Free diabetes: a review essay example

Health & Medicine, Diabetes

Introduction

This review covers the pathophysiology, diagnosis, epidemiology, etiology, clinical presentation, management and complications associated with diabetes mellitus commonly known as diabetes, a disorder that affects more than 385 million people worldwide (idf. org). The long term prognosis and impact on the quality of life are also discussed. Diabetes is defined by the American diabetes association as a group of disorders that are characterized by hyperglycemia stemming from deficiency in the activity of insulin or reduced insulin secretion, or both. There are three main types of diabetes namely type 1, type 2 and gestational diabetes. Diabetes mellitus has no cure. It is a lifelong chronic condition that needs to manage by medication, diet, weight management, and physical activity. The hyperglycemia associated with diabetes can lead to a number of complications affecting multiple organs including, neuropathy, macular degeneration, amputation of limbs, vascular diseases, kidney diseases, etc. The risk for cardiovascular disease also increases with diabetes.

Classification

The classification of diabetes is based on the physiological process resulting in hyperglycemia. The two main types of DM include the type 1 and type 2 diabetes. The type 1 diabetes occurs as a manifestation of near total or absolute deficiency of insulin by the pancreas. Type 2 diabetes is a more heterogeneous disease in which a deficiency of insulin secretion, insulin resistance or increased glucose production can result in hyperglycemia. Type 2 diabetes occurs to a number of risk factors, including, genetics,

environmental factors, and metabolic defects in the patients. It is observed that type 2 diabetes occurs following a period of pre-diabetes. Pre-diabetes, is a critical phase in which while most patients are asymptomatic have an impaired glucose tolerance. If diagnosed and treated many prediabetics can avoid the eventual diagnosis of DM. In the previous system of classification, diabetes was classified as insulin dependent and non- insulin dependent diabetes mellitus. However, it has been shown that many patients with NIDDM require insulin eventually, the use of NIDDM is confusing.

Other types of DM include the gestational diabetes (GDM) and the maturity onset diabetes of the young (MODY). Gestational diabetes is the diabetes that occurs during pregnancy. It is described as increased glucose level in pregnancy or intolerance to the glucose levels. It is usually observed in the second and third trimesters of pregnancy. GD affects 5-7 of all pregnancies (Schoeber, et al., 2006). While most women return back to normal FGL level a substantial 30-50% develop DM later in the life. MODY is diabetes that occurs in young adults due to a number of genetic mutations. The hyperglycemia occurs at < 25 years. The two most commonly identified mutations associated with MODY include the HNF1A and the GCK genes. MODY is very commonly misdiagnosed as either type 1 or type 2.

Diagnosis

The world health organization and the national diabetes association have developed the diagnosis criteria for diabetes mellitus. The criteria have been developed based on the a). Fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) is different in normal and diabetic adults. b). The level

of glycemia has to be defined based on the level at which complications occur in patients (idf. org)

The two main diagnostic criteria include

• Fasting blood glucose level is ≥ 7 mmol/L; Two hour plasma glucose is ≥ 11. 1 mmol/L at the end of an oral glucose tolerance test.

A third rarely used criteria states that following random sampling blood glucose concentration is 11. 1 mmol/L in addition to the presence of various diabetes associated symptoms. According to the ADA protocol, a repeat testing is recommended if an unambiguous result is not obtained. In addition to the diagnostic criteria, the diabetes mellitus patients are also defined based on their glucose tolerance levels. 1. Fasting plasma glucose level of < 5. 6 mmol/L is considered healthy and normal. 2. FPG levels between 5. 6-6. 9 mmol/L is defined as pre-diabetes. 3. FPG level of ≥ 7 mmol/L is diagnosed as diabetes.

Another diagnostic marker that is recommended by some clinicians for DM diagnosis is the Hemoglobin A1C (HbA1C) level at ≥ 6. 5%. However, a clear correlation between the HbA1C level and subjects with mild glucose intolerance or normal tolerance to glucose is not established. A conclusive diagnosis of DM results in a major impact on the life of the patient. As a result, various criteria must be satisfactorily satisfied to impart a diagnosis. As has been stated, DM is not a disease it is a way of life (Alberti and Zimmet, 1998).

Epidemiology

DM is a disease that affects the rich and poor alike. In fact, it is touted as the disease of the rich world. It was demonstrated that an estimated 30 million patients were reported to have DM in 1985. In the year 2014, an estimated 385 million patients have been reported to be suffering from DM (who. org). The number of cases with type 2 diabetes rise at a higher rate than the type 1 as a result of increasing obesity epidemic worldwide and especially as the rate of industrialization increases. It is known that the incidence of DM increases with age. 20. 9 % of all adults over the age of 60 had DM. The occurrence of DM is observed to be similar between men and women, with men > 60 showing a greater prevalence.

Type 1 and type 2 diabetes demonstrate a difference based on the location. The Scandinavia region has been reported to have the highest type 1 incidence while the Pacific rim including Japan and parts of China report to have lowest worldwide occurrence of type 1 diabetes. The occurrence of pre-diabetes and type 2 diabetes is greatest in a few Pacific islands. Nations like US and India demonstrate a medium to high occurrence, and most of the African nations demonstrate a low type 2 DM incidence (idf. org).

Etiology

Insulin is the hormone that is secreted by the ß cells (islets of Langerhans) of the pancreas in response to elevated blood glucose levels following a meal. While glucose is the key modulator of insulin secretion, amino acids, other nutrients, ketones and some neurotransmitters can affect the secretion of insulin. A blood sugar level of > 4 mmol /L followed by the transport of glucose by glucose transporter 2 to the islet cells results in increased

production of insulin and subsequent release. Glucose gets phosphorylated by the glucokinase that can regulate secretion of insulin. Glucose -6 phosphate is further metabolized by glycolysis that inhibits the activity of ATP sensitive K+ channel. Inhibition of the K+ channel results in opening of voltage dependent Ca2+ channels inducing secretion of insulin (Butler et al., 2006). Incretin are proteins released by neuroendocrine cells, and they stimulate the insulin secretion following food consumption. Following the release of insulin, it binds to insulin receptor and activates tyrosine kinase activity of the receptor. The insulin receptor undergoes auto-phosphorylation resulting in recruitment and activation of a number of signaling pathways. One event associated with the activation of insulin receptor involves glucose transporter 4 (GLTU4). GLUT4 gets translocated to the cellular surface resulting in the uptake and absorption of glucose in skeletal muscle and fat (Tisch & McDevitt, 1996). The homeostasis of glucose involves uptake of glucose by muscle and fat cells and production of glucose in the liver. Insulin is the primary regulator of maintaining this homeostasis in humans. In most cells the glucose uptake and release in under the control of insulin except cells such as in the brain.

Type 1 diabetes occurs as a result of genetic and immunological factors that result in the destruction pancreatic beta cells. In most type 1 patients, an autoimmune mediated destruction of the islet cells of pancreas is observed. Individuals have a genetic mutation are born predisposed to developing autoimmunity. They exhibit normal pancreatic function at the time of birth, however, following a certain trigger the functioning beta cells decrease and the beta cell mass gets reduced also. This results in a progressive decrease

in the production and secretion of insulin. Unfortunately most type 1 patients remain asymptomatic for a long time, and clinical symptoms become evident when 80% or more of the beta cells are damaged. The remaining functioning beta cells can produce some insulin that is inadequate to maintain a proper balance of glucose level. The remaining beta cells are destroyed eventually making the patient completely insulin deficient.

The genes most commonly responsible for predisposition to type 1 are located on the HLA region of chromosome 6. This cluster of genes is responsible for the synthesis of major histocompatibility (MHC) II molecules. These MHC II molecules are involved in initiating an immune response resulting in the islet cell death. In addition to the HLA region genes, certain other genes such as the IF1H1, PTPN22, CTLA-4, etc. are responsible for increasing susceptibility to developing type 1 (Davies et al., 1994). The beta cells are infiltrated by T lymphocytes and attacked a number of cytokines resulting in beta cell death (Daneman, 2006).

Type 2 diabetes progression carries a greater genetic component. A person with both parents' diagnosed with type 2 diabetes has a 40% likelihood of developing type 2 diabetes. Identical twins bear a greater degree of co-occurrence. There are a few genes that have been identified as being responsible for increasing susceptibility to type 2. Genetic polymorphism is also associated with increased risk for type 2 diabetes development. However, in addition to the genetic component environmental factors play a vital role too. Obesity, presence/absence of physical activity and diet contribute to the risk for type 2 diabetes. Pre-diabetes is usually identified in obese patients especially centrally or viscerally obese people. Many pre-

diabetics present insulin resistance which is compensated by increased insulin production by the beta cells. The beta cells, however, fail to keep up with the demand and hyperglycemia develops. This state of pre-diabetes is followed by further reduction in insulin secretion and increased glucose production in the liver resulting in type 2 diabetes.

The occurrence of type 2 diabetes is a follow up to an event called “ insulin resistance”. In this condition, the cells are not receptive to the plasma glucose level and cannot utilize the glucose adequately resulting in hyperglycemia. Obesity has been identified as a critical driver for insulin resistance. A greater fat content and fatty acids inhibit the signaling molecules driving the insulin receptor activity (Muoio & Newgard, 2011). Free fatty acids also inhibit the utilization of glucose in skeletal muscle cells and impair the activity of pancreatic beta cells. Insulin resistance is also an indicator of metabolic syndrome. Metabolic syndrome is a term used to describe a number of metabolic deficiencies including hyperglycemia, dyslipidemia, and hypertension. Pre-diabetes is one of the conditions of metabolic syndrome. It has been reported that if identified, pre-diabetes can be treated, and progression to diabetes prevented.

Clinical features

Some of the classical symptoms of diabetes ae frequent urination, increased thirst and increased hunger. These symptoms are commonly presented in patients with type 1 diabetes. Many type 2 patients do not show any of these symptoms. Diabetes affects the blood flow and often leads to a number of microvascular and macro-vascular complications. Diabetes leads to damage to blood vessels. This vascular damage can lead to retinopathy or eye

damage, nephropathy or kidney damage. Damage to nerves is also observed in an ineffective hyperglycemia control. Diabetic neuropathy leads to wasting of nerve cells. As diabetes affects the circulation, the lower extremities including toes and feet can suffer damage and require amputation in uncontrolled cases. Diabetes also increases the risk for peripheral vascular disease, stroke and cardiovascular disease.

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic nonketotic syndrome (HHNS) are two of the severe complications of diabetes. DKA can induce coma and be life threating. DKA manifests as due to inadequate glucose metabolism fat cells are metabolized to derive energy. Excessive breakdown of fat causes production of ketone bodies that are toxic to the human body. HHNS occurs when the body tries to remove all of the excess sugar resulting in excessive urination. This excessive urination can lead to coma and death if not treated in a timely manner (Olokaba, Obateru & Olokaba, 2012).

Treatment and Management

The aim of diabetes treatment is to maintain ‘ normal’ blood glucose level or achieve a state of euglycemia. The maintenance of normal glucose level can be attained by a combination of medication, physical activity, diet, and weight loss. Metformin, a biguanide is the first line of treatment against type 2 diabetes. Metformin induces activation of AMP activated protein kinase responsible for regulating expression of gluconeogenesis genes. It inhibits gluconeogenesis that is the production of glucose from the liver. It has also been shown to increase the sensitivity to insulin by phosphorylating GLUT 4 enhancer receptor. Sulfonylureas are also used to treat hyperglycemia in

patients with type 2 diabetes. They bind to the ATP dependent K+ channel in the beta cells and stimulate the secretion of insulin. These agents are well tolerated but have been associated with hypoglycemia. In addition to sulfonylurea, Meglitinides also act on the ATP dependent K+ channel and induce insulin secretion. Meglitinides have a short duration of action and therefore exhibit a lower risk of hypoglycemia. Thiazolidinedione are the third group of drugs used in the management of type 2 diabetes. They bind to and activate the peroxisome proliferator activated gamma (PPAR- ■) receptor. Alpha-glucosidase analogues such as Acarbose, Miglitol, incretin based agents, DPP-IV inhibitors are other agents used in the treatment of type 2 diabetes (Tehrani, Bailey, Del Parto & Barnett, 2011)

Patients with type 1 diabetes are treated with insulin. Insulin replacement therapy is carried out by using insulin or insulin analogues. The insulin administered to the patients can differ based on the onset of effect. The insulin can be differentiated based on the onset and duration of action (Migdalis, 2001). A fast acting insulin (lyspro) preparation works rapidly and is used to manage glucose levels between meals. A long acting insulin (NPH, lente and ultralente insulin) is absorbed at a slower rate and has longer duration of action. Insulin can be administered as injection or infusion. The insulin syringe is the most common method of insulin administration. However, in recent years insulin pen is becoming more popular. The insulin pen contains a ‘ cartridge’, a replaceable reservoir with needle to puncture the skin for delivery.

In addition to physiological effects, diabetes can cause depression, anxiety and feeling of helplessness in patients due to the lack of cure. Weight gain

can occur due to environmental factors. In addition to diabetes treatment, the care should involve proper education, especially among the poor and the elderly. The importance of physical activity, maintaining healthy diet, controlling alcohol consumption should be imparted in all diabetics. Tobacco intake should be stopped in patients with diabetes. While there is no cure for this disease, novel drugs are being developed. A wholesome approach to the management of this lifestyle can result in patients leading happy and fulfilling lives.

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