CHAPTER 1

INTRODUCTION

1.1 Background

A complicated metabolic ailment called diabetes mellitus (DM), commonly referred to as diabetes, is defined by hyperglycemia, a physiologically abnormal state indicated by persistently increased blood glucose levels. The persistent and varied symptoms of hyperglycemia include abnormalities in the metabolism of carbohydrates, fats, and proteins. Hyperglycemia is caused by abnormalities in either insulin production or insulin action, or both. Diabetes has a complicated etiology and progresses in a gradual manner (Banday Aga S; Nissar Saniya, 2020).

The vast majority of diabetic patients fall into one of two broad categories include type 2 diabetes mellitus, which is characterized by the presence of insulin resistance with an insufficient compensatory increase in insulin secretion, or type 1 diabetes mellitus, which is brought on by an absolute or nearly absolute deficiency of insulin. Additionally, gestational diabetes is a term used to describe women who develop diabetes throughout their pregnancy. Last but not least, there are several unusual and different kinds of diabetes that can be brought on by infections, medications, endocrinopathies, pancreatic damage, and genetic flaws. The "Other Specific Types" section of the diabetes chart includes these unconnected types (Solis-Herrera, C., Triplitt, C., Reasner, C., DeFronzo, R.A. and Cersosimo, E., 2018).

Since the early 1980s, diabetes has been a problem in Indonesia and is seen as a serious health issue. With a prevalence incidence of 6.2% and more than 10 million individuals living with the disease, diabetes is one of the leading causes of mortality in Indonesia. In 2013, Indonesia was listed as one of the 10 nations with the highest percentage of people living with diabetes worldwide. If diabetes prevention and management strategies are not put in place, it is anticipated that the same pattern would persist (Ligita et al., 2019).

Chronically high blood sugar levels disturb homeostasis, lead to oxidative stress, harm the neurological and immunological systems, and ultimately exacerbate the onset of diabetes problems. Increased fatty acid metabolism, decreased myofilament Ca+ sensitivity, mitochondrial dysfunction, oxidative stress, apoptosis, and fibrosis in diabetic cardiomyocytes are all factors that contribute to cardiomyopathy. The structural and functional impairment of blood vessels caused by pathologic glucose metabolism also leads to microvessel apoptosis and fibrosis, which causes diabetic nephropathy, glomerular atrophy, renal fibrosis, renal dysfunction, and renal failure. Microaneurysms and bleeding in the retina can also be caused by microvessel apoptosis and paraplasm, which is known as diabetic retinopathy and ultimately leads to visual loss. Peripheral neuropathy and peripheral vascular disease are brought on by poor glucose regulation, as well as anatomical abnormalities and environmental factors and compromised immunity lead to the development of diabetic foot (Sun et al., 2021).

A frequent side effect of diabetes mellitus known as diabetic retinopathy (DR) is a leading cause of visual loss in middle-aged and older adults. DR affects one-third of diabetic patients. The diabetes duration, high blood sugar levels, and hypertension are all significantly linked to diabetic retinopathy. Although retinal neurodegeneration is also involved, it is typically thought of as a microvascular disease. The development of DR is caused by intricately interconnected pathophysiological pathways that are sparked by hyperglycemia. These processes include vascular endothelial growth factor (VEGF), enhanced synthesis of free radicals, advanced glycosylation end products, genetic and epigenetic variables, and free radical production. The key to avoiding the onset and slowing the course of DR in diabetics is maintaining optimal management of blood sugar and blood pressure (Wong et al., 2016).

One of the factors of diabetic retinopathy is the increase in the incidence of diabetes in the community. Therefore, by considering this situation, the authors are interested in conducting research to find out what is the prevalence of diabetic retinopathy in patients visiting Wahidin Hospital

Sudhirhosodo.

The purpose of this research is to understand and provide an overview of the prevalence of diabetic retinopathy among diabetic mellitus patients in Wahidin Hospital Period 2021. In addition, the characteristics of diabetic retinopathy include non-proliferative (NPDR) and proliferative diabetic retinopathy (PDR) are considered the two clinical stages of DR, Thus, the research will enable the researcher to articulate deeper insight in regards to diabetic retinopathy and promote awareness to the medical associate and general public concerning diabetic mellitus and related diseases.

1.2 Problem Formulation

1. What is the prevalence and the characteristics of diabetic retinopathy in diabetes mellitus patients at Wahidin Sudirohusodo hospital in period 2024?

1.3 Research purposes

1.3.1 General purpose

To report the prevalence and the characteristics of diabetic retinopathy in diabetes mellitus patients at Wahidin Sudirohusodo hospital in period 2024

1.3.2 Special purpose

1. To determine the influence of diabetes mellitus on diabetic retinopathy at Wahidin Sudirohusodo hospital in period 2024.
2. To identify factors that increase the chance of developing diabetic retinopathy in Wahidin hospital patients with diabetes mellitus in period 2024.

1.4 Benefits of research

1.4.1 Clinical Benefits

It is expected that the results of the research will be of objective interest to health workers to prevent and reduce the incidence of diabetic retinopathy in particular due to diabetes mellitus.

1.4.2 Academic Benefits

It is expected that the results of the research will be useful for both the community and patients with diabetes mellitus to predict diabetic retinopathy before it occurs, to improve their quality of life.

1.4.3 Personal Benefits

In order for me to have a future perspective on diabetes and diabetic retinopathy and to gain a lot of knowledge that will be beneficial to me in my professional life as a doctor.

CHAPTER 2

LITERATURE REVIEW

2.1 Pathophysiology of type 1 and 2 DM

In type 1 diabetes mellitus (T1DM), pancreas cells stop generating insulin, usually as a result of autoimmune damage. In order to control this, insulin replacement is essential since it causes hyperglycemia and ketosis. While onset can happen at any age, incidence rises in puberty and the early years of adulthood. However, because people with T1DM have long lives, prevalence is higher in adults. Weight loss, polydipsia, and polyuria are symptoms. Diabetic ketoacidosis is one of the acute consequences that needs to be managed immediately. Microvascular and macrovascular disorders are long-term side effects. T1DM patients are more likely to have additional autoimmune disorders and mental problems (Syed, 2022).

Regarding the pathophysiology of the T2DM, unusually high blood glucose levels are caused by a breakdown of the feedback loops between insulin action and insulin production. As a result of decreased insulin production caused by -cell malfunction, the body's ability to maintain physiological glucose levels is constrained. On the other side, IR helps to reduce glucose absorption in adipose tissue, muscle, and the liver while increasing glucose synthesis in the liver. Even while all of these processes occur early in the pathophysiology and help to cause the illness to manifest, -cell dysfunction is often more severe than IR. However, hyperglycemia is exacerbated and T2DM progresses if both IR and -cell dysfunction are present (Galicia-Garcia et al., 2020)

2.2 Risk Factors for type 1 and 2 DM

Compared to prediabetes and type 2 diabetes, type 1 diabetes risk factors are less well understood. Age and family history are known risk factors for type 1 diabetes, which often develops in adolescents, teenagers, or young adults. Family history includes having a parent, brother, or sister who has the disease.

White persons are more likely to get type 1 diabetes than African Americans, Hispanics, and Latinos are in the United States ("Diabetes Risk Factors | CDC," n.d.)

Age, obesity, bad lifestyle choices, and previous gestational diabetes (GDM) are just a few of the many variables that raise the chance of developing T2DM. T2DM is more common in some racial and ethnic groupings than others, particularly in young and middle-aged persons. Type 2 diabetes is more common in some communities than others, including Native Americans, people from Pacific Island countries, people from the Middle East, and people from South Asia. Strong family, probable genetic, or epigenetic susceptibility is also frequently linked to it. Although studies indicate that some common genetic variations of T2DM occur among various ethnic groups and populations, the genetics of T2DM are complicated and poorly understood (King et al., n.d.)

2.3 Pathophysiology of diabetic retinopathy

Diabetes is a condition that damages the retina's small blood vessels, preventing them from receiving blood. The more prevalent non-proliferative diabetic retinopathy and the more serious progressive diabetic retinopathy are the two different forms of diabetic retinopathy. In nonproliferative diabetic retinopathy, the retinal blood vessel walls deteriorate, resulting in tiny bumps protruding from the blood vessel walls. Advanced diabetic retinopathy causes abnormal new blood vessels to form in the retina when injured blood vessels become occluded. They might, however, break easily and spill fluid into the vitreous. The retina may separate from the back of the eye due to scar tissue created by the development of new blood vessels. When new blood vessels obstruct the eye's natural fluid flow, pressure accumulates inside the eyeball and glaucoma develops. To diagnose DR, a fundus examination is typically combined with fundus fluorescein angiography (FFA), optical coherence tomography (OCT), and more recently, optical coherence tomography-angiography (OCTA). The FFA may be used to qualify and quantify areas of capillary non-perfusion, and the OCT can be used to properly identify and quantify macular oedem (Asia, 2020).

2.4 Epidemiology of DR

The World Health Organization (WHO) reported that DM prevalence has increased over the past several decades in many areas of the world. According to the International Diabetes Federation's (IDF) most recent statistics, 8.8% of adults aged 20 to 79 or 425 million individuals worldwide are projected to have diabetes. About 79% of people reside in low- and middle-income nations. If the age range is extended to 18-99 years, there are 451 million persons worldwide who have diabetes. If these trends continue, 693 million individuals between the ages of 18 and 99, or 629 million people between the ages of 20 and 79, would have diabetes by 2045. According to estimates, half of all diabetics aged 20 to 79, or 212.4 million people, are ignorant that they have the illness. 84.5% of diabetes cases worldwide without a diagnosis are found in low- and middle-income nations. The top three nations with the highest prevalence of DM are still China, India, and the United States, with Indonesia coming in sixth place (Wahyu, 2019)

2.5 Risk factors of Diabetic Retinopathy

2.5.1 Duration of Diabetes

A longer history of diabetes has been linked in certain studies to a higher chance of developing diabetes. According to studies, persons with longer histories of diabetes had a twofold higher frequency of DR than those with newly diagnosed diabetes. They showed that for each year that diabetes continues, the risk of retinopathy increases by around 8% due to an increased risk of retinal vascular damage and neovascularization, for instance, a longer duration of diabetes was detected in DR patients (P 0.001). Additionally, a significant connection between DR and diabetes mellitus duration was found (P 0.001) (Rasoulinejad, 2022).

2.5.2 Hypertension

Vascular disorders and hypertension have a well-

established link. A number of mechanisms, including activation of the coagulation, shearing stress on blood flow, damage to retinal capillary endothelial cells, and interactions between hormonal control of blood sugar levels and the renin-angiotensin-aldosterone system, are involved in the development of DR in diabetic patients with hypertension. According to studies, those with hypertension had a 1.7 times higher relative chance of developing DR than people without the condition. According to research, the chance of developing diabetic retinopathy (DR) and serious retinopathy rose by 1.23 and 1.19 times, respectively, for every 10 mmHg increase in systolic blood pressure, however the rate was reduced when diastolic blood pressure was elevated. Another study revealed that after 10 years, individuals with hypertension had a risk of getting DR that was more than twice as high as that of controls. The clinical fact that diabetes and hypertension typically coexists is supported by this data (Rasoulinejad, 2022).

2.5.3 Age and Sex

According to certain research, men (P 0.001) and elderly patients (P = 0.003) experience considerably higher rates of DR. In a large-scale investigation, it was shown that among those older than 40 years, the incidence of DR was greater in men than in women (38 5.5 and 27.1 4.7%, respectively). Additionally, the Los Angeles Latino Eye Study (LALES) study's multivariate model revealed that men notably had a 50% greater chance of developing DR than women (P = 0.006). The UKPDS 50 study's multivariate model also showed that women had a decreased probability of DR development. According to these data, older ages and male sex can be regarded as separate risk factors for DR. Nevertheless, several research failed to discover any connection between sex and DR (Rasoulinejad, 2022).

2.5.4 Hyperglycemia

Hyperglycemia, a microvascular condition, is a feature of diabetes. It is widely believed to be the primary factor in both types 1 and 2 diabetes that leads to diabetic complications such retinopathy, nephropathy, and neuropathy. The production and buildup of advanced glycation end products (AGE) is one mechanism relating persistent hyperglycemia to diabetic retinopathy. Advanced glycation end products (AGE) are formed in a manner that is related to glycemic control. They cause long-lived proteins to crosslink, increasing vascular stiffness, altering vascular structure and function, and interacting with the AGE receptor to cause intracellular signaling that increases oxidative stress and promotes the production of important pro-inflammatory cytokines. Reactive oxygen species (ROS) generation, binding to certain cell surface receptors, the formation of crosslinks, and AGE effects all play a role in the pathophysiology of vascular disease in diabetes (Moemen et al., 2020)

2.5.5 Gestational diabetes

Gestational diabetes can eventually lead to the serious development of diabetic retinopathy (DR) during pregnancy or the worsening of an already existing DR. Gestational diabetes increases the likelihood of developing diabetes in the future for both the mother and the fetus, further aggravating both situations. Understanding the prevalence, evaluating risk factors causing pathogenesis, and identifying challenges in treating DR in pregnant women have all been fascinating. A risk factor for DR development is pregnancy itself. Pregnancy-related physiological changes in the form of metabolic, vascular, immunologic, and hormonal alterations might aggravate DR as well as contribute to its development. If nothing is done about it

right away, this might potentially cause irreversible vision loss (Chandrasekaran et al., 2021).

2.6 Latest Advances in Pancreatic Repair in Diabetes Mellitus

Recent advancements in pancreatic repair for diabetes have focused on stem cell-derived therapies and beta cell regeneration. A major breakthrough is the use of personalized endoderm stem cell (EnSC)-derived islet tissues for intrahepatic implantation, showing promise in restoring insulin secretion for type 2 diabetes patients, with reduced risks compared to cadaveric islet transplantation. Studies report improved glycemic control and less insulin dependency. Research also targets beta cell regeneration by enhancing replication and neogenesis through pathways like PI3K/Akt/mTOR and JAK2/STAT5, and hormones such as GLP-1, prolactin, and GABA. Pharmacological interventions like GLP-1 agonists further support beta cell regeneration, offering hope for diabetes treatment and reversal (Wu et al., 2024)