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Leucocyte Value as a Signs of Microvascular Inflammation in Type 2 Diabetes Mellitus Patients

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Abstrak

Masalah dalam pengembangan patogenesis Diabetes Melitus Tipe 2 (DMT2) hingga komplikasi sering diabaikan, dan jarang dilakukan tes darah rutin pada individu dengan DMT2. Peradangan adalah tanda awal yang penting untuk mendeteksi komplikasi. Salah satu faktor yang dapat digunakan sebagai indikator peradangan adalah nilai leukosit. Tujuan dari penelitian ini adalah untuk menilai jumlah leukosit pada pasien dengan DMT2 sebagai tanda peradangan pada pasien DMT2. Penelitian ini menggunakan metode pendekatan cross-sectional, dengan data dianalisis secara deskriptif dan korelatif menggunakan perangkat lunak SPSS. Subjek penelitian melibatkan warga binaan Puskesmas Kota Baru dan Kalibaru yang menderita DMT2 pada periode Januari hingga Februari 2019. Hasil uji Pearson menunjukkan nilai p=0,49, yang mengindikasikan bahwa tidak ada hubungan yang signifikan antara leukositosis dan kadar glukosa darah. Kesimpulan dari penelitian ini adalah bahwa tingginya jumlah leukosit pada pasien DMT2 diduga bukan disebabkan oleh kadar glukosa darah yang tinggi, melainkan mungkin dipengaruhi oleh faktor lain terkait perkembangan komplikasi penyakit DMT2. Penelitian ini memiliki implikasi penting dalam memahami patogenesis dan pencegahan komplikasi DMT2.

***Kata kunci*:** *Jumlah Leukosit, Diabetes Melitus Tipe 2, Peradangan*

Abstract

Problems in the pathogenesis of Type 2 Diabetes Mellitus (T2DM) to complications are often overlooked, and routine blood tests are rarely performed in individuals with T2DM. Inflammation is an important early sign for detecting complications. One of the factors that can be used as an indicator of inflammation is the value of leukocytes. The purpose of this study was to assess leukocyte counts in patients with T2DM as a sign of inflammation in T2DM patients. This study used a cross-sectional approach method, with data analyzed descriptively and correlative using SPSS software. The subjects of the study involved residents assisted by the Kota Baru and Kalibaru Health Centers who suffered from DMT2 in the period from January to February 2019. The results of the Pearson test showed a value of p = 0.49, which indicated that there was no significant relationship between leucocytosis and blood glucose levels. The conclusion of this study is that the high number of leukocytes in T2DM patients is thought not to be caused by high blood glucose levels, but may be influenced by other factors related to the development of complications of T2DM disease. This research has important implications in understanding the pathogenesis and prevention of complications of T2DM.

Keywords: Leukocyte Count, Diabetes Mellitus Type 2, Inflammation

1. INTRODUCTION

In 2015, Indonesia has faced serious challenges in terms of type 2 diabetes mellitus, with it ranking seventh in the world and an estimated more than 10 million individuals affected by the disease. In just two years, in 2017, this figure increased to more than 10.3 million people with type 2 diabetes . This fact shows an alarming escalation in the prevalence of type 2 diabetes in Indonesia. Diabetes deaths in Indonesia are a serious problem, ranking second only to Sri Lanka in Southeast Asia. Even more worrying, diabetes with complications is the third highest cause of death in Indonesia (Dayrit et al., 2018; Mahendradhata et al., 2017). Therefore, the risks and impacts caused by type 2 diabetes mellitus have raised an urgent need to undergo deeper and comprehensive research. In addition, the prevalence of diabetes at the provincial level, such as in West Java, shows a clear picture of the magnitude of the challenges faced at the regional level. West Java has a diabetes prevalence of 1.3% with significant variation in its range. In the midst of this

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context, Bekasi city stands out as one of the regions with a significant diabetes rate, reaching 1.9%. This data emphasizes the need for more in-depth and specific research in the management of type 2 diabetes, especially at the regional level such as Bekasi.

Type 2 Diabetes Mellitus is a serious and complex condition that can lead to various complications. One of the early signs of complications that often arise is inflammation. In particular, early complications of type 2 diabetes are often characterized by microvascular damage, which can harm various organs and systems in the body (Chawla et al., 2016; Paul et al., 2020). Some research suggests that creatinine and CRP (C-reactive protein) levels can be used as clinical parameters and biomarkers to detect acute microvascular damage to kidney cells (nephron). This microvascular damage, if not detected and managed properly, can develop into serious complications due to type 2 diabetes (Amelia, 2021; Thayibah et al., 2018). Unfortunately, microvascular damage in patients with type 2 diabetes is often detected late due to delays in clinical laboratory trials (An et al., 2021; Gedebjerg et al., 2018). Some of the factors contributing to this delay include a lack of awareness of the importance of regular health checkups and the high cost of laboratory tests (Alain et al., 2021; Gebreyes et al., 2020). Research has also shown that inflammation can be recognized through increased levels of leukocytes in the blood (Kizilgul et al., 2018; Milosevic & Panin, 2019). Leukocyte count is one of the important components that play a role in insulin resistance, and elevated leukocyte counts often occur in type 2 diabetes patients with complications. Knowing the importance of regular checking of leukocyte counts can be a very important first step in preventing serious complications such as kidney failure, leg amputation, vision loss, and nerve damage in patients with type 2 diabetes.

This study aimed to investigate the role of biomarkers such as creatinine and CRP (C-reactive protein) in detecting acute microvascular damage in type 2 diabetes patients. This microvascular damage, if not detected and properly managed, can develop into serious complications. Unfortunately, microvascular damage in type 2 diabetes patients is often detected late due to delays in clinical laboratory trials. Factors such as lack of awareness of the importance of routine health checkups and high cost of laboratory tests also contribute to this delay. Leukocytes, in particular, can be used as an important clinical parameter to identify inflammation associated with complications of diabetes. In-depth research into the role of leukocytes can be a very important first step in preventing serious complications, such as kidney failure, leg amputation, vision loss, and nerve damage in patients with type 2 diabetes.

In this study, we wanted to provide a parameter solution for hematological examination which could be used as an indicator of microvascular inflammation in patients with type 2 diabetes mellitus to prevent complications. The results of this study can be used as an initial screening of inflammation and prevent complications in patients with type 2 diabetes mellitus.

2. METHODS

This type of research is descriptive research with a sampling method that is purposive sampling. The research was conducted in the target area of the Puskesmas Kalibaru and Kotabaru Bekasi with a research permit from the Dinas Kesehatan Bekasi District with no. 070/69B/Dinkes. SDK. The subjects in this study were residents of Kalibaru and Kotabaru who were diagnosed with type 2 diabetes mellitus and were treated at the Puskesmas Kalibaru and Kotabaru, Bekasi. Data analysis was performed using SPSS by using descriptive test, normality test and Pearson correlation test with variable blood glucose level and leukocyte values. In checking blood sugar using an autoclick, lancet, test strip, and blood sugar checking tool with the Accu-Chek brand. Meanwhile, the tools for sampling used a

mask, handscoon, tourniquet, alcohol swab, syringe, vacutainer needle, and a 6 ml EDTA tube. The tool for sample examination is hematology analyzer the Rayto brand type RT-7200. Sampling was carried out in coordination with puskesmas health workers and posbindu volunteers to collect patients. After the patient was collected, a blood sample was taken. Then the collected samples were taken to the STIKes Mitra Keluarga hematology laboratory using an ice box containing ice gel.

Arms in a straight position tourniquet placed 3 fingers above the elbow clay. The vein to be punctured is palpated. Respondents were asked to make a fist.

The location of the vein to be punctured is first disinfected with an alcohol swab. The vein is punctured with a needle. The tourniquet is removed when the venous blood has entered the syringe. The syringe suction is pulled slowly until the required volume is sufficient. An alcohol swab is placed at the puncture site. The syringe is withdrawn. the alcohol swab is pressed at the puncture site. The syringe is closed. Dry cotton is placed on the puncture. Plaster is attached to the puncture mark. The needle is removed. The blood samples were transferred to the purple EDTA vacutainer tube. The blood sample was homogenized. The blood sample was confirmed to be homogeneous with anticoagulant. type of whole blood sample on tap on the screen. Respondent data is entered by selecting profile in the sample test window and then pressing enter on the screen. The vacutainer tube is placed under the suction needle. Aspirate button is pressed. The suction needle is waiting to go up. Move the vacutainer tube. The hematology analyzer tool is waiting for the results to appear on the screen. The results of the examination of the leukocyte count were recorded.

3. RESULTS AND DISCUSSION

Result

The total respondents obtained in the study were 55 people consisting of 43 women and 12 men. In Table 1 it can be seen that the average value of blood glucose is 283 mg/dL and the average value of leukocyte count is 8,829 cells/ul.

Table 1. Univariate Analysis

Variable	Results (n= 55)
Sex	Female = 43 (78%), Male = 12 (22%)
Age	56 ±56 years (min= 36 year, max 71-year, modus= 47 years)
Blood glucose values	Mean= 393 mg/dL (min = 215 mg/dL, max= 649 mg/dL)
Leukocyte count	Mean= 8.820 cells/µl (min= 3.740 cells /µL, max= 17.220 cells /µL)

Table 2. Correlation Statistical Analysis

Statiscal Analysis	pValue
Normality Test	0.2
Pearson Correlation Test	0.49

The normal value of the leukocyte count is 4,000 - 10,000 cells/µL of blood and the normal value of blood glucose is <200 mg/dl (Kiswari, 2014). In Table 1 blood glucose levels at minimum levels are over the normal value limit> 120 mg/dL with a maximum of 393 mg/dL. The number of leukocytes in the sample has an average value of 8,820 cells/ µL which is still in the normal category. However, the highest value for the number of leucocytes

was 17,220 cells/ µL which had exceeded the normal value limit. To find out whether leucocytes can be used as a parameter for the presence of microvascular inflammation in patients with type 2 diabetes mellitus, continue the normality and correlation tests on random blood glucose variables and leukocyte values. The results of the Kolgomorov-Smirnov normality test showed a value of p = 0.2 (> 0.05). This indicates that the blood glucose data at the time and the leukocyte values were normally distributed. Then a correlation test was performed using the pearson test. Pearson test results in Table 2 the relationship between leukocyte values and sugar levels showed no relationship with the value of p = 0.490 (p> 0.05).

Discussion

Based on Table 1, type 2 diabetes mellitus sufferers are mostly experienced at the age of 47-55 years. Women are more affected by type 2 diabetes mellitus than men because menopause causes a decrease in the hormone estrogen (Paschou & Papanas, 2019; Stuenkel, 2017). Based on Table, a sample data obtained, the average age of the female sample ranges from 47-55 years, this age is the age at which menopause occurs. The hormones estrogen and progesterone function to increase the insulin response in the blood. The decrease in the hormones estrogen and progesterone results in insulin resistance (Yan et al., 2019; L. Zhu et al., 2014). In addition, a women are more at risk of developing type 2 diabetes mellitus because an increase in body mass index, monthly cycle syndrome, and post-menopausal also makes the distribution of fat in the body easy to accumulate, causing type 2 diabetes mellitus (Lee et al., 2021; Nam et al., 2022). During menopause, estradiol levels decrease. Decreased levels of estradiol in the body can affect the body's metabolism so that it can cause hyperusemia and insulin resistance (Amelia, 2021; Thayibah et al., 2018). The associations of sex steroid hormones with insulin resistance are different depending on the estrogen status, in postmenopausal conditions estradiol hormone therapy can reduce insulin resistance. However, in hyperestrogen conditions it can cause insulin resistance (Campello et al., 2017; Gregorio et al., 2021).

The majority of type 2 sufferers are experienced by people aged 40 years and over, because insulin resistance will increase and may also have risk factors for obesity. At the age of 46-64 years, insulin resistance occurs and the aging process causes resistance due to the decreased ability of pancreatic B cells at that age (Li, N., Liu et al., 2019; M. Zhu et al., 2021). Insulin resistance is the inability of cells to respond to insulin causing high blood glucose levels or hyperglycemia so that the body's cells do not get enough glucose to be converted into energy (Daryabor et al., 2020; Prasad et al., 2020). The cause of insulin resistance is obesity because the large number of fat cells causes the secretion of TNF-α and leptin to increase (Tong et al., 2022; Wondmkun, 2020). TNF-α and leptin released by fat cells can inhibit insulin action in the liver by interfering with signaling for insulin receptors (Gan et al., 2018; Zhang et al., 2022). The increase in excess free radicals is also a cause of insulin resistance. The conversion of excess glucose into energy in obesity causes an increase in the formation of excess free radicals so that muscle and fat cells carry out self-protection (Hurrle & Hsu, 2017; Yaribeygi et al., 2020). Self-protection of muscle and fat cells is by becoming resistant to insulin to reduce the entry of glucose and free fatty acids into the cells. Glucose and free fatty acids can stimulate cell dysfunction and cause inflammation at the cellular level (Halim & Halim, 2019; Wronka et al., 2022).

Table 2 shows that there is no relationship between the increase in the number of leukocytes and blood glucose levels. This may be due to several factors such as the drugs the respondent has consumed after being diagnosed with type 2 diabetes mellitus. Previous research stated that higher leuko-cyte counts was correlated with uncontrolled diabetes (Milosevic & Panin, 2019; Narjis et al., 2021). Accompanied by other markers, chronic

inflam-mation that can be shown by this factor could be related to pathogenesis and the progression of these diabetes-related complications. Base on the data in Table 1 above, there are 16 respondents who have glucose values and leukocyte values above normal. Questionnaire data shows that 17 respondents suffer from hypertension. Leukocytes play a role in the inflammatory process in the pathogenesis of type 2 diabetes mellitus and the risk of endothelial activation, vascular dysfunction, and hypertension (Sun et al., 2019; Sung et al., 2017). The inflammatory process also contributes to the pathogenesis of cardiovascular complications in patients with type 2 diabetes mellitus which causes an increase in the number of leukocytes (Bajpai & Tilley, 2018; Daryabor et al., 2020; Ritchie & Abel, 2020). Low insulin levels can stimulate the production of leukocytes in the bone marrow and an increase in leukocytes is found in diabetic patients who have inflammation of the blood vessels (Berbudi et al., 2020; Xia et al., 2017). The chronic inflammatory response causes diabetes complications by inducing massive endothelial injury and an increase in several mediators and oxidative stress (Amelia et al., 2021; Beandrade et al., 2022; Burgos-Morón et al., 2019). C-reactive protein and creatinine are parameters that can be used as a sign of acute inflammation in patients with type 2 diabetes mellitus (Amelia et al., 2019; Zbaar et al., 2022). In addition, the parameter HbA1C value has a relationship with fasting blood glucose levels. High HbA1C results are followed by high hs-C reactive protein (Park & Lee, 2022; Seo & Shin, 2021). This means that high levels of glucose in the blood can trigger an increase in laboratory parameters for signs of inflammation such as leukocytes, hs-CRP. Although the high leukocyte value still requires supporting parameters to prove the presence of inflammation in patients with type 2 diabetes mellitus, this can be used as an early sign to next step diagnose a source of inflammation.

4. CONCLUSION

The conclusion from the results of this study is the increase in a leukocytes count is indicated by the presence of additional complications such as hypertension in patients with type 2 diabetes mellitus.

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