ZooScan: ISSN 0000-0000 (Online) 2023

Contents lists available at KulDevWeb

ZooScan

journal homepage: www.zooscan.kuldevpublication.com

Review Article

Diabetes mellitus: A disease that kills silently an Analysis

*[1]Dinesh S. Kharate

*[1] *Department of Zoology, Sant Ramdas Arts, Commerce and Science College, Ghansavangi, Jalna-431209, India*

ARTICLE INFO

Article history:
Received 17 September 2023
Accepted 30 October 2023
Available online xxxx xxxx

Keywords:
Diabetes,
Insulin,
Blood glucose,
Mellitus.

ABSTRACT

Elevated blood sugar level of the hallmark of diabetes mellitus was very chronic multifactorial progressive illness that is widely recognized. Roughly 8.5% of adult people worldwide suffer from it. The main causes of it are aging, obesity, and metabolic and genetic variables. The real Because over 50% of diabetics do not receive a diagnosis for their condition until ten years after it first manifests, the prevalence of diabetes is comparatively high. This review focuses on the types, causes, and problems of this condition, as well as how to manage and treat it.

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Selection and peer-review under responsibility of scientific committee of editorial board members of ZooScan and author (s) and suggested reviewer.

1) Introduction

The typical symptoms of diabetes mellitus, which include weight loss and frequent urination reflexes, were initially identified by the Egyptians in history. The Greek word "diabetes" meaning "passing through" is the source of the word causes increased urination, which is a typical illness sign. The Latin term "mellitus," which refers to glucose found in diabetic patients' urine, means "honey." Based on recent WHO estimates, diabetes mellitus is considered a chronic global pandemic disease that causes more than 1.6 million deaths yearly.

Diabetes is the cause of 7% of fatalities worldwide for males aged 20 to 69 and 8% of deaths for women in the same age range. Between 1984 and 2013, the projected peoples with having diabetes increased from 112 million to 412 million. According to current polls, its global frequency is estimated to rise from 4.7% in 1980 to 8.5% by 2014. Because over 50% of diabetics go untreated, the true prevalence of the disease is very high. Over the past three decades, its prevalence was sharply increased in low to middle income nations (WHO. Global reports on diabetes, 2017). Patients with diabetes will more likely experience short- term and long-term consequences, which can lead to chronic health issues and early mortality—nearly one death occurs every ten seconds—(Kaul, 2012). According to Pessin and Saltiel (2000), it causes the β subunit to undergo autophosphorylation, which is followed by the extra glucose being converted to glycogen for storage.

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* Corresponding author.
E-mail address: dineshkharate2@gmail.com (Dinesh S. Kharate)

https://doi.org/10

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Uncontrollable risk factors like heredity, family history, and age, as well as poor lifestyle choices like overeating, obesity, and physical inactivity, are the main causes of diabetes mellitus. Diabetes affects mammals, including dogs, cats, and other animals, in addition to humans (Riaz, 2009).

2) The Pathophysiology of Hyperglombia

Each organ system in the human body must function differently and effectively in order to remain a healthy physiological state. Any departure from their typical functioning resulted in the emergence of a pathological condition or disorder. One of the medical conditions known to diabetes mellitus occurs when the body was unable to produced the insulin, which causes the blood to contain abnormal levels of glucose. In order for cells to metabolize glucose, insulin is required for its delivery into the cells. Lethargy, or dizziness, Decreased vision, Ketoacidosis, Polydipsia, Polyuria, Hyperglycemia, dehydration, polyphagia, increased susceptibility to infections, delayed sore healing, weariness are among the frequent symptoms of diabetes mellitus.

3) Mechanism of Blood Glucose Regulation

Since glucose is the main respiratory substrate, blood is typically the source of it. A person is considered hyperglycemic or diabetic if their blood sugar level is higher than 133 mg/dl of blood volume prior to meal blood volume following a meal. Blood glucose level with normal range, two key hormones glucagon and insulin act antagonistically. Elevation in blood sugar level prompts the pancreatic β cells, islets of langerhans to release insulin. The hormone, which was in turn, triggers to transfer of glucose into the liver cells, where it is transformed into glycogen, the food molecule stored in reserve. Insulin is a polypeptide hormone of 51 amino acids that is made up of 2 chains, A and B. linked together by disulfide bonds. Pro-insulin is first secreted in inactive form consisting of 3 chains: A, B, and C. Then, the enzymes convertases and carboxypeptidase transform it into an active form. The blood carries insulin to the liver cells where they interacts to the tyrosine kinase insulin receptor. The receptor is composed of 2 extracellular α subunits and two intracellular β subunits connected by disulfide connections.

Additionally, the translocation of the glucose transporter-4 into the cell surface stimulates the absorption of glucose by adipose and skeletal muscle cells. The blood glucose level returns to normal thanks to this regulatory system. Low blood glucose levels trigger the production of glucagon from the pancreatic α cells. In order to maintain homeostasis, glucose is released into the bloodstream by the liver cells in response to a signal from glucagon. Diabetes was characterized by malfunction in either the production or secretion of insulin, as in type 1 diabetes, or the development of insulin resistance, as in type 2 diabetes.

4. Diabetes Mellitus Types

Maturity-onset diabetes of the young (MODY), Gestational diabetes (GD), Latent autoimmune diabetes in adults (LADA), Type 2 diabetes (T2DM) and (Type -1) diabetes are among the various forms of diabetes mellitus that can affect a person.

4.1 (Type-1) Diabetes Mellitus

Type-1 diabetes referred as insulin dependent, Juvenile diabetes was typically strikes between the ages of 0 and 35. Environmental and genetic factors might be to blame. The HLA gene found on chromosome 6 codes for the cell surface HLA proteins. The immune system's ability to distinguish between self and nonself is attributed to these proteins. Any mutation in the HLA gene leads to the production of faulty HLA proteins and which in turn causes the immune system to mount to autoimmune reaction against pancreatic β cell. Activated T lymphocytes (CD8+ and CD4+) with macrophages infiltrating the islets of langerhans target and kill the pancreatic β cells. Due to decreased insulin production, idiopathic diabetes, an uncommon form of T1DM without autoimmune, is found in Asian and African populations (Harris and Fillegal, 1998). In this situation, regular insulin administration becomes essential to the body's ability to maintain the glucose balance necessary for survival. Patients with Type 1 diabetes may occasionally gain weight or acquire insulin resistance resulted of gene as a factors, which can result the development of double diabetes. (Type- 1) diabetes is commonly characterized by weight loss, weariness, polyuria, polyphagia, increased thirst and weakness.

4.2 Diabetes Mellitus Type 2:

According to NIH, USA data, it is the most prevalent type of diabetes globally, accounting for 90% of diabetic cases. According to reports, people with type 2 diabetes who obesed experience resistance to endogenous insulin as a result of alterations in the cell receptors linked to the accumulation of abdominal fat. In contrast, people without obesity have been shown to have insulin inefficiency at the post receptor levels in addition to a shortage in insulin production and release. Obesity and being overweight are the biggest risk factors for form 2 diabetes. Type 2 diabetes is encouraged by a diet low in healthy foods high in fiber and low in calories, processed carbs, and saturated fats. It is further exacerbated by physical inactivity. According to Mehta and Wolfsdorf (2010), hazy vision, irritability, tingling in the hands and feet, and recurrent bladder, vaginal, and skin infections are typical signs of diabetes.

4.3 Diabetes Gestationale

Women exhibit significant fluctuations in blood glucose levels and frequently go through an earlier stage of hunger during pregnancy. Gestational diabetes is caused by an increase in the mother's blood glucose levels. Most of the time, it ends when the pregnancy ends, but it also raises the child's risk of type-2 diabetes in later life along the mother's health. It is linked to the placenta secreting insulin and causes a temporary state of insulin resistance by decreasing insulin sensitivity at the end of the first trimester. However, because of its potential teratogenicity, it could be fatal to both the mother and the fetus, leading to neuropathy, intrauterine growth retardation, premature delivery, newborn jaundice, respiratory problems in the baby, and even stillbirth (Maria, 2011). Gestational diabetes affects around 4.6 % of pregnant women, (ADA) American Diabetes Association (American Diabetes Association, 2007).

4.4 Young Diabetes with Maturity Onset

It is an uncommon monogenic form of diabetes brought on by a mutation in any one of the following genes: hepatocyte nuclear factor 4α (HNF 4α), HNF‑1β, insulin promoter factor‑1 (IPF‑1), glucokinase gene (HNF‑1α), and NEUROD-1. This kind of diabetes has a 70% correlation with mutations in the α gene (HNF‑1). A significant deficiency in insulin secretion is its defining characteristic (Fajans et al., 2001). Secondary causes such as hyperthyroidism, Cushing's syndrome, Klinefelter's syndrome, and pancreatitis may be the reason.

4.5 Adults with Latent Autoimmune Diabetes:

A type of autoimmune (type-1) diabetes known as Latent autoimmune diabetes (LADs) in adult is identified in people who are older than the typical age at which type 1 diabetes first manifests itself (more than 25 years of age). Other names for "LADA" that have been used are "Slow Onset Type-1" diabetes, Late-onset Autoimmune Diabetes and "Type-1 diabetes," of Adulthood. Because of their age at diagnosis, patients with LADA are frequently misdiagnosed as having type-2 diabetes.

5) Diabetes Causes and Risk Factors

Diabetes is a long-term, complex condition influenced by a person's environment, lifestyle, and genetics. American Diabetes Association reports that there a 10 to 29 % likelihood of type-2 diabetes and a 55% chance of inheritance [3,9]. Lack of regular exercise, weight increase, and central obesity of buildup of fat around the belly that promotes insulin resistance were the main risk factors for type-2 diabetes. It is risk factor for all simple carbohydrate consumption peoples, a diet low in fiber, and excessive soft drink consumption. It is also associated with asthma, hypertension, hypercholesterolemia, and polycystic ovarian syndrome. Blood glucose levels can be altered by hormonal imbalances, especially those caused by glucocorticoids, anabolic steroids, and injectable contraceptives. Type 1 diabetes can be brought on by coxsackie virus infection, rubella, and mumps.

6) Diagnostic Results

The following tests are used in the clinical diabetes mellitus diagnosis is (Diabetes Care, 2004):

1. Plasma glucose at random ≥ 202 mg/dl
2. Plasma glucose when fasting ≥ 112 mg/dl
3. Mouth glucose test (measurement of plasma glucose level two hours after mouth glucose administration >205 mg/dl) for gestational diabetes

7) Hb A1C glycohemoglobin testing (to evaluate glucose management over the long term)

Different forms of diabetes can be distinguished by another test known as the C-peptide test. As a byproduct of producing C-peptide along insulin is present in patients with diabetes but absent or present in very low concentrations in those with Type 1 diabetes.

8) Diabetes Mellitus Management and Treatment

Insulin therapy, oral hypoglycemic medication, and diet and exercise management are all options for managing diabetes. In every situation, diet is an essential component of care. Without proper attention to providing optimal nutrition, treatment cannot be effective. A diabetic patient's diet shouldn't include more than 300 mg of cholesterol or 10% of saturated fats (Zarogoulidis and as N, Kouliatsis, 2011). A minimum of 20 g of dietary fiber should be consumed on a regular basis through wholegrain fruits, legumes, cereals and vegetables.

Consuming too much salt should be avoided. It was restricted especially in individuals with nephropathy and hypertension. The goals of dietary therapy should be to maintain a healthy weight, meet nutritional needs, allow for good glycaemic control with blood glucose levels as close to normal as feasible, and address any abnormalities in blood lipid levels that may be related. A glucometer must be used for routine blood glucose monitoring in order to prevent issues related to diabetes. Insulin is used for treatment individuals with type-1 diabetes. It can be given orally, intravenously, or even through innovative nanotechnology-based delivery systems (Chaillous et al., 2000; Card and Magnuson, 2011).

Patients of type 2 diabetes they do not adhere to the recommended diabetes treatment strategies have higher glycated hemoglobin levels and glucose concentrations (HbA1C of >6.0). Anti-diabetic medication use becomes necessary in these situations (TNCCFC, 2008). Anti-diabetic medications such as biguanides, meglitinides, sulfonylureas, thiazolidinediones, DPP-4 inhibitors, and alphaglucosidase inhibitors are commonly used to treat diabetes.

These anti-diabetic medications can be roughly categorized into four groups [2]:
a) Biguanides, which include Metformin and diminish gluconeogenesis;
b) Insulin secretagogues, which include medications like sulfonylureas and stimulate pancreas release insulin.
c) Insulin sensitizers, such as thialzolidinediones, which increase the sensitivity of peripheral tissues.
d) Insulin/insulin analogues, which give recombinant insulin as an exogenous insulin source.

To prevent diabetic nephropathy, some hypertension medications such as antichloestrol medications, ACE inhibitors and angiotensin II receptor blockers are also advised in addition to these prescriptions. Amylin synthetica is used to treat type 1 diabetes. In cases of severe insulin shock, a glucose kit may be employed. Studies on the pathophysiology and management of diabetes, along with technological advancements, have resulted in the creation of more potent medications that act on the incretin system. These include injectable glucagon-like peptide-1 agonists, which may stimulate oral DPP-4 inhibitors, such as saxagliptin, linagliptin, sitagliptin, and vildagliptin along insulin secretion which block the DPP-4 enzyme and raise levels of the incretin hormone (GLP-1) (Riedel and Kneffer, 2010 and Gallwitz, 2010).

Furthermore, there is ongoing development of sodium-glucose transport protein-2 (SGLT-2) inhibitors, which attempt to obstruct renal glucose re-absorption through the (SGLT-2) transporter (Washburn, 2009). Treatment for type 1 diabetes involves transplanting the entire pancreas or pancreatic islets from a compatible donor; however, organ rejection reaction poses a risk to transplantation therapy, even when immunosuppressive medications are taken (Vardanyan, 2010). Additionally, studies are being conducted to create a stem cell that can produce β-cells that produce insulin (Kroon, 2008). Precautionary steps such as controlling one's diet, exercising, taking care of one's feet and skin, and regularly checking one's cholesterol and blood sugar levels can help prevent diabetes.

9) Complications with Medicine

Diabetes damages several organs, including the eyes, Kidney, heart, and immune system, causing them to malfunction or fail. For this reason, it is also referred to as the "silent killer disease." It may cause diabetes angiopathy, which is damage the blood vessels, and it may also aggravate diabetic neuropathy, nephropathy, and retinal degeneration. Patients with diabetes are 2 to 4 times more likely to develop atherosclerosis, coronary

heart disease, and stroke. Patients with diabetes typically exhibit hypertension, hypercholesterolemia, and hyperinsulinemia. 15% of diabetics get foot ulcers, and 4.6 to 17.5% of those who get them require surgery to remove the ulcer.Nephrotic failure affects 16% of diabetics. In 2010, 2.6% of blind cases and 1.9% of moderate to severe vision impairment worldwide were attributed to diabetic retinopathy. According to Boyle (2007) and Ceriello (2010), it is the second most common cause of blindness and renal disease globally, which can lead to glaucoma and cataracts.

However, retinopathy rates are higher among Caucasian populations, those with type 1 diabetes, those with diabetes for a longer period of time, and maybe those from lower socioeconomic backgrounds (Yau, 2010). More than 60% of diabetic patients experience neuropathy, the most frequent long-term effect of the disease. It can cause discomfort, weakness, loss of hearing or vision, and even limb amputations (Casellini and Vinik, 2007 and Edwards et al., 2008). Autonomic neuropathy can impair digestion and increase the risk of incontinence and sexual dysfunction, whereas peripheral neuropathy frequently results in discomfort or numbness in the limbs. Alzheimer's disease, dementia, memory loss, and other cognitive impairments are more common in diabetics. The primary cause of last stage renal failure was diabetic nephropathy. Which is characterized by a progressive rise in urine albumin, an increase in glomerular blood pressure, and urinary tract infections (Selby, 1990). Dialysis or a kidney transplant are necessary forms of treatment.

10) Summary

World diabetes data show that number of individual living with diabetes 1 and 2 has increased from 111 million, 1984 to 428 million,2017. This indicates that the prevalence of diabetes is rising quite quickly. Arranged. There is an urgent need to create new tactics that include strong leadership, the construction of systems for allocating resources, and advocacy for an integrated non-communicable illnesses program that specifically targets diabetes in order to stop the disease's global expansion. Furthermore, there is a need for the creation of more effective anti-diabetic medications in addition to successful advancements in β-cell regeneration, pancreas or pancreatic transplantation, and stem cell therapy.

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