The Relationship of Neutrophil-Lymphocyte Ratio and Glycemic Control in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Progressivity of type 2 Diabetes Mellitus (DM) is associated with a condition of chronic inflammation. The Neutrophil-Lymphocyte Ratio (NLR) has become a potential new marker of inflammation to detect chronic inflammation. This research aimed to determine NLR differences between controlled type 2 DM and uncontrolled type 2 DM groups. This research conducted an observational with a cross-sectional approach to 56 patients with type 2 diabetes. The identity, anthropometric measurements, and laboratory data of routine blood exam and HbA1c were carried out on each research subject, and then the NLR calculations were performed. The subjects were 20 (35.70%) controlled type 2 DM patients, 36 (64.30%) uncontrolled type 2 DM patients, consisting of 36 (64.30%) male and 20 (35.70%) females. The NLR value was statistically significantly higher in uncontrolled type 2 DM patients than controlled type 2 DM patients, which was 1.90±0.84 compared to 1.52±0.50 (p=0.035). There was a significant difference in the NLR value between the uncontrolled type 2 DM group and the controlled type 2 DM group.

Keywords: Diabetes mellitus, NLR, glycemic control

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterized by hyperglycemia resulting from the failure of the pancreas to secrete insulin adequately, a defect in insulin action, or both. Diabetes mellitus is still a health problem and a significant threat to health nowadays due to the increase of patients and the increase in complications.[1-4]

Diabetes Mellitus type 2 (type 2 DM) is the most common group of types of DM. Long-lasting hyperglycemia can cause various complications, both microvascular and macrovascular. Complications can manifest as retinopathy, nephropathy, neuropathy, coronary heart disease, peripheral vascular disease, and cerebrovascular disease. One factor that plays a role in the pathogenesis of insulin resistance in type 2 diabetes is inflammation. Subclinical chronic inflammation is a process that plays an essential role in the progression and chronic complications of type 2 DM.[3,5,6]

Type 2 DM is associated with chronic inflammatory conditions. The chronic state of inflammation induces hypersecretion of proinflammatory cytokines such as IL-6 and TNF-α,

leading to persistently high neutrophil counts. This situation can interfere with the anti-inflammatory effects of insulin. The Neutrophil-Lymphocyte Ratio (NLR) has become a potential new marker for chronic inflammation. In chronic inflammation, the neutrophil count will increase, and the lymphocyte count will decrease. The NLR examination is widely used as a marker of inflammation because it is relatively easy to do and inexpensive.[7]

METHODS

This research used a cross-sectional design and was conducted at the Hasanuddin University Hospital Clinical Pathology Laboratory Installation for sampling. The examination was done at the Hasanuddin University Medical Faculty Research Unit/Hasanuddin University Hospital throughout August-September 2020.

The research population was all adult patients examined at the Internal Medicine Metabolic Endocrine Outpatient Clinic Dr. Wahidin Sudirohusodo Hospital, Makassar and RSPTN Hasanuddin University type 2 DM patients. Therefore, the research sample was an affordable population that met the research criteria (inclusion criteria). The inclusion criteria were adults aged 18 to

85 years old who came to the Endocrine and Metabolic Outpatient Clinic of Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital and have a history of disease data and routine blood tests, FBG and HbA1c.

Data analysis was performed using SPSS version 22. The statistical analysis carried out was descriptive statistical calculations and frequency distribution as well as the Spearman's correlation and Mann-Whitney tests. This statistical test was a non-parametric test used for data analysis that was not normally distributed. The result of the test was statistically significant if the p-value was < 0.05.

After receiving ethical clearance, this research was conducted by considering respect for subjects, beneficence, non-maleficence, and justice from the Health Research Ethics Commission (KEPK) Faculty of Medicine, Hasanuddin University-RSPTN UH-Dr. Wahidin Sudirohusodo Hospital, Makassar with article number 492/UN4.6.4.5.31/PP 36/2020.

RESULTS AND DISCUSSION

The research was conducted from August to September 2020 using a cross-sectional design involving 56 subjects who met inclusion and exclusion criteria. The research subjects were patients who had been diagnosed with type 2 DM by clinicians who came to the Endocrine Outpatient Clinic of Dr. Wahidin Sudirohusodo Hospital. Subjects consisted of 20 (35.70%) controlled type 2 DM patients and 36 (64.30%) uncontrolled type 2 DM patients, 36 (64.30%) male patients and 20 (35.70%) female patients. The age range of the subjects was 35-84 years, with a mean of 58.39±9.51 years. This data is in line with the 2018 Riskesdas data, which shows that the proportion of DM increases with age, the highest found in the 55-64 year age group.[2] The general characteristics of the research sample are shown in Table 1.

The NLR values varied between 0.62-4.31 with a mean of 1.77±0.75, and HbA1c levels varied between 4.90-12.20 with a mean of 7.85±1.82. Long-suffering from diabetes with a mean of 6.1±5.5. Hemolyzed and icteric samples were not examined.

Table 2 explains that there was a significant difference in the NLR value between the uncontrolled DM group and the controlled DM group with a p-value < 0.05.

Table 2. NLR value according to DM control

Variable	Control DM	n	Mean	SD	p
NLR	Controlled	20	1.52	0.50	
					0.035
	Uncontrolled	36	1.90	0.84	

The NLR value was higher in uncontrolled DM (1.90) than in controlled DM (1.52). The statistical tests showed a p < 0.05, which means that there was a significant relationship between uncontrolled DM and high NLR values (Figure 1).
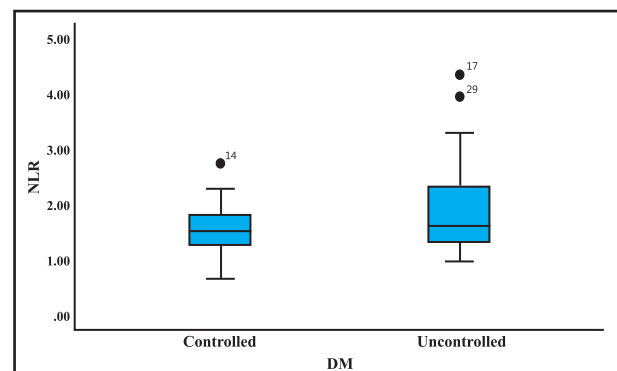

Figure 1. Comparison of NLR according to DM control

Based on Table 2 and Figure 1, the NLR value in uncontrolled type 2 DM was statistically significantly higher than controlled DM. The increase in NLR occurs due to the increase in proinflammatory cytokines that occur in type 2 DM. The increase in proinflammatory cytokines causes neutrophilia and

Table 1. Characteristics of research samples (n=56)

Variable	n (%)	Minimum	Maximum	Mean±SD
Gender				
Male	36 (64.30)			
Female	20 (35.70)			
Age (year)		35	84	58.39±9.51*
HbA1c (%)		5.10	12.2	7.87±1.81*
≤7	20 (35.70)			
> 7	36 (64.30)			
NLR		0.62	4.31	1.77±0.75*
Duration DM (year)		1	27	6.1±5.50

Information: *Kolmogorov-Smirnov test, SD=Standard Deviation, HbA1c= Glycated Hemoglobin, NLR= Neutrophil Lymphocyte Ratio

lymphopenia. Lymphopenia also occurs due to insufficient proliferation of lymphocytes.[8,9]

The results of this research are in line with a study conducted by Sefil *et al.*, which stated that there was a statistically significant difference between NLR in type 2 DM patients with HbA1c ≤ 7% and > 7%. The results of this research were different from the study conducted by Dik, who stated that there was no statistically significant difference between NLR in type 2 DM patients with HbA1c < 10% and ≥ 10%.[9,10]

In DM patients, there is a low level of chronic inflammation. This inflammation causes hypersecretion of inflammatory factors such as CRP, IL-6, TNF-α, and MCP-1, stimulating an increase in neutrophil production. In DM patients, there is also interference with T-cell signal transduction, which causes a decrease in the number of T-cells.[10]

CONCLUSIONS AND SUGGESTIONS

There was a significant difference in the NLR value between the uncontrolled and controlled DM groups.

Further research needs to be carried out using a larger sample population with other useful variables to assess glycemic control in preventing more severe complications of DM.

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