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Abnormal hemoglobin A1C (hba1c) value in a men patient with diabetic pedis ulcer and uncontrolled reactive hyperglycemia

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ABSTRACT

Glycated hemoglobin (HbA1c) is the gold standard test to identify average plasma glucose in the last 2-3 months with a fast, convenient and accurate test since 1968 for DM diagnostic. Indonesian Society of Endocrinology (PERKENI) 2021 determines that the diagnosis of HbA1c is above 6.5%. HbA1c assays can be used in diagnosis and treatment to identify clinical scenarios and factors contributing to bias. It is important to recognize the factors that can cause results to be inaccurate. The following is a case presentation of abnormal HbA1c values in a man patient with diabetic foot ulcers and uncontrolled reactive hyperglycemia who was treated at a hospital in Semarang.

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INTRODUCTION

Glycated hemoglobin (hemoglobin A1c, HbA1c, A1C, or Hb1c) is a form of hemoglobin measured to identify the average plasma glucose concentration over a long period (Kemenkes RI Dirjen P2P, 2020). HbA1c is irreversibly glycated at one or both N-terminal valine of the beta chain. HbA1c is the most widely used and accepted test to monitor glycemic levels in individuals with diabetes (Chauhan, 2017).

In normal adults, Chromatography of Hemoglobin A1 and Hemoglobin A1c is divided into two parts, namely HbA (HbA0) 92-94% and HbA1 (6-8%), where chain B has an additional glucose group (Liu et al., 2021). HbA1c is generally measured by isoelectric focus or electrophoresis. Glycation of hemoglobin occurs in a variable (non-linear) at any time according to red blood cells (RBC), i.e., 120 days. The relative proportion of HbA1c depends on the average glucose level over the previous 120 days (Chauhan, 2017).

HbA1c is an important indicator for long-term glycemic control with capabilities that reflect the cumulative history of glycemic from the previous two to three months (Chauhan, 2017; Goyal & Jialal, 2022). Venous blood sampling is a diagnostic tool in clinical practice when determining the risk or onset of diabetes. The American Diabetes Association recommends glycated hemoglobin (HbA1c) as a possible fasting blood glucose substitute for diabetes diagnosis.

PERKENI 2021 divides the interpretation of HbA1C into normal (<5.7%), pre-diabetes (5.7 – 6.4%), and diabetes (>6.5%) standardized by the National Glycohaemoglobin Standardization Program (NGSP) (Soelistijo, 2021). Diabetes is a global endemic with a rapidly increasing prevalence in developing and developed countries (Chauhan, 2017; Goyal & Jialal, 2022).

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It occurs due to impaired insulin secretion, insulin resistance, or both. According to the *I*nternational Diabetes Federation (IDF), about 415 million adults aged 20 to 79 had diabetes mellitus in 2015 (Genova et al., 2018; You et al., 2018). DM is a global public health burden, and its number is expected to rise to another 200 million by 2040. Chronic hyperglycemia that synergizes with other metabolic disorders in diabetes mellitus patients can cause damage to various organ systems and lead to the development of health complications, such as microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications that lead to a 2-4-fold increased risk of cardiovascular disease (Goyal & Jialal, 2022).

Hyperglycemia persisting in patients with uncontrolled diabetes mellitus can cause some complications, both acute and chronic. Acute complications include hypoglycemia, diabetic ketoacidosis, hyperglycemic hyperosmolar state, and hyperglycemic diabetic coma. Chronic microvascular complications include nephropathy, neuropathy, and retinopathy, while chronic macrovascular complications are coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease. Peripheral artery disease (PAD) is important in the etiology of leg ulceration in patients with diabetes mellitus (Goyal & Jialal, 2022; Tresierra-Ayala & Garcia, 2017).

The following explanation presents an abnormal case of HbA1c values in a man with diabetic pedis ulcer and uncontrolled reactive hyperglycemia treated at one of Semarang's public hospitals. This case is interesting to be chosen as an internal case because, in the case of diabetic pedis ulcers, an HbA1c examination is generally carried out to monitor the increase in blood sugar levels. However, the patient has elevated blood sugar levels that are not followed by increased HbA1c. These similar cases have never been obtained by anyone before.

RESEARCH METHOD

This type is qualitative research with a case study approach (Sugiyono, 2017, 2018, 2019). Case taking was carried out at the working area of at a hospital in Semarang.

RESULTS AND DISCUSSIONS

A 60-year-old man came to the hospital with a persistent complaint of pain in the injured left big toe four months ago, with a VAS score of 8. The wound was accompanied by blood and pus that had been bandaged at home but still seeped. The patient has a history of uncontrolled diabetes mellitus and is a vegetarian. The physical examination found the general state looked weak, and the consciousness of the composing is with vital signs within normal limits. On examination of the status of localis, it was found that the wound on the right thumb, redness, swelling, blood, pus seeped, and fragile bleeding easily. In the lab examination, there were increases in leukocyte levels (16.8/uL), the number of neutrophils (71.3%), absolute neutrophils ($12.09x10^3$ ul), GDS levels (222 mg dL), normal HbA1C levels (5.4%), platelet increase (435/uL), and D-dimer (920.3 ng/mL). Duplex Sonography (DUS) examination of the right lower extremity was performed to obtain dextra peripheral artery disease. Histopathological examination obtained non-specific chronic inflammation.

The initial response was provided with an infusion of 0.9% 20 tpm NaCl, antibiotics cefotaxime and metronidazole, and fast-acting insulin for 8 hours for hospitalization until the patient's condition stabilized. Follow-up therapy was performed pedis digiti I amputation by the surgeon. After the surgery, no bleeding was found, then postoperative treatment and modification

of the DM diet were carried out until the patient's condition stabilized, and heparin was given 12,000 units/12 hours.

A diabetic foot ulcer is a chronic complication of diabetes mellitus (DM) that affects the patient's quality of life and is associated with high healthcare costs. The prevalence of diabetic foot ulcers ranges from 4-10% during hospitalization and is the leading cause of non-traumatic amputations worldwide. Frisk people with diabetic foot ulcers include the male gender, diabetes over ten years old, peripheral neuropathy, structural foot abnormalities (bone changes, calluses, thickening of the nails), smoking, a history of dyspepsia or amputation, non-routine glycemic control, and peripheral artery disease (PAD). It is defined as a clinical disorder of stenosis or occlusion of the arteries of the lower extremities. The main cause of PAD in people over 40 is atherosclerosis. The risk of atherosclerosis increases, especially in diabetics, and epidemic studies have confirmed the correlation between diabetes and the increased prevalence of PAD. Diabetes was associated with a two to four-fold increase in the incidence of PAD compared to non-diabetic individuals. Among the adult population≥40 years old, the prevalence of PAD was 9.5% in diabetic subjects and doubled the prevalence of 4.5% in non-diabetics. The American Diabetes Association (ADA) consensus recommends that brachial artery (ABI) should be performed as a measure of detection in all diabetic individuals over 50 years of age or those who have DM for more than ten years. PAD is an important predictor of foot ulceration in diabetic patients (Tresierra-Ayala & Garcia, 2017).

Diabetes mellitus (DM) is the most common chronic metabolic disorder in the world, caused by a combination of two main factors, namely insulin secretion damaged by pancreatic β cells and the inability of insulin-sensitive tissues to respond to insulin (Goyal & Jialal, 2022; Galicia-Garcia *et al.*, 2020). According to the World Health Organization (WHO), diabetes mellitus is a chronic metabolic disease characterized by increased blood glucose levels and, over time, causing damage to the heart, blood vessels, eyes, kidneys, and nerves (Galicia-Garcia et al., 2020; Goyal & Jialal, 2022; Richardson et al., 2020).

Diabetes mellitus type 2 (T2DM) accounts for approximately 90% of all cases of DM, characterized by a reduced response to insulin in pancreatic beta cells initiated by increased compensation in insulin secretion to maintain glucose levels within the normal range. However, the overtime beta cells are not able to perform homeostasis, so a state of hyperglycemia called T2DM arises. Most patients with T2DM are obese or have a high percentage of body fat, with the most distribution in the abdominal area. T2DM is often finished in people older than 45 (Goyal & Jialal, 2022; Silvia et al., 2022).

Patients with diabetes mellitus often come with clinical symptoms of increased thirst, urination, lack of energy and fatigue, bacterial and fungal infections, and delayed wound healing. Some patients may also complain of numbness or tingling in the hands or feet or blurred vision. Diagnosis diabetes used hemoglobin A1c (HbA1c) criteria by giving average blood glucose for the last 2-3 months. Patients with HbA1c greater than 6.5% (48 mmol/mol) were diagnosed with DM. HbA1c is a standard test that is convenient, fast, and shows less variation (Goyal & Jialal, 2022).

HbA1c was measured using a National Glycohemoglobin Standardization Program (NGSP) certified method standardized for the Diabetes Control and Complications Trial (DCCT) test (Goyal & Jialal, 2022). HbA1c represents the percentage of glycated hemoglobin circulation. Glycation is a non-enzymatic process and measures glucose levels over time, a biomarker that reflects the average plasma glucose over the previous 8-12 weeks. HbA1c is used for diabetes diagnosis and management. It is recommended as the gold standard in the assessment of diabetes-related outcomes. The increase in HbA1c levels in diabetic patients was first reported by Rahbar *et al.* in 1968 and over the next decade, arguably the most important indicator of blood glucose control. It is widely used to assess the adequacy of diabetes treatments (Chehregosha *et al.*, 2019).

The results can be inaccurate due to several factors. False positives result of HbA1c can occur due to hemoglobinopathy, liver disorders, and iron or vitamin B12 deficiency anemia, so its

use with a high prevalence of anemia is less than optimal (Chehregosha *et al*., 2019; Goyal & Jialal, 2022). According to Bennish's study, improper blood glucose measurement in patients can miss a significant glycemic period leading to a mismatch between HbA1c levels and plasma glucose levels resulting in false low results (Fayyaz *et al*., 2019). According to Iran J, the causes of cases with abnormally low HbA1C are excessive control of the patient's diet, the excessive use of anti-diabetic drugs, laboratory errors, hemolytic anemia, or bleeding that may be the cause of reduced HbA1c (Joob & Wiwanitkit, 2018).

CONCLUSION

It is not yet known for certain the cause of the HbA1c abnormality values in diabetic pedis ulcer patients with a history of uncontrolled DM with this high glycemic index. Many internal and external factors can influence, such as how often the patient exercises excessive dietary control, the use of anti-diabetic drugs at improper dosage, the patient has unknown hemoglobinopathy, and potential process errors at the time of collection and laboratory processing. Thus, it is necessary to conduct a further evaluation to find out the specific cause.

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