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Complication of Diabetes Mellitus

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Abstract

Diabetes mellitus define as a chronic metabolic disorder ,each of hyperglycemia and poor control lead to many complication in human body , that complication lead to sever mortality and morbidity. The complication of DM can divided into two main types the microvascular complication that effected on small vascular in each of retinal , peripheral nerve and kidney that lead to retinopathy, neuropathy and nephropathy disease respectively. And macrovascular complication that effected on large vascular including Peripheral Artery Disease, Coronary Artery Disease and Cerebrovascular disease.

Keywords: Diabetes mellitus, Microvascular complication, Macrovascular complication.

1. Introduction

1.1 Diabetes Mellitus:

Diabetes mellitus describes a metabolic condition , in the 14th century known as black-death and the oldest known man-made condition in which insulin hormone is not adequately developed or used in the human body, which involved the transformation of carbohydrates into energy, The imperfections in the secretion or function of insulin hormone may trigger certain metabolic abnormalities that indicate the development of the condition of hyperglycemia as a result of these defects (Deepthi *at el.*,2017),(Mezil *at el.*,2018).Diabetes affects nearly two million people, or 7.43% of Iraq 's total population , and 415 million people worldwide(Mansour *at el.*,2008),(Zheng *at el.*,2018). For both clinical and scientific purposes, the classification developed for the etiology or pathogenesis of many types of diabetes would be extremely useful. Unfortunately, such a classification is impossible because of inadequate knowledge on the causes of diabetes. For the bulk of this century, the terms juvenile onset and adult onset have been used to characterize the two most prevalent diabetic syndromes. However, since juvenile diabetes can start late in life and adult diabetes can start early in life, the initial age range was never adequate. A classification system for insulin tolerance was set up in 1979(National Diabetes Data Group,1979).

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The National Diabetes Committee has adopted T1DM diabetes, T2DM, and GTM. diabetes will contribute, if left untreated, to a multitude of serious health problems affecting on both smaller and large vessels, i.e. microvascular and macrovascular complications respectively, the microvascular risks affect the renal , the most expensive complication with diabetes, with persistent kidney failure (nephropathy) and nerve injury (neuropathy) raising the likelihood with diabetic foot ulcers and/or amputations. Furthermore, eye injury (retinopathy) can due to blindness, while macrovascular disorders (coronary heart failure, peripheral artery disease , and stroke) can lead to blindness (Saeedi *at el.*,2019).The disturbance of the body's vascular system, combined with hyperglycemic disease, is due to compromised digestion of sugars, protein and electrolytes. Under this condition, owing to disproportionate glucose accumulation in certain cells, lipid metabolism dysfunction, better reactive growth, the retina, glomerulus, middle, and peripheral nerves are all pretentious endothelial cells (Federation,2017).

1.2 The Microvascular Complication of Diabetes

1.2.1 Retinopathy:

A microvascular condition that may affect each of the peripheral retina, macula, or both is characterized by diabetic retinopathy is a serious cause of vision loss and blindness in diabetics. Vitreous hemorrhage or retinal objectivity may cause a total or partial loss of vision(Abdulwahab ,2020). In the previous arrangement, It can be segregated into two kinds "proliferative diabetic retinopathy" (PDR) and "non-proliferative diabetic retinopathy" (NPDR). As a general, NPDR is distinguished by capillary divider deficiency, enhancement of micro aneurysm and liquid spillage, and more prominent endothelial attachment of leukocytes and monocytes(Cade,2008). Diabetic retinopathy disorder characterized by endothelial cell and pericytes retinal capillary degeneration due to the incidence of ischemia and micro-aneurysm. At an advanced stage of the disease, proangiogenic mediators, especially vascular endothelial growth factor, are upregulated, resulting in pathological retinal vessel proliferation (VEGF)(Bloom *at el.*,1975). Changes in the retinal microvasculature, as well as increased retinal vessel leakage, can result in vision loss.

Retinal capillary degeneration or occlusion is closely linked with poor prognosis (Hammes *at el.*,2011).Because of the subsequent discharge of antigenic elements related to hypoxia, this is most likely the consequence of ischemia. This propels the disease into a proliferative stage, where visual impedance, called macula oedema, and liquid collection within the retina are triggered by neovascularization. Dying with associated retinal engineering mutilation will occur in more realistic situations, counting the deterioration of a fibro vascular film that may result in retinal separation a short time later (Liu *at el.*,2020).Several hyperglycemic-mediated pathways are needed for diabetic retinopathy pathogenesis, like activation of each of the protein kinase C and the polyol pathway, accumulation of advance glycated end products, and increased hexosamine flux. These pathways facilitate retinal blood flow enhancements, improved vascular permeability, activation of multiple growth factor receptors, pericytes loss, capillary basement membrane thickening, and microaneurysms hemorrhage (Frank.,2004).

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1.2.2 Neuropathy:

In more than 15 percent of chronic diabetics, diabetic neuropathy tends to be the biggest and least known complication (Herat ,2018). A heterogeneous collection of clinical or subclinical manifestations that, as a complication of diabetes mellitus (DM), affect the peripheral nervous system (PNS), it can have various clinical types, pathways of pathophysiology, beginning and development (Oyenihi, *at el*., 2015).Distal symmetric polyneuropathy is the most common form of diabetic neuropathy. Depending on the classification of sensory fibers involved, symptoms differ. Small fiber intervention is the most frequent early symptom that involves pain (e.g. acute, shooting) that synesthesia (e.g. burning). In the case of a regular clinical examination and regular nerve conduction experiments, which are a measure of broad fiber efficiency, discomfort can be present (Thrainsdottir *at el.*,2003) .Big fiber involvement can result in numbness , tingling and loss of protective sensation. Unlike DR, both vascular and non-vascular metabolism appear to be related to PN pathogenesis, but this theory is uncertain (Cameron *at el.*,2001).

Neuropathy studies, such as electrophysiology and predictive research, are progressively shown to predict not only endpoints, such as foot ulceration, but also mortality (Feldman at el.,2017).The exact knowledge of DPN pathophysiology remains uncertain (Gross *at el.*,2005). Pathological neuronal changes: oxidative stress, polyol pathway activation, early end product glycation development, and protein kinase C activation are only several of the molecular pathways linked to functional nerve dysfunction (Gross *at el.*,2005),(Shillo,2019). In all cases, the precise causal associations among hyperglycemia and clinical DPN are unknown. Our current hypothesis is that both hyperglycemia and risk factors for artery disease create barrier pathways in the long run, resulting in disruption to the microvessel endothelium, nerve back cells, and nerve axons (Shillo,2019). Recent advancements propose that through the generation of reactive oxygen species and mitochondrial dysfunction, the combined impact of these injurious events might result in neuronal death. In comparison, there is no discrimination between painless and painless DPNN in mechanical and pathological studies (Lee *at el.*,2019).

1.2.3 Nephropathy:

Nephropathy is a chronic complication characterized by increased urinary albumin excretion (Proteinuria) or reduced kidney glomerular filtration rate (GFR) in both forms of diabetic mellitus, T1DM and T2DM (Alicic *at el*.,2017).Proteinuria was seen in about 30% of type 1 diabetes (T1D) patients and 40% of type 2 diabetes patients (T2D). It's also the major source of end-stage renal disease (ESKD) development in the world, accounting for about 40% of new renal replacement therapies (Ritz *at e*l.,2011), (Viberti *at el.*,1982).This includes the creation of basement membrane thickening and the growth of micro-aneurysms. In addition, the development of the extracellular matrix and the progression of tubular and glomerular sclerosis are consistent with glomerular hyperfiltration (American Diabetes Association,1998).

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An notable source of oxidative drive is enhanced glucose flux by means of the polyol pathway. In addition , chronic hyperglycemia invigorates vascular porousness, vasoconstriction, amalgamation and turnover of the extracellular network (ECM), cell improvement, angiogenesis, cytokine enactment, and leukocyte attachment pathway (Noh & King,2007). Recently, more and more evidence indicates that inflammation is involved in the development of DN (Mezil *at el.*,2018). A major obsessive discovery of DN in expansion of that could be glomerulosclerosis. Diabetic glomerulosclerosis is distinguished by the set of mesangial developing extracellular network proteins and tubulointerstitial fibrosis (Mauer *at el*.,1984).Glucose transporter 1 intracellular hyperglycaemia stimulates the release of cytokines or developmental elements linked to glomerulosclerosis enhancement(Ibrahim & Hostetter,2007).

1.3 The Macrovascular Complication of Diabetes

Diabetic mellitus is a complicated and persistent condition that includes lifelong medical treatment, consisting of coronary artery disease, cerebrovascular disease and peripheral artery disease, with a high risk of disease on patients with multiple macrovascular complications associated with it. Among diabetic cases, The frequency of acute myocardial infarction is 2.13 times greater in males and 2.95 times higher in females than in non-diabetic groups(Vergès,2015), (Salman *at el.*,2019)The primary contributing factor in the occurrence of diabetic vascular complications has been identified as chronic hyperglycemia (Zelniker, *at el.*,2019).The cause of endothelial dysfunction is hyperglycemia, which is the main activating factor in diabetic vascular pathogenesis(Shi & Vanhoutte,2017).

1.3.1 Peripheral Artery Disease

One of the most dangerous diabetes complications is peripheral artery disease its characterized as arterial obstructive excessive disease that lowers arterial blood fluid during rest and advanced exercise , by multiple studies success attained Peripheral artery disease has been found to be a very dangerous complication of diabetes naturally, but most frequently asymptomatically (PD *at el.*,2018). The German Ankle Brachial Index Epidemiological Analysis (GETABI) showed that diabetic patients aged sixty five years or older had a 2-fold greater occurrence of peripheral artery disease (ABI less than 0.9) and a 2.5-fold increased risk of sporadic claudication (Lange *at el.*,2004).

Hyperglycemia has been identified as an independent risk factor for peripheral artery disease., specifically hemoglobin glycation. In diabetic patients , detecting peripheral artery disease will present difficulties. Diabetes mellitus is synonymous with medial calcinosis, which, due to the incomprehensibility of the leg arteries, will unnecessarily raise the ankle-brachial index despite significant occlusive artery disease and reduction of the real ankle perfusion pressure (Dolan *at el*.,2002).

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Peripheral artery disease signs are difficult especially in DM patients who may have concomitant peripheral neuropathy, since before its advanced stage it is often undiagnosed. As a result, The promotion of arterial inflammation and endothelial cell damage in diabetic patients and causes vessel wall degeneration. Smooth muscle cells and platelets are examples of blood cell abnormalities and hemostasis causes. Until DM is diagnosed, these vascular deficiencies that cause atherosclerosis in patients with DM are always present, and their incidence rises as blood glucose control and DM cycle worsen. In DM patients, causes of PAD include vascular wall derangements by fostering artery inflammation and endothelial cell dysfunction; defects of blood cells, including smooth muscle cells and platelets; and hemostasis factors. In patients with DM, these artery abnormalities causing atherosclerosis are often present before DM is diagnosed, and their frequency increases as blood glucose increases. regulation and DM period deteriorate. Sub-optimal therapy that can prevent disease development is often resorted to (McCarthy *at el*.,2019).

In DM patients, causes of PAD include vessel wall derangements in DM patients by fostering artery inflammation and endothelial cell dysfunction; blood cell abnormalities, including smooth muscle cells and platelets; and influences of haemostasis. These vascular defects which cause atherosclerosis in patients with DM are often present before DM is diagnosed, and their prevalence increases as blood glucose regulation and DM period deteriorate. Causes of PAD include vascular wall derangements by fostering inflammation of the artery and dysfunction of endothelial cells; abnormalities of blood cells, including smooth muscle cells and platelets; and causes of haemostasis. These vascular defects which cause atherosclerosis in patients with DM are often present before DM is diagnosed, and their prevalence increases as blood glucose regulation and DM period deteriorate (Cade,2008).

1.3.2 Coronary Artery Disease:

Coronary heart disease is the main cause of morbidity and mortality around the world (Thiruvoipati *at el.*,2015).. It is a big reason of death in Western nations and is becoming a significant reason of death in developed countries. This increase may be attributed to the rising prevalence of one of the most significant risk factors of this type, multiple risk factors for coronary heart disease such as diabetes. In the Middle East and globally, the prevalence of diabetes is increasingly increasing and has attained pandemic proportions (Rubler *at el.*,1972).Diabetes is associated with an increased risk of coronary heart disease. In patients with no previous history of myocardial infarction, the seven-year risk of myocardial infraction is 20.2 percent and 3.5 percent, respectively, for diabetics and non-diabetics. Likewise, the 7-year MI risk for diabetics and non-diabetics is 45.0 percent and 18.8 percent, respectively, for patients with a history of MI (Haffner *at el*.,1998). .ASCVDD is jointly encouraged by diabetes-related hormonal and physiological disorders, including oxidative stress, insulin resistance, reactive oxygen production, advanced glycation end products and increased inflammatory cytokine development(Rhee & Kim,2018).

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In most cases, atherosclerotic plaques in diabetes mellitus are distinguished by large volumes and lipid cores, which induce elevated remodeling rates in the pretentious vascular section, and thin fibrous caps with extreme inflammatory processes, which render them more susceptible to break up and may cause an acute coronary event. Diabetics are more likely to experience greater, more frequent, and more severe coronary artery injury, which is linked to a worse prognosis. In diabetic patients with no CAD results, necropsy tests revealed that in the late stages, 50 percent and 75 percent of patients under and over the age of 65, respectively, had CAD (Eddy *at el*.,2009).

Among diabetes cases, coronary heart disease is once again the most common cause of death. Any risk factors linked to elevated atherosclerosis are prevalent in diabetes, such as hypertension , dyslipidemia, smoking, and obesity. Metabolic and hematological risk factors that lead to atherosclerosis include microalbuminuria, macroalbuminuria, serum creatinine elevation, platelet impairment, elevated inflammation, oxidative stress, endothelial dysfunction, and hypercoagulation. Insulin resistance, which is linked to high levels of the plasminogen inhibitor activator (PAI) and fibrinogen inhibitor (FI), promotes atherothrombosis (Goraya *at el.*,2002).

1.3.3 Cerebrovascular disease:

Macrovascular and microvascular conditions cause complex cerebrovascular conditions in patients with DM. Brain artery disorders can be categorized as ischemic cerebrovascular disease and hemorrhagic cerebrovascular disease, depending on pathogenesis and anatomy, in DM cases (Adams *at el.*,1993). CVBDs are complex and distinct types of neurological disorders affecting the brain's blood vessels, including ischemic strokes, intracerebral hemorrhagic strokes, aneurysms, arteriovenous malformations, cardiac arrests, and neurological diseases, i.e. functional artery dysfunction and artery dementia, occluded and stenotic carotid arteries(Greger&Stone,2016). Multiple risk factors, including diabetes mellitus are associated with CVBDs (Goldstein,2019).

Prolonged untreated DM results in micrangium, hypoxic and ischaemic damage to the skin, which increases the likelihood of apoplexy and exacerbates cortical lesions induced by inadequate blood. In diabetic patients, its incidence is 2-6 times greater than in patients with non-DM, and its complications and resulting prevalence are much greater. Demonstrate patients with elevated atherosclerosis and intensified vascular response to vascular constrictors in the cerebral arteries, a deregulated response to vascular dilators, and decreased function of the artificial blood supply of the brain. Improved small artery endothelial function and compromised resistance vessel vascular motor function may suggest improvements in local blood stream arbitration and inadequate tissue perfusion in patients with diabetes (Portik-Dobos *at el.*,2002).

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1.4 Another Type of Diabetic Complication

1.4.1 Diabetic cardiomyopathy:

Diabetic cardiomyopathy is referred to as a pathological heart type and presentation in the absence of other cardiac risk factors, such as coronary artery disease, hypertension and severe valve dysfunction (Jia, *at el.*,2018).Diabetic cardiomyopathy is categorized as weakened heart structure and presentation, such as coronary artery disease, hypertension and severe volvuli disease, in the absence of other cardiac risk factors (Rubler *at el.*,1972).Clinical trials show the commonness of cardiac insufficiency in diabetic patients ranging from 19 to 26 %. The Framingham Heart Study showed that the risk of heart failure was elevated relative to age ranges of both male and female diabetes patients, and this association was liberated of obesity (Lee & Kim, 2017).DCM's pathophysiologic processes have still not been fully elucidated. The incidence of DCM is multifactorial and numerous causes are indicated, including insulin resistance, microvascular failure, subcellular component defects, metabolic disorders, autonomic cardiac dysfunction, renin-angiotensin system changes, and maladaptive immune response (Alavi *at el*.,2014).

1.4.2 Diabetic foot:

Diabetic foot ulcers are lacerations that usually occur on the soles of the feet in patients with diabetes mellitus due to peripheral neuropathy or peripheral arterial disease on all skin layers, necrosis or inflammation ,around 15% to 25% of diabetic patients will grow foot ulcers during their lives, the leading cause of non-traumatic subtraction worldwide (Delgado ,2018). Endothelial cell inflammation and smooth cell imperfections are caused by hyperglycemia in peripheral arteries. Endothelial dysfunction is the most serious condition causing microcirculation, due to developments in endothelial cell differentiation, thickening of the vault membrane, reduced nitric oxide secretion, elevated blood viscosity, improvements in microvascular tone and decreased blood volume (Atlas,2015).

2. Conclusion:

Diabetic mellitus consider from metabolic condition, effected on many system in body that lead to molality or morality ,hyperkalemia is a main factor to many defect in human system that resulted from complications of diabetic in both of small and largest vascular.

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