

Differences of Erythrocyte Index in Patients With Diabetes Mellitus Given The Criteria for Prediabetes And Diabetes at Kedungdoro Public Health Center Surabaya

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Differences of Erythrocyte Index in Patients With Diabetes Mellitus Given The Criteria for Prediabetes And Diabetes at Kedungdoro Public Health Center Surabaya

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ABSTRACT

Diabetes Mellitus is a metabolic disease characterized by high blood glucose levels due to impaired insulin secretion, decreased insulin action, or both. Diabetes mellitus is divided into prediabetes criteria, namely when fasting blood sugar levels are 100-125 mg/dL and diabetes criteria when fasting blood sugar levels are 126 mg/dL. Elevated blood sugar levels are associated with a deficiency of *Erythropoietic Stimulating Factors* (ESF) which can affect the process of erythrocyte formation to have an impressive effect on the erythrocyte index (MCV, MCH, and MCHC). This study aims to determine the difference in index of erythrocytes in patients with prediabetes and diabetes in Puskesmas Kedungdoro Surabaya. This research was observational analytic with *crosssection* conducted from January to April 2021 in 15 patients with prediabetes and 15 diabetic patients at the health center Kedungdoro Surabaya using materials EDTA blood test. Complete blood counts were carried out at the Bakti Analytical Clinical Laboratory using the *ABX Micros 60 Hematology Analyzer*. The results showed the average MCV value of prediabetic patients was 86.80 m³ while in diabetic patients it was 82.00 m³, the average MCH of prediabetic patients was 29.48 pg and in diabetic patients is 27.25 pg, and the average MCHC of prediabetes is 33.94 g/dL while in diabetic patients it is 33.20 g/dL. So that further research is needed on risk factors that can increase the value of the erythrocyte index in people with diabetes mellitus.

Keywords: Diabetes, Prediabetes, Erythrocyte Index

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disease characterized by high levels of glucose in the blood (hyperglycemia), which occurs due to impaired insulin secretion, decreased insulin action, or the result of both. Several pathological processes are involved in the development of diabetes, ranging from destruction of cells in the pancreas with consequent insulin deficiency, to abnormalities leading to insulin resistance.⁽¹⁾ Diabetes is one of the most important public health problems and is categorized into four non-communicable diseases. This is due to the increasing number of cases and prevalence of diabetes over the last few decades. The World Health Association (WHO) predicts that the number of people with diabetes in Indonesia will increase from 8.4 million in 2000 to 21.3 million in 2030.⁽²⁾

Increase in the prevalence of diabetes in Indonesia from 5.7% in 2007 increased to 6.9% or around 9.1 million in 2013. Based on a preliminary survey conducted by researchers at the Kedungdoro Health Center Jl. Kaliasin Pump Gang No. 79-81, Tegalsari, Surabaya, it is known that the number of type 2 diabetes mellitus patients from 2019 to 2020 was 1,426 patients and the period from September to November was 120 patients. Data from the International Diabetes Federation in 2015 shows the estimated number of people with diabetes in Indonesia is estimated at 10 million. The increase in the prevalence and control of Diabetes Mellitus shows the importance of preventing and controlling Diabetes Mellitus.⁽³⁾

Examination of the diagnosis of diabetes mellitus is very necessary by being enforced on the basis of examination of blood glucose levels. The results of laboratory tests for diagnosing diabetes mellitus can be divided into several criteria, namely the criteria for prediabetes where the results of blood sugar levels do not meet the normal criteria and the criteria for diabetes mellitus, namely with fasting blood sugar levels of 100-125 mg/dL,

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while the results of the examination show a diagnosis of diabetes when the blood sugar levels are high. fasting blood 126 mg/dL.⁽⁴⁾ In connection with the higher blood sugar levels that affect the criteria for the incidence of diabetes mellitus, it can inhibit the formation of the hormone erythropoietin (HPO) which functions to regulate the production of red blood cells in the bone marrow.⁽⁵⁾ In patients with Diabetes Mellitus, bone marrow is one of the body's tissues with a high proliferation rate that produces all types of blood cells every day, one of which is red blood cells through the erythropoiesis system by erythropoietin (EPO).

The persistent increase in blood sugar levels associated with diabetes is associated with a deficiency of *Erythropoietic Stimulating Factors* (ESF) which can affect the process of erythrocyte formation to have an impressive effect on one of the red blood cell indices, which include mean corpuscular volume (MCV), corpuscular hemoglobin. (MCH), means the corpuscular hemoglobin concentration (MCHC).⁽⁶⁾ According to research, cases of Diabetes Mellitus are often found to have disturbances in various systems, one of which is interference with erythrocytes. Disorders of erythrocytes are closely related to the mean erythrocyte index which consists of the mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) which are important indicators to reflect the condition of erythrocytes.⁽⁷⁾

Alamri's research (2019), on the effect of hyperglycemia on red blood cell (erythrocyte) index, showed that hyperglycemia was proven to reduce corpuscular volume (MCV), average corpuscular hemoglobin (MCH), and corpuscular hemoglobin concentration (MCHC). According to research conducted by Jaman (2018), regarding diabetes and red blood cell parameters, it shows that in diabetics, glycemic control affects the RBC count, RDW, and erythrocyte index consisting of MCV, MCH, and MCHC. MCH values were lower in patients with high glycemic levels than in patients with low glycemic control. In patients with diabetes mellitus, disorders are often found in various systems, one of which is in erythrocytes. An important indicator that can reflect the state of erythrocytes is the erythrocyte index (MCV, MCH, and MCHC).⁽⁸⁾

Therefore, researchers want to know the characteristics of the erythrocyte index that can be used as an indicator to see the presence of erythrocyte disorders in people with diabetes mellitus with prediabetes and diabetes criteria.

Research Objectives and Benefits

This study aims to determine the difference in erythrocyte index in patients with diabetes mellitus with prediabetes and diabetes criteria through hematological examination, namely erythrocyte index.

This study is expected to be an alternative examination in determining the diagnosis of diabetes mellitus by providing information about the criteria for prediabetes and diabetes through the erythrocyte index which includes MCV, MCH, and MCHC.

METHODS

This research is an analytical observational study, comparing two groups, namely the prediabetes group and the diabetes group. With approach *cross section*, that each subject will be examined for the erythrocyte index at one time and the research design is *the post control group design*, namely the study uses the results of the final examination with limitations on the research group. Research This research was conducted at the UPTD of the Kedungdoro Health Center, Surabaya City and laboratory examination tests were carried out at the Bakti Analysis laboratory from October 2020 to April 2021. Sample in this study was 30 samples taken according to the population with inclusion criteria, namely patients categorized as prediabetes with fasting blood glucose levels of 100-125 mg/dL and categorized as diabetes with fasting blood glucose levels 126 mg/dL. The sampling technique used primary data from blood sugar examination and erythrocyte index obtained by *purposive consecutive sampling technique*, sampling namely done by selecting samples that meet the research criteria for a certain period of time.

Data Collection Techniques

Using primary data from the results of examination of blood glucose levels, erythrocyte index and the results of the respondent's questionnaire in accordance with the consent *informed*. research data is quantitative data, then normality test is carried out using the Kolmogorov Smirnov test. Because the data were normally distributed ($p > 0.05$), performed *Independent Samples T-Test* was to determine the difference in erythrocyte index in prediabetes and diabetic patients.

Research Stages

DM patients were measured blood glucose levels then conducted interviews, filled out questionnaires, and *informed consent* in DM patients who had blood sugar levels according to the sample criteria, namely 100-125 mg/dL (prediabetes) and 126 mg/dL (diabetes). Perform venous blood collection then complete blood examination with Horiba ABX Micros 60 Hematology Analyzer (MCV, MCH, and MCHC). Data is collected and analyzed statistically to obtain results and conclusions in the study.

RESULTS

Based on the results of the study in the form of examining the erythrocyte index in patients with diabetes mellitus with prediabetes and diabetes criteria using the Horiba ABX Micros 60 Hematology Analyzer, the following results were obtained:

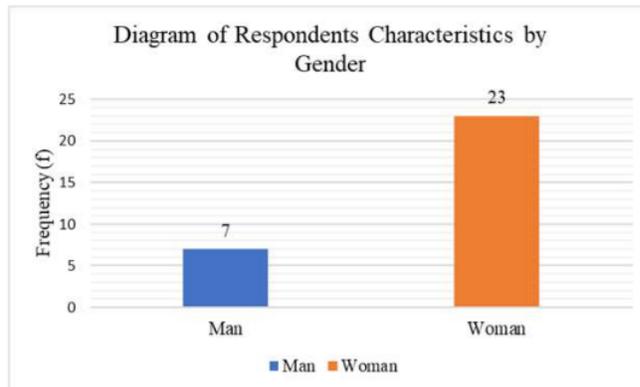


Figure 1. Diagram of Respondents Characteristics by Gender

Based on the gender distribution, it shows that there are more female respondents than male respondents, namely 23 samples (76%), while 7 samples are male (24%).

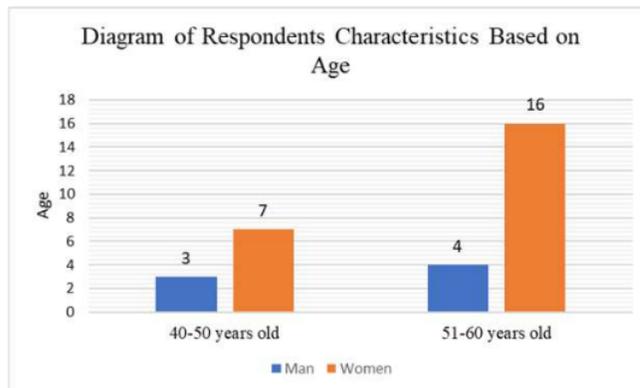


Figure 2. Diagram of Respondents Characteristics Based on Age

Based on Figure 4.2 above, there are respondents with an age range of 40-50 years as many as 10 samples (34%) consisting of 3 samples of men and 7 samples of women. While the age range of 51-60 years was 20 samples (66%) consisting of 4 male samples and 16 female samples. So it can be seen that DM is more at risk of being suffered by the 51-60 year age group.

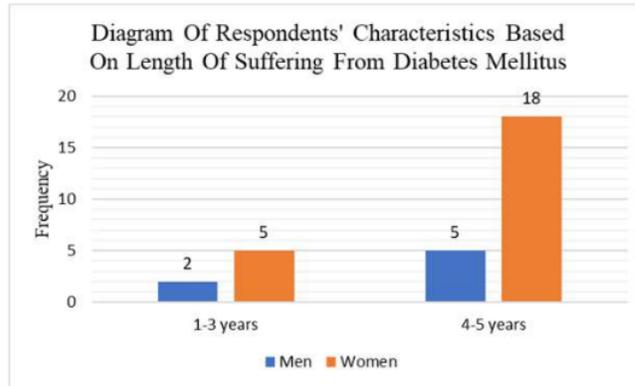


Figure 3. Diagram Of Respondents' Characteristics Based On Length Of Suffering From Diabetes Mellitus

Based on Figure 4.3, as many as 2 samples of men and 5 women experienced Diabetes Mellitus for 1-3 years. A total of 5 samples of men and 18 women had experienced Diabetes Mellitus 4-5 years. The period of time the respondent has diabetes mellitus can be an influencing factor for the formation of erythrocytes which is reflected in the erythrocyte index value.

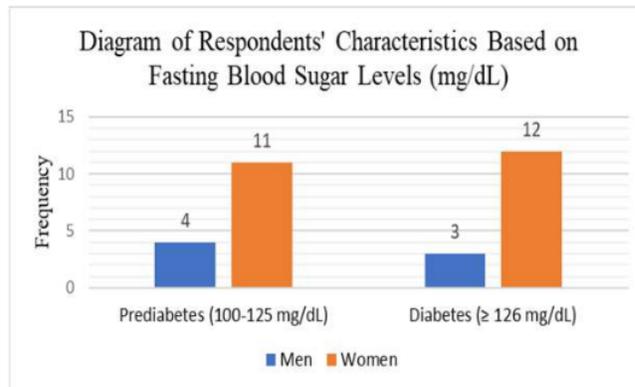


Figure 4. Diagram of Respondents' Characteristics Based on Fasting Blood Sugar Levels (mg/dL)

Based on fasting blood sugar levels, respondents with prediabetes criteria (100-125 mg/dL) were 15 samples, namely 4 men and 11 women. And the criteria for diabetes (≥ 126 mg/dL) were 15 samples consisting of 3 men and 12 women

Table 1 Results of Erythrocytes Index In Patients With Pre-Diabetes Index

Erythrocyte Index	Normal Value	Minimal	Maximum	Mean
Erythrocyte Index in Prediabetes				
MCV	80-97	83	92	86,80
MCH	26,5-33,5	27,9	31,6	29,48
MCHC	31,5-35,0	32,8	35,4	33,94

Based on the index of erythrocytes in patients with prediabetes, MCV value of at least $83\mu\text{m}^3$ a maximum of $93\mu\text{m}^3$ and an average of $86.8\mu\text{m}^3$. The minimum MCH value is 27.9 pg, the maximum is 31.6 pg and the average is 29.48 pg. The minimum MCHC value is 32.8 g/dL, the maximum is 35.4g/dL, and the average is 33.94 g/dL.

Erythrocyte Index	Normal Value	Minimal	Maximum	Mean
Erythrocyte Index in Diabetes				
MCV	80-97	65	89	82,00
MCH	26,5-33,5	20,1	30,0	27,25
MCHC	31,5-35,0	31.0	34,7	33,20

Based on the results of the erythrocyte index in diabetic patients, the minimum MCV value is 65 m³, the maximum is 89 m³, and the average is 82.00 m³. The minimum MCH value is 20.1 pg, the maximum is 30.0 pg and the average is 27.25 pg. The minimum MCHC value is 31.0 g/dL, the maximum is 34.7 g/dL, and the average is 33.20 g/dL.

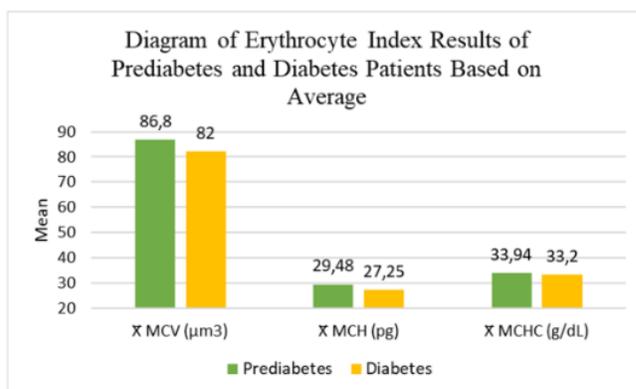


Figure 5. Diagram of Erythrocyte Index Results of Prediabetes and Diabetes Patients Based on Average

Based on Figure 4.5, it can be seen that the average MCV, MCH, and MCHC in patients with glycemic levels included in the prediabetes criteria is higher than respondents with diabetes criteria.

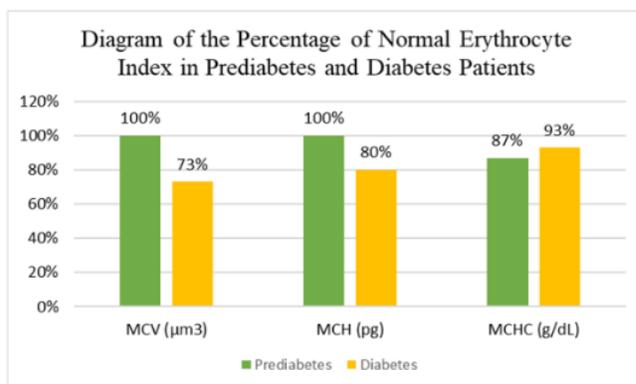


Figure 6. Diagram of the Percentage of Normal Erythrocyte Index in Prediabetes and Diabetes Patients

Based on the results table above, it is known that the MCV and MCH values of prediabetic patients are normal (100%), normal MCHC with a percentage of 87% and an increase of 13%. Whereas in diabetic patients, MCV was 73% normal, MCH 80% normal, and MCHC 93% normal. The normal percentage of prediabetes patients is higher than diabetes

DISCUSSION

From the research that has been conducted on the blood of prediabetic and diabetic patients at the Kedungdoro Public Health Center, Surabaya, the results showed that the mean MCV value of prediabetic patients and diabetic patients was in the normal range but the MCV in prediabetic patients was higher, namely 86.80 m^3 while in diabetic patients of 82.00 m^3 . The decrease in MCV values at higher glucose levels can be caused because hyperglycemia is able to affect serum sodium levels which are extracellular cations through the mechanism of increasing and moving solutes from the intracellular to extracellular compartments, the increase in glucose will cause an osmotic gradient that causes a decrease in sodium levels, so that the volume of blood cells decreases and affects changes in cell size.⁽⁹⁾

Based on table 4.5 regarding the results of the erythrocyte index in prediabetic patients, it can be seen that the average number of MCH values in patients with prediabetes category is higher than patients with diabetes category, which is 29.48 pg while in diabetic patients is 27.25 pg. There were 3 diabetic patients who were below the normal MCH value (26.5-33.5 pg), while the MCH value of prediabetic patients was in the normal range. Chronic hyperglycemia can cause hypoxia in the renal interstitium so that it affects the glomerular filtration rate (GFR) and indicates that there are fewer nephrons that function in the production of erythropoietin produced by peritubular fibroblast cells in stimulating the bone marrow to produce erythrocytes so that the formation of hemoglobin is not optimal.⁽¹⁰⁾

The average MCHC in prediabetic patients was 33.94 g/dL while in diabetic patients it was 33.2 g/dL so it was found that the average MCHC value in prediabetic patients was higher than in diabetic patients. A consistent increase in sugar levels can cause functional and structural changes in the hemoglobin molecule including the hemoglobin concentration and the cytoplasmic environment inside each red blood cell.⁽¹¹⁾

Based on the results of questionnaires and interviews, it can be seen that most of the respondents have an uncontrolled lifestyle, respondents routinely consume oral antidiabetic drugs (OAD) such as metformin and glimepiride obtained from the Puskesmas or insulin obtained from a referral hospital, but most of the respondents not exercising regularly, especially during the Covid-19 pandemic. Uncontrolled diabetes can occur if a diabetic takes medication or insulin not according to the doctor's instructions accompanied by eating too little food and or too much physical exercise and as a result of diabetes' response to excessive anti-diabetic drugs so that blood glucose levels drop too low.⁽¹²⁾ The number of female respondents was 76% more than male respondents which was 24%. The female sex tends to be more at risk of developing diabetes mellitus than men, this is related to the body mass index that women have which tends to be greater so that there will be a buildup of fat that inhibits the transport of glucose to enter the cells and there is a phase of pregnancy that can increase insulin resistance.⁽¹³⁾

The majority of respondents were in the age range of 51-60 years (20 samples) while the age group of 40-50 years consisted of 10 samples, so that it can be seen that DM is more at risk of being suffered by the 51-60 year age group. This can be caused by the increasing age of a person, the higher the risk of the body experiencing physiological changes that can reduce body functions.⁽¹⁴⁾ Based on the duration of suffering from diabetes mellitus, it is known that 60% of respondents had diabetes mellitus for 4-5 years and 40% of respondents had diabetes for 1-3 years. The results of this study are in line with research conducted by Mildawati (2019), that the length of time suffering from diabetes can affect the occurrence of complications where the longer you have diabetes, the higher the risk of complications.⁽¹⁵⁾

Based on the reference values used by the Bakti Analysis Surabaya clinical laboratory, the MCV values of 15 prediabetic patients were in the normal range ($80-97 \text{ m}^3$) and a total of 4 patients with diabetes criteria were below the normal range of 65 m^3 , 76 m^3 , 78 m^3 , and 79 m^3 . MCH values from 15 prediabetic patients were in the normal range (26.5-33.5 pg) and 3 patients with diabetes criteria were below the normal range of 20.1 pg; 26.0 pg; and 26.2 pg. As for the MCHC value, there were 2 samples of prediabetes patients who were above the normal value (31.5-35 g/dL) which was 35.4 pg and 35.3 pg, there was one sample of patients with diabetes criteria who were below normal, namely 31, 0 g/dL. From the distribution of the results of the examination, it can be seen that the MCV, MCH and MCHC values of prediabetic patients have higher values than patients with diabetes category.

The results of this study are in accordance with the theory that has been described previously. According to Wijaya, Kusnadi, & Zen, in connection with the higher blood sugar levels that affect the criteria for the incidence of diabetes mellitus, it can inhibit the formation of the hormone erythropoietin (HPO) which functions to regulate the production of red blood cells in the bone marrow.⁽¹⁶⁾ Erythropoietin affects erythrocyte production by stimulating the proliferation, differentiation and maturation of erythrocyte precursors. The hormone erythropoietin

is used to stimulate erythropoiesis by increasing the number of progenitor cells bound to the process of erythropoiesis.⁽¹⁷⁾

Statistical tests conducted in this study on the results of the erythrocyte index examination which included MCV, MCH, and MCHC in diabetes mellitus patients with prediabetes and diabetes criteria showed that the Asymp value. Sign (2-tailed) < 0.05 then H_a is accepted and H_o is rejected. Thus, it can be concluded that there is a significant difference between the MCV, MCV, and MCHC values of prediabetic patients and diabetic patients. This is in line with another study conducted by BN Alamri (2019) which stated that the MCV and MCH values in hyperglycemia conditions would decrease. Research conducted by Jaman also states that in diabetics, glycemic control affects the number of RBC, RDW, and erythrocyte index consisting of MCV, MCH, and MCHC. MCHC values were lower in patients with high glycemic levels than in patients with low glycemic control.⁽¹⁸⁾ In patients with diabetes mellitus, disorders of various systems are often found, one of which is in erythrocytes. An important indicator that can reflect the state of erythrocytes is the erythrocyte index (MCV, MCH, and MCHC)⁽¹⁹⁾

Based on the results of statistical tests carried out, it can be concluded that there are differences in the erythrocyte index which includes MCV, MCV, and MCHC between patients with diabetes mellitus with prediabetes criteria and patients with diabetes mellitus with diabetes criteria at the UPTD Puskesmas Kedungdoro Surabaya City.

CONCLUSION

1. Fasting blood sugar levels in patients with diabetes mellitus with prediabetes criteria are 100-125 mg/dL, and diabetic patients are 126 mg/dL.
2. Erythrocyte index (MCV, MCH, MCHC) in diabetes mellitus patients with prediabetes criteria obtained
MCV (*Mean Corpuscular Volume*) of 86.80 m³
MCH (*Mean Corpuscular Hemoglobin*) of 29.48 pg
MCHC (*Mean Corpuscular Hemoglobin Concentration*) of 33, 94 g/dL
3. Erythrocyte index (MCV, MCH, MCHC) in patients with diabetes mellitus with diabetes criteria obtained:
MCV (*Mean Corpuscular Volume*) of 82.00 m³
MCH (*Mean Corpuscular Hemoglobin*) of 27.25 pg
MCHC (*Mean Corpuscular Hemoglobin Concentration*) of 33 ,20 g/dL
4. There is a difference between the erythrocyte index in patients with diabetes mellitus with prediabetes criteria and diabetes criteria at the UPTD Public Health Center Kedungdoro Surabaya City.

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GRADEMARK REPORT

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GENERAL COMMENTS

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