Exploring the Correlation of Body Mass Index (BMI), Hemoglobin A1c (HbA1c), and Diabetes Mellitus: A Literature Review

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Abstract

Obesity, a predominant cause of T2DM, is analyzed through the lens of BMI, with higher values indicative of increased free fat accumulation. The Asia-Pacific Guidelines' BMI range for obesity is defined as ≥25 kg/m². Notably, a substantial percentage of diabetes patients are found to be overweight, and over half of those classified as obese exhibit impaired glucose tolerance. This comprehensive literature review delves into the intricate relationships among Body Mass Index (BMI), Hemoglobin A1c (HbA1c), and Type 2 Diabetes Mellitus (T2DM). Investigating the metabolic intricacies within individuals with T2DM, the review underscores the process of protein glycosylation resulting from prolonged high blood sugar levels and their interaction with protein N groups. Monitoring T2DM patients, particularly through HbA1c levels, emerges as a critical aspect of glycemic control. Drawing from research, this review emphasizes a correlation between elevated BMI and increased HbA1c levels in obese individuals. Furthermore, it discusses findings revealing a significant portion of T2DM patients with poorly controlled and elevated HbA1c levels. The accumulation of excess fat in the bodies of obese individuals is highlighted as a pivotal factor leading to the development of T2DM, marked by heightened blood sugar levels. The literature review synthesizes these insights, providing a comprehensive understanding of the metabolic dynamics involving BMI, HbA1c, and T2DM. This nuanced exploration contributes to the broader comprehension of metabolic disorders and offers valuable insights for future research and clinical practice.

Keywords: Diabetes mellitus, HBA1c, body mass index.

1. Introduction

The global surge in metabolic disorders, notably Type 2 Diabetes Mellitus (T2DM), has prompted extensive exploration into the complex interactions between various physiological parameters. Among these, Body Mass Index (BMI) and Hemoglobin A1c (HbA1c) have emerged as pivotal indicators, offering insights into the metabolic intricacies underlying T2DM (Fatimah, 2016). This comprehensive literature review aims to unravel the interconnected relationships among BMI, HbA1c, and T2DM, providing a nuanced understanding of their roles in the intricate landscape of metabolic health. Type 2 Diabetes Mellitus, characterized by insulin resistance and impaired glucose metabolism, has reached epidemic proportions globally. With the prevalence

of T2DM escalating, particularly in the context of lifestyle changes and a surge in obesity rates, there is an urgent need to dissect the contributing factors influencing its onset and progression (Saputra et al., 2020).

BMI, a metric widely employed for assessing the nutritional status of individuals, serves as a fundamental parameter in this investigation. The Asia-Pacific Guidelines designate specific BMI ranges, and research consistently highlights the association between obesity, reflected by an elevated BMI, and the increased risk of developing T2DM. As a critical component of metabolic health, BMI provides a tangible measure of adiposity, allowing for the classification of individuals into distinct weight categories. Concurrently, HbA1c, a glycosylated form of hemoglobin, stands out as a robust marker for long-term glycemic control (Marbun, 2018). Serving as a crucial diagnostic tool, HbA1c reflects the average blood glucose levels over the preceding three months, offering a comprehensive snapshot of glycemic management. Its reliability in capturing sustained glucose exposure positions HbA1c as an essential parameter in assessing and monitoring T2DM (Makful, 2018).

This literature review navigates through existing research, synthesizing evidence to illuminate the intricate relationship between BMI, HbA1c, and T2DM. By delving into the underlying mechanisms of these interactions, we aim to contribute to a more profound comprehension of the metabolic dynamics that shape the landscape of T2DM. The global burden of T2DM underscores the urgency of unraveling the complexities surrounding its etiology and progression. As the prevalence of obesity continues to rise, understanding the role of BMI in the context of T2DM becomes paramount. Simultaneously, recognizing the significance of HbA1c as a key biomarker enables clinicians and researchers to gauge long-term glycemic control and tailor interventions accordingly.

In the subsequent sections, this review will systematically explore the epidemiology of T2DM, elucidating the prevalence and trends globally. It will delve into the classifications and etiological factors contributing to T2DM, shedding light on the diverse pathways leading to its manifestation. Furthermore, the discussion will extend to encompass the metabolic implications of T2DM, emphasizing the critical roles played by BMI and HbA1c in this multifaceted landscape. Through a meticulous analysis of existing literature, we aim to distill valuable insights that inform both research trajectories and clinical practices in the realm of metabolic health and Type 2 Diabetes Mellitus.

2. Review Content

2.1 Definition and Classification of Diabetes Mellitus

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from abnormalities in insulin secretion, insulin action, or both (Perkeni, 2021). Hyperglycemia can lead to symptoms such as polyphagia (increased hunger), polydipsia (increased thirst), and polyuria (frequent urination) (Shouip, 2020). Diabetes Mellitus can be classified into several types, including Type 1 (DMT1), Type 2 (DMT2), Gestational Diabetes, and Other Types of Diabetes (Kardika, 2017). Type 1 Diabetes (DMT1) is an autoimmune disease characterized by increased blood glucose levels due to the body's failure to produce insulin (Katsarou, 2017). Type 2 Diabetes (DMT2) is a condition where the body cannot maximize insulin use in peripheral tissues (insulin resistance) and experiences beta cell dysfunction, often leading to overweight conditions (Kardika, 2017). Gestational Diabetes occurs during pregnancy in women without a history of diabetes (Kardika, 2017). Other types of Diabetes are caused by other diseases or severe infections (Tandra, 2017).

Epidemiology of Diabetes Mellitus

According to WHO data, in 2014, 8.5% of the adult population aged 18 and older had diabetes. In 2019, diabetes directly caused 1.5 million deaths, with 48% occurring in individuals under 70 years. Between 2000-2016, there was a 5% increase in premature deaths (before 70 years) due to diabetes. The impact varied between high-income and low- to middle-income countries, with a decrease in high-income countries from 2000-2010 but an increase from 2010-2016. In low- to middle-income countries, there was an increase in both periods (WHO data). In 2012, WHO estimated that diabetes contributed to 6% of all causes of death in Indonesia. By 2020, more than 6% of approximately 172 million adults in Indonesia were reported to have diabetes (IDF). According to Basic Health Research (Riskesdas) Indonesia for 2013 and 2018, diabetes prevalence in the population aged 15 and above increased, with the highest cases in the age group above 45 (Tanoey & Becher, 2021). Of the various types, IDF reported that in 2015, 415 million people had diabetes, with 98% having DMT2 (Nuraisyah, 2018). DMT2 affected nearly 90% of the total diabetic population (Decroli, 2019).

Etiology of Diabetes Mellitus

Type 1 Diabetes (DMT1) results from pancreatic beta cell damage due to infectious agents or environmental factors like toxins, viruses (mumps, coxsackievirus, cytomegalovirus, rubella), and certain foods (sugar, coffee, soy, wheat, and cow's milk) (Homenta, 2012). DMT1 has a genetic component but is not strictly hereditary. Individuals with DMT1 have genetic mutations due to antibodies targeting the enzyme Glutamic Acid Decarboxylase (GAD) in the pancreas (Kousar, 2019). Type 2 Diabetes (DMT2) involves the body's failure to use insulin, leading to weight gain and reduced physical activity (Kardika, 2017). DMT2 is a heterogeneous condition caused by a combination of genetic factors related to insulin secretion disorders, insulin resistance, and environmental factors. Individuals with DMT2 can still produce insulin, but often at higher-than-normal levels, resulting in relative insulin deficiency. DMT2 is commonly associated with individuals aged over 30 with poor activity patterns, leading to 80-90% of cases being obese (Chairunnisa, 2020). Gestational Diabetes (DMG) is defined as glucose intolerance that occurs during pregnancy. Most DMG cases happen in women with no prior history of diabetes, experiencing elevated blood glucose levels during pregnancy. DMG can lead to complications during childbirth, such as macrosomic babies, stillbirths, and neonatal metabolic disorders. Offspring of mothers with DMG are more susceptible to an increased risk of diabetes and obesity. Other types of diabetes can result from other diseases or serious infections occurring first, such as pancreatic exocrine disease, endocrinopathy, genetic damage to beta cell function, genetic damage to insulin function, and other genetic syndromes related to diabetes (Kurniawaty, 2015).

2.2 Pathophysiology of Diabetes Mellitus

Type 1 Diabetes (DMT1)

Autoimmune damage to pancreatic cells leads to insulin secretion deficiency, causing metabolic disturbances associated with Insulin-Dependent Diabetes Mellitus (IDDM). In addition to insulin deficiency, beta cell function becomes abnormal, and there is excessive glucagon secretion in DMT1 patients (Ozougwu, 2013). DMT1 is characterized by autoimmune CD4+ and T CD8+ cells, along with macrophages infiltrating islet cells, and specific islet antibodies. Factors classifying DMT1 as an autoimmune disease include immune cell infiltration into pancreatic islets, specific islet antibodies, involvement of monokines and TH1 cells in interleukin production, and disease response to immunotherapy. Besides insulin deficiency, abnormal alpha cell function leads to excessive glucagon secretion, unlike normal conditions where hyperglycemia reduces glucagon secretion (Negm, 2004).

Type 2 Diabetes (DMT2)

DMT2 involves two conditions in the body—insulin resistance and dysfunction of pancreatic beta cells. DMT2 occurs when insulin target cells cannot provide normal feedback, resulting in insulin resistance (Fatimah, 2016). In cases dominated by insulin resistance, beta cell mass changes to compensate by increasing

insulin availability. In situations of insulin resistance, the body prevents glucose absorption mediated by insulin in the periphery, incomplete hepatic glucose output, and impaired triglyceride uptake by fat. To counter insulin resistance, the body increases islet cell numbers, leading to elevated insulin levels both in fasting and postprandial states. DMT2 patients experience increased fasting blood glucose disturbances (Baynest, 2015).

2.3 Diagnosis of Diabetes Mellitus

The primary examinations used to confirm the diagnosis of Diabetes Mellitus are blood glucose and HbA1c level tests. Diagnosis cannot be established solely based on glucosuria. Various characteristic complaints and symptoms can be used to support the diagnosis of DM, such as classic signs and symptoms of DM: polyuria, polydipsia, polyphagia, and sudden weight loss and other signs and symptoms: fatigue, weakness, lethargy, blurred vision, erectile dysfunction in men, and vulvar pruritus in women (IDAI, 2017). According to PERKENI, the diagnostic criteria for Diabetes Mellitus are as follows:

a. Fasting plasma glucose test (body in a state of no caloric intake for a minimum of 8 hours): ≥126 mg/dL
b. Plasma glucose test 2 hours after an Oral Glucose Tolerance Test (OGTT) with 75 grams of glucose: ≥200 mg/dL
c. Random plasma glucose test (for patients with classic DM complaints or hyperglycemic crisis): ≥200 mg/dL
d. HbA1c test using a method standardized by the National Glycohaemoglobin Standardization Program (NGSP) and the Diabetes Control and Complications Trial Assal (DCCT): >6.5% (Perkeni, 2021).

2.4 Body Mass Index (BMI)

Body Mass Index (BMI) is a metric measurement currently used to describe anthropometric height/weight characteristics in individuals and classify them into various groups. BMI is also used as an indicator of risk factors for several health issues (Nuttall, 2015).

BMI is a tool used to determine the nutritional status of adolescents and adults by comparing body weight (BW) and height (Ht). Indirectly, BMI can serve as an indicator of an individual's body fat levels (Matin & Veria, 2013). BMI is an easy, cost-effective, and non-invasive measure. It requires only height and weight, allowing individuals to accurately measure and calculate BMI. Additionally, BMI is estimated to predict morbidity, mortality rates, and an individual's health risks (Cdc, 2011).

2.5 Definition of HbA1c

HbA1c results from the chemical reaction between glucose and hemoglobin (part of red blood cells) (Marbun, 2018). Glycated hemoglobin (HbA1c) is the form of hemoglobin used to identify an individual's average blood glucose levels over the past three months and correlates with complications from high blood sugar, also known as Diabetes Mellitus. HbA1c is formed by non-enzymatic glycation of beta hemoglobin A chains by plasma glucose. This glycation is irreversible and occurs continuously throughout the lifespan of red blood cells, approximately 120 days (three months). HbA1c or glycated hemoglobin increases predictably based on the average plasma glucose level (Rawal Gautam et al., 2016). The HbA1c test is used for long-term blood sugar control, diagnosis, prognosis determination, and diabetes patient management. By measuring glycohemoglobin, it is possible to determine the proportion of hemoglobin containing sugar (Marbun, 2018). This test is the Gold Standard for assessing blood sugar balance in the body because HbA1c values are not dependent on daily fluctuations in blood sugar concentrations. The test reflects glycemic metabolic control over 3-4 months and is a valuable indicator for monitoring glycemic control and the effectiveness of diet, exercise, and treatment in diabetes patients (Kemas et al., 2014). The HbA1c test is recommended by various international diabetes control organizations such as the International Diabetes Federation (IDF) and the American Diabetes Association (ADA). They recommend checking HbA1c levels at least twice a year for

patients with controlled blood sugar and every three months for patients with uncontrolled sugar levels or in diabetes therapy (Rawal Gautam et al., 2016).

Advantages and Disadvantages of the HbA1c Test

Here are some advantages and disadvantages of the HbA1c test compared to other tests such as convenient for patients as it does not require special preparation like fasting, can be performed at any time of the day without time constraints, relatively stable after collection, better marker of chronic glycemic exposure, and lower variability compared to fasting blood sugar (Rawal Gautam et al., 2016). Despite the various advantages of the HbA1c test, it is relatively expensive, and its availability is limited to certain regions (Wyn, 2019). The American Diabetes Association (ADA) has established an estimated relationship between HbA1c concentration and average blood glucose levels because both a decrease and an increase in HbA1c values are positively correlated with blood sugar levels in the body. According to WHO, an HbA1c ≥6.5% is recommended as the cutoff for diagnosing diabetes (WHO, 2011). IDF and ADA recommend checking HbA1c levels at least twice a year for patients with controlled blood sugar and every three months for patients with uncontrolled sugar levels or in diabetes therapy (Rawal Gautam et al., 2016). The interpretation of HbA1c levels can be divided into three categories: well-controlled diabetes (<7%), moderately controlled diabetes (7-8%), and poorly controlled diabetes (>8%) (ADA, 2022).

2.6 Relationship between BMI and HbA1c

In individuals with type 2 diabetes (DM), a process of protein glycosylation occurs, where high blood sugar levels persisting over a prolonged or chronic period interact with protein N groups. Monitoring blood glucose levels in type 2 diabetes patients can be done by determining the level of glycosylation of hemoglobin (HbA1c). One of the most common causes of type 2 diabetes is obesity. Measurement and classification of nutritional status can be achieved by assessing Body Mass Index (BMI). A higher BMI value indicates an elevated accumulation of free fat in the body (Saputra et al., 2020). BMI is a measurement that compares weight and height. For obesity, the Asia-Pacific Guidelines define the BMI range as ≥25 kg/m². Approximately 70% of diabetes patients are overweight, and more than 50% of obese patients experience impaired glucose tolerance (Siagian & Simanjuntak, 2021). Research conducted by Wyn indicates that in obese individuals, the HbA1c levels in their bodies increase in line with the rise in BMI (Wyn, 2019). Similar results were found by researcher Wulandari, where a significant number of type 2 diabetes patients had high and uncontrolled HbA1c levels (Wulandari et al., 2020). In obese individuals, there is an accumulation of fat in the body that exceeds normal limits. This accumulation leads to the development of Diabetes Mellitus, characterized by an increase in blood sugar levels. One marker for measuring glucose is the elevation of HbA1c in the body (Makful, 2018).

3. Conclusion

In conclusion, this literature review illuminates the intricate interplay between Body Mass Index (BMI), Hemoglobin A1c (HbA1c), and Type 2 Diabetes Mellitus (T2DM). Emphasizing the crucial role of monitoring HbA1c levels in glycemic control for T2DM patients, the review underscores the significant impact of obesity, as reflected by elevated BMI, on metabolic dynamics. The findings affirm a direct correlation between increased BMI and higher HbA1c levels in obese individuals. Recognizing the pivotal role of excess fat accumulation in fostering T2DM, this review contributes valuable insights for comprehending metabolic disorders, providing a foundation for future research and clinical applications.

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