ORIGINAL ARTICLE

Correlation Between Eosinophil to Leukocyte Ratio (ELR) and HbA1c in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Introduction: : Diabetes mellitus is one of metabolic diseases characterized by an increased blood glucose levels. Eosinophil, one of leukocyte components, have an important role in metabolic homeostasis, especially in type 2 diabetes patients. Leukocyte are responsible for cellular defense and humoral response to inflammatory cells in blood vessels. Glycated hemoglobin (HbA1c) is a test to measure and control blood glucose levels. A higher serum HbA1c level indicates a greater risk of a development of DM-related complications. This study used an observational analytic design with a cross sectional approach and involved 100 research subjects. Data were analyzed with Kolmogorov-Smirnov and Pearson correlation test with significance of p> 0.05 and p <0.05, respectively. There was no significant correlation between ELR and HbA1c in type 2 DM patients with r=-0,181 and p=0,071 (p>0,05). Further research was needed to determine the correlation between ELR and other fasting blood glucose parameters or inflammatory markers, in addition to HbA1c levels.

Keywords: Diabetes Mellitus, Eosinophil to Leukocyte Ratio, HbA1c

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INTRODUCTION

Diabetes Mellitus (DM) is a group of symptoms caused by increased blood glucose levels due to insulin deficiency (1). The results of the Basic Health Research in 2007 by the Ministry of Health in Indonesia showed the average DM prevalence of 5.7% among a population above 15 years old in the urban area. The lowest DM prevalence of 1.7% was reported in Papua Province, while the largest prevalence of 11.1% was reported in West Kalimantan and North Maluku Provinces. In addition, the prevalence of impaired glucose tolerance (IGT) in West Papua Province ranged from 4.0% to 21.8%, while an average prevalence of 10.2% was reported in Jambi Province. This data shows a great number of DM patients in Indonesia with the possibility of further increasing numbers in the future (2).

There are several types of diabetes mellitus, namely type 1 diabetes, type 2 diabetes, and gestational diabetes. Type 2 Diabetes Mellitus is a metabolic disease characterized by increased blood glucose levels due to decreased insulin secretion by beta cells of the pancreas or insulin resistance (3). Insulin resistance in muscles and liver and failure of beta-pancreatic cells are known as pathophysiological damage of type 2 DM. Systemic inflammatory markers are risk factors for the development of type 2 DM and micro and macrovascular complications. Chronic inflammation in DM patients, characterized by increased production of acute-phase cytokines and reactants and activation of inflammatory signals are known to be associated with the pathogenesis of type 2 DM. Inflammation will affect insulin signals which indirectly increase the risk of non-obese type 2 DM. In addition, inflammation subsequently triggers beta-cell death. However, the correlation between inflammation and type 2 DM is not clearly understood (4).

Glycated hemoglobin (Hb) or HbAlc is formed when Hb binds to glucose in the blood. Regularly controlled type 2 Diabetes Mellitus is indicated by HbA1c levels <7%, while uncontrolled type 2 DM is indicated by HbA1c levels >7% normal range. A higher serum HbA1c level indicates a greater risk of the development of DM-related complications (2). Eosinophil, a type of leukocyte components, have an important role in metabolic homeostasis. Immune response and metabolic regulation as a mechanism of homeostasis are able to

cause chronic metabolic diseases, especially in type 2 DM patients (5). Leukocyte or white blood cells contain nuclei and have an important role in cellular defense and the humoral response of organisms to foreign substances. Previous epidemiological studies showed a correlation between the number of leukocytes, non-specific marker for inflammation, and the risk of DM (4).

The purpose of this study was to determine the correlation between ELR and HbA1c in type 2 DM patients. This research was expected to contribute to knowledge and insight of researchers about type 2 DM and to determine the correlation between ELR and HbA1c in type 2 DM patients.

MATERIALS AND METHODS

This study was an observational analytic study with a cross-sectional approach to determine the correlations between ELR and HbA1c in type 2 DM patients by involving 100 research subjects. The study was performed in March-May 2018 at the Clinical Pathology Installation of Regional General Hospital Dr. Moewardi in Surakarta with type 2 DM inpatients and outpatients as accessible population, while the target population was inpatient and outpatient type 2 DM patients at the Clinical Pathology Installation of Dr. Moewardi Surakarta in March 2011-April 2015.

The data were then presented in tabular form and statistically analyzed using Kolmogorov-Smirnov to determine the normality and the Pearson correlation test with 95% confidence intervals and significance of $p < 0.05$.

RESULTS

Table I shows the ELR and HbA1c in type 2 DM patients. The mean age of the study subjects (respondents) was 55.51 ± 9.96 years. The gender of research subjects (respondents) was dominated by female patients (63.00%) compared to males (37.00%). The mean of total leukocyte and total eosinophil counts in this study was 11688.00 ± 6133.71/pL and 162.19 ± 148.77/pL, respectively.

Table I : Characteristics of Research Subjects

Variable	Total (%)	Mean	SD
Age(year)		55.51	9.96
Sex			
Male	37(37.00)		
Female	63(63.00)		
Total		11688.0	6133.1
Leukocyte counts (/µL)			
Total eosinophil counts (/µL)		162.19	148.77

SD=Standard deviation
/µL= per micro litre.

To determine the correlation between ELR and HbA1c in type 2 DM patients, a normality test using Kolmogorov-Smirnov test was first performed to determine the data distribution of ELR and HbA1c to select the proper statistical test. $p > 0.05$ indicated normal data distribution, while $p < 0.05$ indicated abnormal data distribution. The results of the normality test can be seen in Table II.

Table II : The Results of Normality Test Using Kolmogorov-Smirnov

Variable	P	Interpretation
Eosinophil to Leukocyte Ratio (/µL)	0.001	Abnormal data distribution
HbA1c (%)	0.358	Normal data distribution

p>0,05 indicated normal data distribution in Kolmogorov-Smirnov test
HbA1c= Hemoglobin A1c.

Based on the results of the one-sample Kolmogorov-Smirnov test in Table II, the probability value (p) of ELR and HbA1c in type 2 DM patients was 0.001 and 0.358, respectively. The probability value of the ELR did not exceed the significance level of 5% ($p < 0.05$), suggesting an abnormal data distribution. Due to abnormal data distribution of one of the subjects, a data transformation test was performed, with the results as shown in Table III.

Table III : The Results of Normality Test Using Kolmogorov-Smirnov (After Data Transformation)

Variable	P	Interpretation
Log of eosinophil to leukocyte ratio (/µL)	0.538	Normal data distribution

p>0.05 indicated normal data distribution in Kolmogorov-Smirnov test.

Based on the one-sample Kolmogorov-Smirnov test in Table III, the probability value (p) of log ELR in type 2 DM patients was 0.538. The probability value of the ELR exceeded the significance level of 5% ($p > 0.05$), suggesting normal data distribution and a need to further statistical analysis using the Pearson correlation test.

Data were then analyzed to determine the correlation between ELR and HbA1c in type 2 DM patients using computer assistance. The results were shown in Table IV.

Table IV : Correlation between eosinophil to leukocyte ratio and HbA1c levels

Variabel	Mean±SD	R	P
Log eosinophil – leukocyte ratio (/µL)	-2.00±0.51	-0.181	0.071
HbA1c (%)	9.56±3.70		

SD = Standard Deviation
r = pearson correlation coefficient, p = significance level, <0.05(significant),
HbA1c= Hemoglobin A1c.

Based on the results shown in Table IV, the mean of the log eosinophil to leukocyte ratio and that of HbAlc was -2.00 ± 0.51 / pL and 9.56 ± 3.70%, respectively. Analysis of the results was carried out with the assistance of the computer and the significance value of 0.071 (p> 0.05) showed no correlation between ELR and HbAlc in type 2 DM patients.

DISCUSSION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia due to disruption in insulin secretion and/or insulin actions. The mechanism of inflammation is involved in the pathogenesis of type 2 DM, resulting in insulin resistance, reduced insulin secretion from the pancreas, and beta-cell dysfunction (6).

Based on the calculation of ELR and the measurement of HbAlc in type 2 DM patients, the research subjects (Table 1) were dominated by female patients (63.00%) followed by males (37.00 %), suggesting a higher prevalence of type 2 DM in women. This was probably due to less activity of women compared to men. The mean of total leukocyte and that of total eosinophil was 11688.00 ± 6133.71/pL and 162.19 ± 148.77/pL, respectively, suggesting a relatively higher mean of leukocyte count and normal eosinophil count. The high leukocyte count in this study was in accordance with a research by Xu et al., 2013 in patients with diabetic ketoacidosis and diabetic ketosis. However, this study found that the eosinophil count was within normal limit, contradictory to a study by Xu et al., 2013 which showed low eosinophil count.

Table IV showed that the log ELR and the mean of HbAlc levels was -2.00 ± 0.51/gL and 9.56 ± 3.70%, respectively. > 8% increase of HbA1c indicated uncontrolled DM and relatively high risk of long-term complications. In this study, no correlation was found between ELR and HbA1c in type 2 DM patients (r = -0.181 and p = 0.071). In addition, this study showed a different HbA1c level from the results of a study by Zhu et al., 2013 which showed average HbA1c of 5,8 ± 1.0% indicating a normal level.

A study by Xu et al., in 2013 found a correlation between the number of leukocytes and blood glucose in diabetic ketoacidosis patients with r = 0.722 and p <0.05 (7). In addition, a research by Konishi et al., in 2017 suggested that there was significantly weak correlation of Eosinophil to Leukocyte Ratio (ELR) in STEMI patients (8). Contrastingly, this study found no correlation between REL and HbA1c in type 2 DM patients (r = -0.181 and p = 0.071). This is caused by the adherence of eosinophils in STEMI patients to coronary thrombosis, increased cortisol concentrations, and eosinophil aggregation at the site of inflammation. However, in type 2 DM patients it is caused by several possibilities as follows: no adherence of eosinophils to coronary thrombosis, no increase in cortisol concentrations, tissue necrosis, the presence of other undetected trauma, and the presence of a disease that affects the eosinophil-leukocyte ratio in type 2 DM patients.

Limitations of this study were the use of secondary data, no control of possible external variables such as the length of DM in patients, regularity of blood glucose control, drug use, history of other diseases, genetic factors, and other risk factors including age and obesity that potentially affected research results.

CONCLUSION

There was no correlation between ELR and HbA1c levels in type 2 DM patients (r= - 0.181 and p= 0.071).

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