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Type 2 Diabetes Mellitus: A Review of Determinants, Pathophysiology, Diagnostics, Management, and Complications

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ABSTRACT

The prevalence and incidence of diabetes mellitus are both on the rise, making it a continuing problem on a global scale. There are multiple factors that contribute to the development of type 2 diabetes mellitus. The disease is characterized by the presence of both a genetic component and an equally significant environmental component. A process of chronic hyperglycemia is the first step in the development of diabetes mellitus. This hyperglycemia is caused by the inability of pancreatic beta cells to secrete insulin, as well as insulin resistance in the muscles and the liver. Diabetes Mellitus Type 2 that is not treated with either medication will result in a variety of problems, including chronic consequences such as microangiopathy, retinopathy, nephropathy, and macroangiopathy. These complications can be caused by a number of different factors. The determinants, pathophysiology, diagnosis, management, and complications of type 2 diabetes mellitus are all topics that are covered in this study.

Keywords: *Type 2 diabetes mellitus, Determinants, Management*

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INTRODUCTION

Type 2 Diabetes Mellitus is a metabolic disorder caused by insulin resistance or progressive insulin secretion impairment, leading to high blood sugar levels (Kemenkes RI, 2020). Various epidemiological studies show a tendency for an increase in the incidence and prevalence of Type 2 Diabetes Mellitus in different parts of the world. WHO estimates a significant increase in Type 2 Diabetes Mellitus patients in Indonesia in the coming years. As reported by the IDF Diabetes Atlas, the global prevalence of diabetes in the age group 20-79 years in 2021 will reach 10.5% (536.6 million people) and will increase to 12.2% (783.2 million) by 2045 (Sun et al., 2022). Type 2 Diabetes Mellitus is the most common type among all Diabetes Mellitus patients in Indonesia in 2023, accounting for 50.2% of the total weighted sample (n) of 14,935 people. The elderly aged 65-74 are the most affected, at 52.5%, followed by those aged 55-64 at 51.8%, and those aged 75 years and above at 50.8% (Kemenkes RI BKPK, 2023).

Diabetes Mellitus is commonly referred to as a silent killer because this disease can attack all organs of the body and cause various complaints. The diseases that will be caused include eye vision disturbances, cataracts, heart disease, kidney disease, impotence, wounds that are difficult to heal up to gangrene, lung infections, vascular disorders, stroke, and so on (Saputri, 2020). Seeing that Diabetes Mellitus will impact human quality of life and significantly increase healthcare costs, a Type 2 Diabetes Mellitus control program is very much needed.

DETERMINANT FACTORS

1. Gender

   The prevalence of Type 2 Diabetes Mellitus in women is higher than in men (Kemenkes RI BKPK, 2023). Women suffer more from diabetes because, physically, women have a higher chance of increased body mass index. Premenstrual syndrome and postmenopause, which cause body fat distribution to easily accumulate due to hormonal processes, lead women to suffer from type 2 diabetes mellitus (Widiasari, Kusuma Wijaya, & Suputra, 2021).

2. Age

   Age < 45 years is a group with a lower risk of suffering from Type 2 Diabetes Mellitus. The risk in that group is 72 per cent lower than those aged 45 years (Delfina, Carolita Maharani, Habsah, & Ayatillahi, 2021). There is a significant relationship between age and the incidence of diabetes mellitus. The age group that suffers the most from diabetes mellitus is the 45-52-year age group (47.5%). The increased risk of diabetes with age, especially after the age of 40, is caused by the onset of increased glucose intolerance at that age. The ageing process leads to a decrease in the ability of the inner pancreatic β cells to produce insulin (Nora, Gultom, Harahap, Edi, & Sipahutar, 2025). As age increases, mitochondrial activity in muscle cells decreases by up to 35%. This is associated with a 30% increase in muscle fat content, triggering insulin resistance.

3. Body mass index

   Individuals who are obese have a 2.7 times greater risk of developing diabetes mellitus. This is caused by a lack of physical activity and high consumption of carbohydrates, proteins, and fats, which are risk factors for obesity. This causes an increase in free fatty acids (FFA) within the cells. This increase in FFA will reduce the translocation of glucose transporters to the plasma membrane, leading to insulin resistance in muscle and adipose tissue (N. N. Sari, 2019). Individuals with a BMI ≥ 23 kg/m2 have a risk of developing type 2 diabetes mellitus (Widiasari et al., 2021).

4. History of hypertension

   There is a significant relationship between blood pressure and diabetes mellitus. The research results show that people with hypertension have a greater risk of suffering from diabetes, with a 6.85 times higher chance compared to those without hypertension. Some literature links hypertension with insulin resistance. The influence of hypertension on the incidence of diabetes mellitus is caused by the thickening of arterial blood vessels, narrowing the blood vessel diameter. This disrupts the glucose transport process from the blood (Dharma Hita & Pranata, 2021).

5. Cholesterol levels

High cholesterol levels pose a risk of type 2 diabetes mellitus. They lead to an increase in free fatty acids, which result in apoptosis. This will damage pancreatic beta cells, leading to type 2 diabetes mellitus. Patients with type 2 diabetes mellitus show low HDL levels (37.3%) compared to high HDL levels (25.6%). High triglyceride levels (57.1%) significantly increase the risk of developing type 2 diabetes mellitus (Delfina, Carolita, et al., 2021).

6. Physical activity

An active body is beneficial for controlling blood sugar. This is important because when the body engages in activity, the sugar will be burned and converted into energy, thereby reducing the amount of insulin. When someone does not engage in enough physical activity, the nutrients that enter the body will accumulate and be stored as fat, increasing the risk of type 2 diabetes mellitus. There is a relationship between physical activity and the incidence of type 2 Diabetes Mellitus (N. Sari & Purnama, 2019).

PATHOPHYSIOLOGY

Type 2 diabetes mellitus is characterized by metabolic disorders, namely impaired beta cell function and insulin resistance in peripheral tissues such as muscle and fat tissues, as well as insulin resistance in the liver. Insulin resistance is considered one of the underlying mechanisms of type 2 diabetes (Decroli, 2019).

Insulin cannot work optimally on muscle, fat, and liver cells, forcing the pancreas to produce more insulin to compensate. If insulin production by the pancreatic beta cells is insufficient to compensate for the increased insulin resistance, blood glucose levels rise, and chronic hyperglycemia develops over time. Chronic hyperglycemia in type 2 diabetes mellitus, on the one hand, further damages beta cells and, on the other hand, worsens insulin resistance (Decroli, 2019).

Pancreatic beta cells cannot produce enough insulin to compensate for increased insulin resistance because the normal function of beta cells is reduced by up to 50%. In type 2 diabetes mellitus, pancreatic beta cells are replaced by amyloid tissue, which leads to decreased insulin production. As people age, the number of beta cells decreases because the process of apoptosis exceeds reproduction and regeneration. This explains why older people are more susceptible to type 2 diabetes mellitus. In type 2 diabetes mellitus, pancreatic beta cells are exposed to hyperglycemia, which produces reactive oxygen species (ROS). Excessive ROS increases and damages the beta cells in the pancreas. Chronic hyperglycemia is a condition that, in turn, can reduce insulin synthesis and secretion and gradually destroy beta cells (Decroli, 2019).

DIAGNOSTICS

The diagnosis of diabetes mellitus is established based on blood glucose level examination. Diabetes mellitus is suspected if there are classic complaints of diabetes mellitus (polydipsia, polyuria, polyphagia, and unexplained weight loss) or other complaints (weakness, tingling, itching, blurred vision, erectile dysfunction in men, and vulvar pruritus in women). The diagnosis of diabetes mellitus or prediabetes can be established if one of the criteria for HbA1c, fasting blood glucose, or plasma glucose is met 2 hours after an oral glucose tolerance test. The random blood glucose (RBG) test result = 200 mg/dL can also confirm the diagnosis of diabetes mellitus if it is accompanied by classic symptoms (Kemenkes RI, 2020).

Table 1: Blood glucose levels for the diagnosis of diabetes and prediabetes

	HbA1c (%)	Fasting blood glucose (mg/dl)	Tolerance test oral glucose (mg/dl)
Diabetes	≥ 6.5	≥ 126	≥ 200
Prediabetes	5.7 – 6.4	100 – 125	140 – 199
Normal	< 5.7	< 100	< 140

(Kemenkes RI, 2020).

MANAGEMENT

The management of diabetes mellitus generally aims to improve patients' quality of life. To achieve this, control of blood glucose, blood pressure, body weight, and lipid profile is required through comprehensive management. The general management of diabetes mellitus includes medical evaluation, which encompasses medical history, physical examination, laboratory tests (FPG, OGTT, and HbA1c), and complication screening. Complication screening is conducted through fasting lipid profile tests (high-density lipoprotein [HDL], low-density lipoprotein [LDL], and triglycerides), liver function tests, kidney function tests (serum creatinine and estimated GFR), routine urine tests, quantitative urine albumin, current albumin-creatinine ratio, electrocardiogram (ECG), chest X-ray if indicated (tuberculosis, heart failure), and comprehensive foot examination (Kemenkes RI, 2020).

Specific management of diabetes mellitus consists of four pillars, namely education, medical nutrition therapy (MNT), physical exercise, and pharmacological treatment (PERKENI, 2021), which are:

1. Education

   Education is conducted to promote healthy living behaviours, which is part of prevention efforts and an essential aspect of holistic diabetes mellitus management. One of the educational materials that will be delivered is about foot care.
2. Medical Nutrition Therapy

   The principle of meal management is a balanced composition of calories and nutrients according to individual needs. Diabetes mellitus patients need to understand the importance of meal schedules, types, and amounts of calories, especially for those using medications to increase insulin secretion or insulin therapy. The recommended food composition consists of carbohydrates (45-65% of total calorie intake), fats (20-25% of total calorie intake), proteins (10-20% of total calorie intake), and other micronutrients (sodium [< 2300 mg per day] and fibre [20-35 grams per day]). Patients' calorie needs are determined by considering the basal calorie needs, ideally 25-30 kcal/kg of body weight. This amount can be increased or decreased depending on several factors, such as gender, age, activity level, body weight, and others.

3. Physical Exercise

   Physical exercise is performed 3-5 times weekly for 30-45 minutes, totaling 150 minutes weekly. Blood glucose testing is recommended before physical exercise, where if the level is < 100 mg/dL, the patient should consume carbohydrates first, while if the level is > 250 mg/dL, it is advised to postpone physical exercise. The recommended physical exercise is moderate-intensity aerobic exercise (50-70% of maximum heart rate), such as brisk walking, leisurely cycling, jogging, and swimming.

4. Pharmacological Therapy

   Pharmacological therapy, consisting of oral antihyperglycemic medications and insulin, is administered alongside meals and physical exercise. This therapy is conducted using the AACE 2019 glucose control algorithm for oral therapy and insulin therapy or a complication-based algorithm for obese patients.

COMPLICATION

As has been stated, hyperglycemia is a central complication in diabetes mellitus. In certain conditions, hyperglycemia will enhance the polyol pathway, increase the formation of non-enzymatic protein glycation, and elevate the glycosylation process itself, leading to increased oxidative stress and ultimately causing complications such as vasculopathy, retinopathy, neuropathy, or diabetic nephropathy (PERKENI, 2021).

Decroli (2019) explains the complications of type 2 Diabetes Mellitus as follows:

1. Microvascular Complications

   It occurs due to the blockage of small blood vessels, especially capillaries. This complication is specific to diabetes mellitus. Suspicion of diagnosing diabetes mellitus sometimes arises, and the symptoms include decreased visual acuity or the possibility of other eye disorders that can lead to blindness. Diabetic retinopathy is divided into two groups: non-proliferative retinopathy and proliferative retinopathy. Non-proliferative retinopathy is the early stage characterized by microaneurysms, while the growth of capillary blood vessels, connective tissue, and retinal hypoxia characterizes proliferative retinopathy.

   In the early stages, retinopathy can be improved with reasonable blood sugar control. In contrast, disorders that have already been suffered are almost impossible to repair with just blood sugar control and may even worsen if blood sugar levels are reduced too drastically.

Type 2 diabetes mellitus is also the cause of most nephropathy, as it leads to end-stage renal failure. Specific kidney damage in diabetes mellitus causes changes in filtration function, allowing large molecules such as proteins to enter the urine. As a result, diabetic nephropathy can lead to progressive kidney failure. Diabetic nephropathy is characterized by persistent proteinuria (> 0.5 g/24 hours), the presence of retinopathy, and hypertension.

2. Macrovascular Complications

   As a result of atherosclerosis in large blood vessels, especially arteries, there is an accumulation of atheromatous plaques. Various epidemiological studies show that the mortality rate due to cardiovascular diseases and diabetes increases 4-5 times compared to normal individuals. Macroangiopathy complications are generally not related to reasonable blood sugar control. However, epidemiologically, it has been proven that hyperinsulinemia is a risk factor for cardiovascular death, where high insulin levels lead to a higher cardiovascular risk. Fasting insulin levels > 15 mU/mL will increase the risk of coronary death by five times. Hyperinsulinemia is now recognized as an atherogenic factor and is considered to play an essential role in the emergence of macrovascular complications.

   The initial process of vascular abnormalities is atherosclerosis, which can occur in all blood vessels. If it appears in the coronary blood vessels, it will increase the risk of myocardial infarction and, eventually, heart failure. Death can occur 2-5 times more frequently in diabetes patients compared to normal individuals. This risk will increase if there are conditions such as dyslipidemia, obesity, hypertension, or smoking. In diabetes patients, peripheral vascular disease is usually diagnosed late. Neuropathy, macroangiopathy, and microangiopathy factors accompanied by infection are the main factors in the process of diabetic gangrene development.

3. Neuropathy

   Generally in the form of diabetic polyneuropathy, its clinical manifestations can include sensory, motor, and autonomic disturbances. The neuropathy process is usually progressive, where there is degeneration of nerve fibres with symptoms of pain or even numbness. What is generally affected are the nerve fibres of the feet or arms. Neuropathy is caused by damage and dysfunction to the nerve structure due to the increased polyol pathway, decreased formation of myo-inositol, and decreased Na/K ATPase, resulting in damage to the nerve structure, segmental demyelination, or axonal atrophy.

CONCLUSION

Type 2 diabetes is a chronic condition that requires careful management to prevent complications. Diagnosis involves measuring fasting blood glucose levels, oral glucose tolerance tests, and monitoring haemoglobin A1c. Management involves lifestyle modifications, medication, and lifestyle changes. Complications can range from microvascular to macrovascular and neuropathy issues. Routine monitoring, adherence to medication, and maintaining a healthy weight can improve outcomes and quality of life.

Type 2 Diabetes Mellitus requires proper and routine management to prevent complications. An accurate diagnosis using blood glucose and haemoglobin A1c measurements is crucial for treatment. Lifestyle changes, including a healthy diet and regular activity, can improve the quality of life for patients. Consistency and routine in medication, limiting the consumption of fats and sugars, emphasizing protein and meat, and maintaining stable cholesterol levels are essential. Collaboration with patients, doctors, and nutritionists is necessary. Research on diabetes management involves exploring the effects of medications on blood sugar regulation, the role of genetics in type 2 diabetes, and the impact of exercise routines on insulin sensitivity, which is essential to conduct.

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