# GAMBARAN KADAR HbA1c PADA PENDERITA DIABETES MELITUS DI PUSKESMAS DUNGALIYO

Wilan Hamzah<sup>(1)</sup>, Niluh Arwati<sup>(2)</sup> dan Mindy Eka Astuti<sup>(3)</sup> <sup>1,2,3)</sup> Universitas Bina Mandiri Gorontalo Email: wilanhamzah6@gmail.com

#### ABSTRAK

Diabetes Mellitus is a metabolic disorder disease marked by the increase of blood sugar due to the decreased of insulin secretion by the pancreas beta cell and insulin resistance. By measuring the glycohemoglobin (HbA1C), it can be ascertained how much the percentage of hemoglobin pigment containing glucose is. This study aimed atinvestigating the description of HbA1c levels in diabetes mellitus patients at Puskesmas Dungaliyo.

It was a descriptive study with a quantitative approach. The data were primary data collected form the evaluation result on HbA1c levels in diabetes mellitus patients and secondary data collected from questionnaires and medical records of diabetes mellitus at Health Center Dungaliyo. The technique of sampling was accidental sampling by having 39 respondents as samples..

Findings revealed that out of 39 samples, 35, or 89.7% had abnormal HbA1c levels, while, the rest 4 samples or 10.3% had normal HbA1c levels. It can be recommended that Diabetes Mellitus patients should regularly check with the docror and check in the laboratory as well as maintain a healthy life style to have good Diabetes Mellitus control.

Keywords: Diabetes Mellitus, HbAI level

#### **INTRODUCTION**

According to Riset Kesehatan Dasar (2018), the prevalence of Diabetes Mellitus in Gorontalo Province was ranked eighth in the prevalence of diabetes in 2018 with a prevalence of >2%. [2] Based on Riskesdas in 2018, the total number of people with diabetes mellitus in Gorontalo City was 2.97%, in Regency was 1.78%, Gorontalo in Boalemo Regency was 0.83%, in Pohuwato Regency was 1.43%, in North Gorontalo Regency as much as 1.93%, and in the District of Bone Bolango 1.34% [2].

Based on data obtained at the Dungaliyo Health Center, diabetes mellitus decreased in 2020 starting from January to December as many as 253 patients divided into 10 villages, while in 2021 there was an increasing in diabetes mellitus patients starting from January to June there were 335 patients who were diagnosed with diabetes mellitus divided into 10 villages [1].

The increasing prevalence of diabetes mellitus will indirectly result in morbidity and mortality due to complications of DM itself. Diseases that will be caused are including impaired vision, cataracts, heart disease, kidney disease, sexual impotence, wounds that are difficult to heal and rot/gangrene, lung infections, blood vessel disorders, stroke and so on. Commonly, people with severe diabetes mellitus will experience limb amputation due to decay [8].

To reduce the incidence and severity of diabetes mellitus, prevention such as lifestyle modification and treatment such as oral hyperglycemic drugs and insulin are needed. Evidence shows that diabetes complications can be prevented with optimal glycemic control. Optimal glycemic control is controlled blood glucose concentration HbA1c (glycosylated hemoglobin), cholesterol, triglycerides, nutritional status, and blood pressure. In addition to blood and urine glucose concentrations, an indicator for long-term glycemic control over the initial few weeks can be identified from the glycemic hemoglobin concentration (HbA1c). HbA1c is a major glycemic component and has been shown in many studies to be associated with mean blood glucose [4].

The benchmark of controlling whether or not Diabetes Mellitus is by checking HbA1c in the blood. If the level is more than 7% then it needs to be treated with insulin or anti-diabetic drugs. Within 6 months the levels should be back to normal. This decrease in HbA1c levels to within normal limits is believed to reduce the risk of cardiovascular disease [3].

The measurement of HbA1c is the most accurate way to determine high blood glucose levels over the past 2-3 months. <sup>[5]</sup> HbA1c is also the best single test to assess the risk of tissue damage caused by high blood glucose levels. Based on this consideration, the researcher is interested in conducting further research on the analysis of HbA1c levels in people with Diabetes Mellitus [4].

Based on the description of the background above, the researcher is interested in conducting a study entitled Description of HbA1c Levels in Patients with Diabetes Mellitus at the Dungaliyo Health Center

Diabetes mellitus or commonly known as diabetes is a metabolic disorder characterized by an increase in blood sugar due to decreased insulin secretion by pancreatic beta cells and impaired insulin function (insulin resistance). Diabetes mellitus is а disease characterized by the occurrence of hyperglycemia and disturbances in the metabolism of carbohydrates, fats and proteins associated with nutritional deficiencies absolute or relative action of insulin secretion. Symptoms that are often complained of by people with diabetes mellitus are polydipsia, polyuria, polyphagia, weight loss and tingling [3].

Diabetes Mellitus (DM) is a chronic disease that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycemia, or increased blood sugar, is a common effect of uncontrolled diabetes and over time causes serious damage to many body systems, particularly the nerves and blood vessels [3].

Diabetes mellitus is also characterized by a state of chronic hyperglycemia accompanied by various metabolic disorders due to hormonal disturbances, which cause various chronic complications in the kidneys, eyes and blood vessels. Currently, diabetes mellitus cannot be cured, but it can be prevented by minimizing its symptoms [4].

There are several tests to detect diabetes mellitus, namely:

1. Capillary Blood Glucose Test Screening

This screening method is fast and cheap, namely by pricking your finger to take no more than a drop of capillary blood. This test is called finger-prick blood sugar screening or commonly abbreviated Stick blood sugar. Can be used to check fasting blood glucose, 2 hours after meal, and blood sugar when [6].

2. Venous Blood Glucose Test

It is usually done by the laboratory by taking blood from a vein in the inner arm to assess blood glucose levels after fasting for at least 8 hours and blood glucose 2 hours after eating (2 hours pp-post prandial) [6].

3. Glucose Tolerance Test

This test is more thorough. After 10 hours of fasting, the next morning the blood glucose was checked. Then, drink 75 grams of glucose (approximately 2-3 times sweeter than Softdrink drinks), and 2 hours later check your blood glucose again [6].

4. Urine Glucose Test

Glucose that builds up in the blood will come out through the urine and be detected on a urine test. The presence of glucose in the urine is an indication that a person has diabetes mellitus [6].

5. HbA1c test (Glycated Hemoglobin or Glycosylated Hemoglobin)

This test provides an overview of the state of blood glucose in the last 2-3 months. High blood glucose will bind to hemoglobin (Hb) molecules in the blood, and will last in the blood according to the age of hemoglobin, which is 2-3 months. The higher the blood glucose, the more hemoglobin molecules bind to sugar. This test is used to monitor diabetes treatment, as well as assess the success of diet and exercise [6].

Hemoglobin consists of four polypeptide chains, 2 alpha chains and 2 beta chains. Human hemoglobin can be separated into three minor components which are more negatively charged than HbA, migrate faster than HbA in an electric field, called HbA1 and henceforth known as HbA1a, HbA1b, HbA1c. All types of HbA1 have a carbohydrate group (glucose or its derivatives) attached to one of their globin chains. Carbohydrates can be attached to the N-terminal residue of the amino acid (valine) of the  $\alpha$  or  $\beta$ chain, or to lysine residues [6].

Hemoglobin A1c is a stable glucose bound to the N-terminal group of the HbA0 chain forming a posttranslational modification so that glucose unites with the free amino group on the valine residue N-terminus of the hemoglobin  $\beta$  chain. The resulting Schiff base is unstable, then through an irreversible rearrangement (Amadori rearrangement) forms a stable ketoamine. Glycation can also occur at certain lysine residues of the hemoglobin  $\alpha$  and  $\beta$ chains; the measurable total glycohemoglobin or total glycated hemoglobin, is known as HbA1c [9].

Glycation of hemoglobin is not catalyzed by enzymes, but through chemical reactions due to exposure of glucose circulating in the blood to red blood cells. The rate of synthesis of HbA1c is a function of the concentration of glucose bound to erythrocytes during The HbA1c concentration exposure. depends on the blood glucose concentration and the age of the erythrocytes [6].

levels HbA1c had a good correlation with average fasting, daily and peak blood glucose levels over the past 12 weeks, there was no difference between insulin dependent and non insulin dependent, nor was it influenced by sex differences. Based on the interim A1c-AG study, it was proven that HbA1c levels were strongly correlated with average glucose levels, enabling diabetic patients to know their average blood glucose levels over the previous 3 months [9].

HbA1c levels can be influenced by genetic factors and hematological diseases. A decrease in the number of erythrocytes can cause a false decrease in HbA1c levels. Patients with episodic or chronic hemolysis, chronic renal failure, anemia cause the blood to contain more young erythrocytes so that HbA1c levels can be found at very low levels [10].

Hemoglobin normally does not contain glucose when the erythrocytes leave the bone marrow for the first time, but after a life span of 120 days, hemoglobin is bound to glucose. Glycoin hemoglobin or HbA1c is the fraction of hemoglobin that binds directly to glucose which shows blood sugar levels for 8-12 weeks. HbA1c examination is a standard examination to assess long-term glycemic status and is effective in all types of people with Diabetes Mellitus. The HbA1c test has been very successful in providing a level of control over diabetes. This test shows the average amount of blood sugar in 2-3 months, therefore diabetics are advised to routinely control it at least 2 times a year [9].

If the blood sugar level is high for several weeks, the HbA1c level will also be high. The HbA1c bond that is formed is stable which can last up to 2-3 months. HbA1c levels will reflect the average level in the period 2-3 months before the examination. By measuring HbA1c levels, it is possible to determine the quality of diabetes mellitus control in the long term, so that patient adherence is known in undergoing meal planning and medication [5].

There are several methods that are often used in the examination of HbA1c levels, including:

### a. Ion Exchange Chromatography Method

The principle of this method is that the isoelectric point of HbA1c is lower and migrates faster than other Hb components. At the moment of using this method, changes in reagent and column temperature, ionic strength and pH of the buffer must be controlled. The disadvantage of this method is the variable interference of hemoglobinopathies, HbF and carbamylated Hb (HbC) which can give false negative results. The advantage of this method is that it can examine the Hb variant chromatogram with a high degree of precision.

## b. High Performance Liquid Chromatography Method

This method has similar principle with Ion Exchange Chromatography, where it can be automated and has excellent accuracy and precision. This method is also recommended as a reference method for the examination of HbA1c levels [7].

## c. Agar Gel Elektroforesis Method

This method has results that correlate well with HPLC but have less precision than HPLC. HbF gives false positive results but ionic strength, pH, temperature, HbS and HbC have little effect on this method [7].

## d. Immunoassay Method (EIA)

The principle of this method is the bond that occurs between the antibody and glucose and between the 4-amino acid and the 10 N-terminal chain. The disadvantage of this method is that it is affected by impaired hemoglobinopathies with complete amino acids on the binding site and some disorders originating from HbF so that this method is only able to measure HbA1c and cannot measure labile HbA1c or HbA1A and HbA1B. The advantage of this method is that it is not affected by HbE and HbD or carbamylated Hb, is relatively easy to implement in different formats and has good precision.

### e. Affinity Chromatography Method

The principle of this method is that glucose bounded to maminophenylboronic acid. The weakness of this method is not only measuring valine glycation at the Nterminal  $\beta$  chain but also chain glycation  $\beta$  in other parts and  $\alpha$  chain glycation so that the measurement results with this method are higher than with the HPLC method. The advantages of this method are nonglycated hemoglobin and the labile form of HbA1c does not interfere with determination of the glycated affected hemoglobin, is not by temperature, has good precision, HbF, HbS and HbC only slightly affect this method.

## f. Chemical Analysis Methods by Colorimetry

This method requires a long incubation time aprocimately about 2 hours but the advantage is more specific because it is not affected by glycosylated or glycosylated labile. The disadvantages are its long time, large sample and the unit of measurement that clinicians are not familiar with is mmol/L. Spectrophotometric method The principle of this method is the removal of the labile fraction of hemoglobin by

means of haemolysate then added a cationic ion exchange agent and then read with a spectrophotometer instrument at a wavelength of 415 nm.

### g. Enzimatis Method

HbA1c examination by enzymatic method has two steps. The first step was measurement of glycosylated N terminal dipeptide (fructo-syl-valinehistidine, f-VH) of HbA1c beta chain which was broken down by protease levels enzymes. then Hb were measured at absorbences of 600 nm and 800 nm. The second step is hydrogen peroxidase produced by the f-VH reaction and fructosyl peptide oxidase (FPOX) is allowed to react with a color fixative in the presence of peroxidase, which will form a color and the absorbance is measured. HbA1c calculated the percentage of Hb levels. The enzymatic HbA1c measurement method was not affected by Hb variance in general, but samples with high HbF (>2.0%) could give higher results when compared.

### h. Boronate Affinity Assay Method

The boronate affinity method is a method that has been standardized by the National Glycohemoglobin Standardization Program (NGSP). This method is also included in the HbA1c checklist accepted by the Food and Drug Administration (FDA). The sensitivity and specificity of the boronate affinity method for the 6.5% HbA1c cutoff were 82.9% and 100%, respectively. The boronate affinity method has the advantage of being slightly affected by hemoglobin variance and providing excellent precision and accuracy.

#### i. Method Immunoturbidimetri

The principle of this method is the binding of antibodies with glucose and between the 4-amino acid and the 10 N-terminal chain. Examination was not affected by HnE, HbD or Carbomylated Hb. The Immunoturbidimetric method can already be automated, it can be used for laboratories with smaller sample sizes because it is examined with an analyzer for other chemistry.

#### **METHOD OF RESEARCH**

This research used a quantitative approach with a descriptive type of research in order to see the description of the results of the examination of HbA1c levels in diabetes mellitus at the Dungaliyo Public Health Center. The primary data in this study were the results of the examination of HbA1c levels in patients with diabetes mellitus carried out at the ProUs Clinical Laboratory, Gorontalo City, while the secondary data was in the form of medical records for patients with diabetes mellitus at the Dungaliyo Public Health Center. Gorontalo Regency.

The population in this study were all patients with diabetes mellitus at the Dungaliyo Public Health Center. The population in the Dungaliyo health center was 335 people. The samples taken from this study were people with diabetes mellitus who were in the Dungaliyo health center with a total of 39 samples based on the calculation of the sample size. The sampling technique was carried out by accidental sampling. The data collection method used in this study is the Immunoassay method (EIA). The data analysis in this study used Univariate Analysis, the data in this study were presented in tabular form and reported in percentages.

### FINDINGS

Based on the results of research that has been carried out at the Dungaliyo Health Center, Dungaliyo District, Gorontalo Regency, Gorontalo Province for 19 (nineteen) days, namely from 07 to 25 October 2021 on 39 samples of people with Diabetes Mellitus, the following results were obtained :

Table1. Distribution of Samples of<br/>HbA1c Levels in Patients with<br/>Diabetes Mellitus at Dungaliyo<br/>Health Center.

HbA1c level examination results	Frequency	Percentage(%)
Normal	4	10,3
Abnormal	35	89,7
Total	39	100

Based on Table 4.1 above, it shows that from 39 respondents with diabetes mellitus who were examined roughly for HbA1c, 35 people (89.7%) obtained abnormal results and 4 people (10.3%) had normal HbA1c levels. The normal limit or reference value for HbA1c is 4.5 - 6.5%.

### a. Karakteristik Responden Berdasarkan Jenis Kelamin

Based on the results of the research, the characteristics of respondents based on gender can be seen in table 4.2

Table 2. Distribution of Samples by<br/>Gender

Gender	Frequency	Percentage (%)
Male	2	5,1
Female	37	94,9
Total	39	100
Source: Data Primer Penel	litian 2021	

Source: Data Primer Penelitian, 2021

### b. Characteristics of Respondents Based on Age

Berdasarkan hasil penelitian untuk karakteristik responden berdasarkan umur dapat dilihat di table 4.3.

Age	Frequency	Persentage (%)
20 - 29 years	1	2,6
30 - 39 years	1	2,6
40 - 49 years	23	59,0
50 - 59 years	8	20,5
> 60	6	15,4
Total	39	100
Source : Data Primer Peneli	tian, 2021	

## c. Characteristics of Respondents Based on Drug Consumption

Based on the results of the research, the characteristics of

respondents based on drug consumption can be seen in table 4.4

**Table 4** Distribution of Samples Based onDrug Consumption

Drug Consumption	Frequency	Persentage (%)
Routine	15	38,5
Not Routine	24	61,5
Total	39	100
Source : Data Primer Penelitian, 2021		

#### DISCUSSIONS

Based on the results of research that haD been carried out on patients with Diabetes Mellitus at the Dungaliyo Health Center, it was found that the HbA1c value in patients with abnormal values > 6.5%was 35 (89.7%). While the normal HbA1c value is 4.5-6.5% as many as 4 respondents (10.3%) of 39 respondents. This was due to the lack of attention of patients with diabetes mellitus. They were not implementing regular exercise habits, uncontrolled food intake and not regularly taking drugs. While the result of normal HbA1c levels in patients was because they could control their diet, take medication regularly and apply diet and exercise regularly.

Elevated HbA1c levels in patients with diabetes mellitus who were uncontrolled and were at high risk for long-term complications such as nephropathy, retinopathy, or cardiopathy. HbA1C examination was recommended to be done routinely in people with diabetes mellitus. The results of this research were in accordance with the research of Keszia M, (2018) that from 40 samples of patients obtained abnormal HbA1c levels as many as 34 samples (85%) and normal HbA1c levels as many as 6 samples (15%). It was proven again by the results of research by Simatupang M. (2020) from 30 samples, 21 samples obtained abnormal results of 70% and normal HbA1c results as many as 9 samples of 30%.

Based on the results of the study, it was found that the majority of people with diabetes mellitus were female, as many as 37 people (94.9%). This was due to the lack of male patients in controlling diabetes mellitus, so that the more women come to know about diabetes mellitus to control the results of HbA1c levels.

Basically the chances of getting DM between men and women, it can only be seen from the risk factors, women have a greater chance due to a greater increase in STIs. Monthly cycle and postmenopausal syndrome which makes the distribution of body fat easy to accumulate due to the hormonal process.

The results of this study are in accordance with Simatupang M. (2020), which found that the percentage of HbA1c 6.5% in 12 women (57.1%) was higher than 9 men (19.6%). The amount of comparison between the compositions in the form of estradiol would make the Estrogen Receptor (ER) and Estradiol Receptor (ER) genes activated, this caused the metabolic process to work and the two genes would coordinate in insulin sensitivity and increased glucose uptake in the blood. In line with increasing human age, the hormone estrogen would decrease in the female body. Activation of the expression of the Estrogen Receptor and Estradiol Receptor genes where this condition caused insulin sensitivity and sugar uptake would also decrease, so that sugar would accumulate in the form of fat in the body which could lead to obesity.

People with diabetes mellitus usually complain of typical symptoms such as polyphagia (a lot of eating), polydipsia (a lot of drinking), polyuria (a lot of urine/frequent urination at night), increased appetite but weight lossed rapidly (5-10 kg in 2-4 days), easily tired, and tingling. The incidence of Type II DM was more common in women because women have a greater chance of increasing their body mass index

Based on the results of the research, it was found that the majority of people with diabetes mellitus occurred at the age of 40-49 years, namely as many as 23 people (59.0%). This was because those aged over 40 years usually had reduced movement activities, both sports and activities that require a lot of calories. And genetic factors could also appear at the age of over 40 years.

The results of this research were in accordance with the research of Keszia M, (2018), which found that the highest percentage was at the age of 47-57 years, namely 13 people (32.5%). The risk of diabetes increases with age, especially at the age of more than 40 years, because at that age, glucose intolerance begins to increase. The aging process causes a decrease in the ability of  $\beta$  pancreatic cells to produce insulin. In addition, in older individuals there was a decrease in mitochondrial activity in muscle cells by 35%. This was associated with an increase in muscle fat levels by 30% and triggered insulin resistance.

Based on the results of the research, the percentage of respondents taking drugs showed that most respondents did not take drugs regularly as many as 24 respondents (61.5%) and respondents who consumed drugs regularly as many as 15 respondents (38.5%). This was due to uncontrolled and not taking medication eating regularly. The results of this research was in line with the research of Utomo, et al (2015) In this study, 13 of the 22 respondents who took drugs according to the doctor's recommendations got an average HbA1c level of 9.1%, which was lower than the average HbA1c level of respondents who did not consume drugs according to doctor's recommendations that was equal to 10.4%.

#### **KESIMPULAN**

Based on the results of research regarding the examination of HbA1c levels in patients with diabetes mellitus at the Dungaliyo Public Health Center, Kab. Gorontalo, it can be concluded that:

The results showed that the HbA1c value in patients was at an abnormal value > 6.5% as many as 35 (89.7%) while the normal HbA1c value was 4.5-6.5% as many as 4 respondents (10.3%) from 39

respondents. Meanwhile, based on gender, namely the female sex as many as 37 people (94.9%), based on age the highest percentage was at the age of 40-49 years as many as 23 people (59.0%) based on the percentage of and respondents taking drugs, it showed that most of the respondents did not take drugs. routinely many as as 24 respondents (61.5%) and respondents who consume drugs regularly as many as 15 respondents (38.5%

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