, lack of exercise, stressful lifestyle, and aging (Goodpaster, 2010). The genetic make-up, family history, ethnicity, health, and environmental factors that influence the patient can all have an impact on the causes of diabetes (WHO, 2002).

9. Prevention of Diabetes

Usually in urbanized societies, sedentary lifestyle and over nutrition often lead to obesity. Eating a healthy diet and increase of physical activity a person can lead a healthy life (Harris, 1991). DM patients try to avoid animal fat, salt, and refined foods, and try to take foods high in fiber, vegetables and fruits (Schellenberg et al., 2013). Obesity people can take attempts to roughly loss 7% to 10% of their body weight (maximum one pound per week) by dietary and exercise improvements that can find opportunity of about 60% reduction in their chance of acquiring diabetes (Pasinettig et al., 2011). About 30 minutes or more of moderate to vigorous aerobic exercise, such as brisk walking, biking, swimming, jogging, running, etc. per day a total of at least 150 minutes a week can reduce weight successfully (Goodpaster, 2010).

10. Risk Factors and Complications of Diabetes

In 2004, diabetes is ranked as the sixth leading cause of death by disease in the USA (National Diabetes Fact Sheet, 2004). In men, it is responsible for erectile dysfunction, low testosterone levels and emotional factors, such as depression, anxiety or stress that can interfere with sexual feelings. In women, pregnancy brings the risk of gestational diabetes, even those who do not have diabetes (Wang et al., 2011). The risk factors of DM are obesity, physical inactivity, uncontrolled and unhealthy eating, increasing age, insulin resistance, family history of diabetes, genetic factors, and race and ethnicity. Uncontrolled diabetes for a long time due to high level of glucose can cause serious damage every part of the body, such as heart, kidneys, brain, eyes, skin, feet, etc. (Boulton et al., 2005).

People with diabetes are at a greater risk of various complications of cardiovascular diseases, such as coronary artery disease with chest pain, ischaemic heart disease (IHD), heart attack, stroke, peripheral vascular disease (PVD), narrowing of arteries (atherosclerosis), high blood pressure, and high cholesterol (American Diabetes Association, 2022). In it's the most severe forms; ketoacidosis or a non-ketotic hyperosmolar state may develop and lead to stupor and coma. In absence of effective treatment complications can even be life-threatening, and death may happen (WHO, 1999).

DM patients may also have elevated risks for sight loss, foot and leg amputation due to damage to the nerves and blood vessels, and renal failure requiring dialysis or transplantation (Pasinetti, 2011). Sometimes kidney damage arises and need dialysis or a kidney transplant due to kidney failure; eye damage can cause blindness and increase risk of glaucoma and cataracts among DM patients. Frequently, uncontrolled diabetes nerve damage problems, such as numbness, tingling, pain, or burning in fingers or toes may confront. Various other problems, such as skin infections, swelling in the legs and feet, loss of hearing, dental problems, poor healing of wounds, erectile dysfunction, dementia, and depression are common to DM patients (Schellenberg et al., 2013).

DM increases the risk of various microangiopathy damage problems, such as retinopathy, nephropathy, peripheral neuropathy, and autonomic neuropathy that are associated with reduced life expectancy, and significant morbidity. Due to specific diabetes related microvascular complications, increased risk of macrovascular complications (ischaemic heart disease, stroke and peripheral vascular disease), and diminished quality of life (WHO, 2002).

11. Diagnosis of Diabetes

Uncontrolled diabetes (hyperglycemia) progressively affects our various vital organs sometimes without symptoms. Therefore, early diagnosis and treatment are essential for the welfare of the DM patients (WHO, 1999). The most common test of DM is the HbA1c (or A1c) that is used to diagnose and monitor diabetes, which measures average blood sugar level for the past two to three months. From the diagnosis A1c 6.5% or above indicates DM (WHO, 2002). Some other common different options to diagnose diabetes are; i) fasting plasma glucose (FPG) level ≥ 126mg/dl (7.1mmol/l), a person has not eaten overnight or for the last 8 hour, ii) plasma glucose (PG)≥200mg/dl two hours after a 75g oral glucose load (OGL), and iii) random plasma glucose

(RPG)≥200mg/dl (11.1mmol/l) with unequivocal signs of hyperglycemia (International Diabetes Federation, 2017; García, 2017). A random blood sugar of between 7.1mmol/l and 11.1mmol/l refer to hospital to confirm diagnosis. The FPG test is the preferred test for diagnosing diabetes because of its convenience and low cost (WHO, 2002).

12. Treatments of Diabetes

More than 80% of DM patients are living in low-to-middle income countries, which pose additional challenges in effective treatment (Galicia-Garcia et al., 2020). With the treatment of DM some regular monitory systems are necessary for the welfare of the patients, such as insulin administration, blood glucose monitoring, meal planning, and screening for diabetes-related complications. Recently modern pharmaceuticals, such as insulin, biguanides, sulfonylureas and thiazolidinediones are discovered for the treatment of diabetes (Goodpaster, 2010). The treatment procedures for pre-diabetes are lifestyle changes, such as exercising regularly, losing weight, and following a healthy eating pattern. Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk reduction strategies beyond glycemic control (American Diabetes Association, 2019).

Inhibitors of dipeptidyl peptidase 4 (DPP-4) are a class of oral hypoglycemics that block the enzyme DPP-4. These inhibitors prevent the breakdown of incretin hormones that help the body for producing insulin to lower elevated blood sugar levels. A new class of drugs incretinmimetics works to stimulate insulin release and helps lower blood sugar, and are taken by injection, either once or twice a day (Gkaliagkousi, 2007). The most common five categories of oral hypoglycemic agent, anti-diabetic medication, are sulphonylureas and similar (secretagogues), biguanides (sensitizers), thiazolidindiones, alpha glucosidaseinhibitors, and incretineanalogues/agonists (Boulton, 2005). The sulphonylureas block the ATP-sensitive K+ channel and as a result can stimulate the insulin secretion (Aversano et al., 1991). The biguanides reduce the hepatic synthesis and the output of glucose, and increase the insulin uptake in the skeletal muscle by reducing LDL cholesterol and triglyceride levels (Makimattila et al., 1999).

The thiazolidinediones are selective agonists of PPARγ receptors, and activate the insulinsensitive genes regulating the glucose and fat metabolism, and consequently increase the insulin sensitivity in the periphereal tissue (Martens et al., 2006). The alpha-glucosidase reduces the intestinal absorption of starch, dextrins, and disaccharides, and reduces the postprandial plasma glucose. The GLP-1 agonists are metabolized by the dipeptidyl peptidase IV enzyme (DPP-IV). The GPP-4 inhibitors increase the blood concentration of the incretin GLP-1 the GPP-4 inhibitors (gliptines) is that they increase the blood concentration of the incretin GLP-1 (glucagon-like peptide-1) by inhibiting its degradation by DPP-4 (Gkaliagkousi, 2007).

13. Conclusions

Diabetes mellitus is a group of metabolic diseases that is related to carbohydrate, lipid, and protein metabolism. Rapid globalization, industrialization, and the normalization of a sedentary lifestyle, along with increased obesity; diabetes and its related comorbidities are increasing worldwide very rapidly. A balanced diet and an increase of the level of physical activity can help to maintain a healthy weight, staying healthier for longer and to reduce the risk of diabetes.

We hope that the DM patients always follow some healthy techniques for the lifelong well-being, such as always eat a heart-healthy diet, get adequate sleep, be physically active, keep blood pressure under control, keep cholesterol in normal level, maintain a healthy weight according to height, avoid alcohol, avoid smoke and second-hand smoke, manage stress, and have regular medical check-ups.

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