CONTENTS

RESEARCH

Proportion of Isomorphic Erythrocyte Urine in Diabetic Kidney Disease with Flow cytometry Methods
Erica Catarina, Coriejati Rita, Basti Andriyoko, Ida Parwati ........................................................................................................ 1 - 6

Analysis of Ret-He in Chronic Kidney Disease Patients at Dr.Wahidin Sudirohusodo Hospital, Makassar
Febrina Rovani, Asvin Nurulita, Mansyur Arif .......................................................................................................................... 7 - 10

Analysis of Red Blood Cell Distribution Width Coefficient of Variation on Stroke Patient
Kartika Paramita, Agus Alim Abdullah, Mansyur Arif .................................................................................................................. 11 - 15

IgA Anti-Dengue Profile in Samples with Positive Dengue PCR or NS1
M Thohirin Ramadhan, Aryati, M Vitanata Arfijanto .................................................................................................................. 16 -20

The Association of Insulin Resistance and Lipid Profile Ratio in Metabolic Syndrome
Rini Rahmayani, Adi Koesoema Aman, Santi Safri ....................................................................................................................... 21 - 25

Correlation of Free Hemoglobin Level and Plasma Nitric Oxide in Packed Red Cell during Blood Bank Storage Period
Ricca Fitria, Rismawati Yaswir, Zelly Dia Rofinda, Desywar ....................................................................................................... 26 - 30

Correlation of Lipid Profile with Interleukin-12 in Type 2 Diabetes Mellitus
Meri Ponda Sari, Hanifah Maani, Ellyza Nasrul, Zelly Dia Rofinda ............................................................................................... 31 - 34

Platelet Indices for Predicting Liver Fibrosis in Patients with Chronic Hepatitis B Infection
Shendy Sherly Soeliliawan, Darwati Muhadi, Mutmainnah ........................................................................................................... 35 - 37

The Relationship between the Level of Interleukin-6 and Procalcitonin in Severe Sepsis Patients at the Adam Malik Hospital
Sesily C Nainggolan, Adi Koesoema Aman, Achsanudin Hanafi .................................................................................................. 38 - 41

Spontaneous Platelet Aggregation in Third-Trimester Pregnancy at Adam Malik Hospital, Medan
Rezqi Maulani Jusuf, Hotma Partogi Pasaribu, Herman Hariman ................................................................................................ 42 - 46

Correlation between Presepsin and Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score as an Organ Dysfunction Marker in Sepsis
Stevi Dwiyani, Agnes Rengga Indrati, Leni Lismayanti, Adhi Kristianto S .................................................................................... 47 - 52

Correlation of Atherogenic Index of Plasma with Stenosis Level of Coronary Artery in Acute Coronary Syndrome
Iliamifithri, Rismawati Yaswir, Eugeny Alia, Efrida ..................................................................................................................... 53 - 57
The Compatibility of Neutrophil to Lymphocyte Count Ratio with Serum Procalcitonin as Bacterial Infection Markers in Sepsis Patients
Elvinawaty, Hanifah Maani, Zelly Dia Rofinda, Husni ................................................................. 58 - 63

The Diagnostic Value of Troponin I Testing to Coronary Angiography with a Point of Care Testing Instrument in Patients with Acute Myocardial Infarction
Riska Anton, Sheila Febriana, Asvin Nurulita, Uleng Bahrun ............................................................. 64 - 67

Comparisons of Fibro Q Index and FIB-4 in Various Stages of Chronic B Hepatitis
Evy Adrianti, Liong Boy Kurniawan, Ibrahim Abdul Samad ............................................................... 68 - 72

Microorganism Pattern on Nasal Cavity of End Stage Renal Disease Patients with Regular Hemodialysis and Staffs in Hemodialysis Installation Adam Malik Hospital Medan
Imelda Damayanti, Ricke Loesnihar, Syafrizal Nasution ...................................................................... 73 - 78

The Correlation between the Mean Platelet Volume Values with Thrombocyte Aggregation in Nephropathy Diabetic Patients
Agus Sunardi, Nadjwa Zamalek Dalimoentoe, Coriejati Rita, Adhi Kristianto Sugianti .......................... 79 - 85

The Role of Platelet Concentration Transfusion on The Correlation between Platelet Number and Maximum Amplitude with Bleeding Volume Post Cardiopulmonary Bypass
Ryan Bayusantika Ristandi, Nida Suraya, Leni Lismayanti, Sylvia Rachmayati ........................................ 86 - 90

The Relationship between Nitric Oxide and Glycemic Control in Controlled and Uncontrolled Type 2 Diabetes Mellitus Patients in the Adam Malik Hospital Medan
Yessy Suziarty, Ratna Akbari Ganie, Santi Syafril ................................................................................ 91 - 94

Analysis of Red Blood Cell Distribution Width Value Towards Fibrotic Stage in Chronic Hepatitis B
Fatma Idris, Darwati Muhadi, Mutmainnah ............................................................................................ 95 - 98

Correlation of Serum High-Density Lipoprotein Cholesterol and Homocysteine Level in Patient with Acute Myocardial Infarction
Yayie Dwina Putri, Rismawati Yaswir, Lillah, Tuty Prihandani .................................................................. 99 - 103

Correlation between Galectin 3, Creatinine and Uric Acid on Stage V Chronic Renal Failure
Indranila KS, Guruh AI, Meita H ........................................................................................................... 104 - 110

LITERATURE REVIEW
Role of Delta Check in Clinical Laboratory Services
Osman Sianipar ........................................................................................................................................ 111 - 114

CASE REPORT
Primary Myelofibrosis
Muhammad Irhamsyah, Darwati Muhadi, Mansyur Arif ....................................................................... 115 - 120

Malignant Lymphoma with Leukemic Phase in Children
Sahriany S, Agus Alim Abdullah, Mansyur Arif ....................................................................................... 121 - 128
THE RELATIONSHIP BETWEEN NITRIC OXIDE AND GLYCEMIC CONTROL IN CONTROLLED AND UNCONTROLLED TYPE 2 DIABETES MELLITUS PATIENTS IN THE ADAM MALIK HOSPITAL MEDAN

Yessy Suziarthy, Ratna Akbari Ganie, Santi Syafri

1Department of Clinical Pathology, Faculty of Medicine, University of Sumatera Utara/Adam Malik Central Hospital Medan, Indonesia. Email: yessy_suziarthy@yahoo.co.id
2Department of Internal Medicine, School of Medicine, University of Sumatera Utara/Adam Malik Central Hospital Medan, Indonesia

ABSTRACT

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia. Hyperglycemia and other metabolic changes can cause Nitric oxide (NO) production disturbance. This study investigated the difference in the levels of NO and its relationship with HbA1c in controlled and uncontrolled diabetes mellitus type 2 patients in the Adam Malik Hospital. This study was a cross-sectional study, conducted in Outpatient Clinic and Inpatient Ward of Internal Medicine Section of Endocrinology in the Adam Malik Hospital on June through October 2016, involving 70 patients type 2 Diabetes Mellitus (DM) consisting of 35 controlled type 2 diabetes patients and 35 uncontrolled type 2 diabetes patients that fulfill this study's criteria. Nitric oxide examination conducted by using Chemwell analyzer with the principle of double-antibody sandwich using Enzyme-Linked Immunosorbent Assay (ELISA). There was no significant relationship between HbA1c and Nitric oxide in patients with controlled (r = 0.264) (p = 0.125) and uncontrolled (r = 0.194) (p = 0.265) type 2 diabetes mellitus. But there was a significant relationship between HbA1c and NO in patients with type 2 DM (r = 0.636) (p = 0.0001). In this study, there was no significant association between HbA1c and Nitric oxide levels in patients with controlled and uncontrolled type 2 diabetes mellitus. There is a statistically significant relationship between HbA1c and NO in patients with type 2 diabetes.

Key words: Type 2 diabetes mellitus, HbA1c, nitric oxide

INTRODUCTION

Diabetes mellitus is a metabolic disorder, which prevalences increases annually.1 It is prevalence in Indonesia is in the seventh highest under China, India, United States, Brazil, Russia, and Mexico. World Health Organization predicts that the number of diabetes mellitus patients in Indonesia will increase from 8.4 million in 2000 to 21.3 million in 2030.2

Diabetes mellitus is the disease with the highest incidence in Medan in September–October 2009.3 Based on an initial survey from medical records done by researchers in the Adam Malik Hospital Medan, it stated that the number of patient visits with diabetes mellitus diagnosis in inpatient ward was 1,660 patients in 2013, 1,013 patients in 2014, and 1,014 patients in 2015. Meanwhile, the number of Diabetes mellitus patients visits were 8,567 patients in 2014, 13,802 patients in 2014 and 14,968 patients in 2015.

Diabetes mellitus patients are expected to undertake a medical examination and receive treatment routinely to monitor their metabolic status. HbA1c nowadays is still considered as a single parameter that stands for the most prominent and independent to control metabolic condition, to evaluate the risk factors of diabetes complications and to monitor the treatment.4

Diabetes mellitus is a metabolic condition characterized by chronic hyperglycemia. The long-term effects of diabetes mellitus are cellular damage, inflammation and multiorgan failure. The diabetes complications are differentiated into two major parts, macrovascular complications (coronary artery disease, peripheral vascular disease, and stroke) and microvascular complications (diabetic nephropathy, retinopathy, and neuropathy).5 Endothelial dysfunction is the most common problem among the other complications. The endothelial cells secrete a different mediator such as vasodilator, i.e. nitric oxide and vasoconstrictor such as endothelin-1. The hyperglycemia and other metabolic disruption can cause disorder in NO production.6 Endothelial dysfunction in type 2 diabetes mellitus patients, can cause cardiovascular disease. Therefore, endothelial dysfunction is the
first feature of cardiovascular complication in type 2 diabetes mellitus.\(^5\)

This research was aimed to know wheather there is a relationship between NO concentration with glycemic control (HbA1c) in controlled and also uncontrolled type 2 diabetes mellitus patients in the Adam Malik General Hospital Medan.

**METHODS**

This study was a cross-sectional study conducted in patients of Outpatient Clinic and Inpatient Ward of Endocrinology Section, Department of Internal Medicine Adam Malik General Hospital Medan in June-October 2016 the inclusion were male/female and type 2 diabetes mellitus patient. The exclusion criteria were pregnant, smoking, hypertension, dyslipidemia, and coronary heart disease. This study involved 70 type 2 diabetes mellitus patients that consisted of 35 controlled type 2 DM patient and 35 uncontrolled type 2 DM patients.

The patient’s serum samples were used for nitric oxide examination. Nitric oxide was measured with Chemwell analyzer. The principle of this examination is a double antibody sandwich Enzyme-Linked Immunosorbent Assay (ELISA). Meanwhile, the HbA1c examination was measured from EDTA blood sample. Thermo Fischer Scientific Indiko automatic analyzer was used to measure the HbA1c. The principle of this device is turbidimetric immununoassay using latex particles conjugated in monoclonal antibodies.

The statistical analysis was done to know the differences of NO concentration among controlled and uncontrolled type 2 diabetes mellitus patient. The independent t-test was used if the data were normally distributed; otherwise, Mann-Whitney test was used. The correlation between nitric oxide and HbA1c in controlled and uncontrolled type 2 diabetes mellitus was assessed with Pearson correlation test if the data were normally distributed and Spearman’s rho test if the data were not normally distributed.

**RESULT AND DISCUSSION**

This study involved 70 patients diagnosed as type 2 diabetes mellitus with age ranged from 22-80 years old. The mean age was 54.64 years old. The number of female subjects (n=28) was higher than male (n=42).

As shown in Table 1, the mean age of controlled type 2 DM was 55.6 years old, older than the mean age of uncontrolled type 2 DM that was 53.69 years old. The mean age between the two groups was significantly different with p=0.008. However, there was no significant difference in the field of sex between the two groups with p=0.333.

As shown in Table 2, the median concentration of NO in uncontrolled type 2 diabetes mellitus was 1063.5 pg/mL. This concentration was higher than in

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type 2 DM</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controlled</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>23 (65.7)</td>
<td>19 (54.3)</td>
</tr>
<tr>
<td>Male</td>
<td>12 (34.3)</td>
<td>16 (45.7)</td>
</tr>
<tr>
<td>Female</td>
<td>55.60 ± 15.4</td>
<td>53.69 ± 9.8</td>
</tr>
</tbody>
</table>

Significantly different if p<0.05, the differential test used: * = independent t-test and ^ = Mann-Whitney U test

| Table 2. Characteristics of the subjects based on laboratory examination results |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | N               | HbA1C(%) Median (Min-Max) | NO (pg/mL) Median (Min-Max) | p                |
| Controlled type 2 DM | 35               | 6.2 (4.2-6.9) | 535.9 (279.3 - 4494.6) | <0.0001 ^        |
| Uncontrolled type 2 DM | 35              | 9.9 (7.0-17.4) | 1063.5 (520.3 - 5725.7) | <0.0001 ^        |
| Total           | 70               |                 |                 |                 |

Significantly different if p < 0.05. The differential test was Mann-Whitney U test
controlled type 2 DM patients which the median value was 535.9 pg/mL. Statistical analysis result showed significant differences in NO concentration between uncontrolled type 2 diabetes mellitus and controlled type 2 diabetes mellitus patients ($p<0.0001$).

As shown in Figure 1, Spearman’s rho test results showed that there was no correlation between HbA1c and NO concentration in controlled type 2 diabetes mellitus patients ($r=0.264$) and the statistic analysis results also showed that there was no significant correlation between HbA1c and NO concentration in controlled type 2 diabetes mellitus patients ($p=0.265$).

![Figure 1. Correlation of HbA1c and NO in controlled type 2 diabetes mellitus patients](image1)

Figure 2 showed, the Spearman’s rho test results there was no correlation between HbA1c and NO concentration in uncontrolled type 2 DM patients ($r=0.194$) and the statistic analysis results also showed that there was no significant correlation between HbA1c and NO concentration in uncontrolled type 2 DM patients ($p=0.636$).

![Figure 2. Correlation of HbA1c and NO in uncontrolled type 2 DM](image2)

Free radical, the NO, has emerged as a primary signal that regulates every essential cellular function and acts as a potent mediator for cell damage in many conditions. Vascular injury in diabetes as a result of hyperglycemia has been related to oxidative stress which causes intracellular glutathione depletion by increasing extracellular superoxide dismutase in plasma which inhibits lipid peroxidation and causes complications in diabetes. The increase in superoxide dismutase concentration can cause endothelial nitric oxide synthase (eNOS) isof orm dysfunction by trigger advanced glycation end product, and poly (ADP-ribose) polymerase take place. Nitric oxide is a gas molecule secreted by endothelial cells that act as the central regulator of endothelial function. Nitric oxide can be synthesized as conversion products from L-arginine precursor into L-citrulline. This reaction is catalyzed by nitric oxide synthases (NOSs), i.e. neuronal NOS (nNOS), endothelial NOS (eNOS) and inducible NOS (iNOS). Nitric oxide is the central molecule to regulate the process related to metabolic, vascular and cellular function.7

A study in coronary heart disease patients with and without diabetes mellitus by Widiaswill showed decreased production of anti thrombotic and vasodilator compound such as NO, thrombomodulin, and tissue plasminogen activator (tPA).8

The recent study found a strong positive correlation between HbA1c and NO concentration in type 2 DM patients ($r=0.636$). Statistical test result found a significant correlation between HbA1c and NO concentration in type 2 DM patients ($p=0.125$) (Figure 3).

![Figure 3. Correlation between HbA1c and NO concentration in type 2 DM](image3)
NO concentration in type 2 DM (p=0.0001). According to Naveen and Renuka study in 2014, they studied 55 diabetes and 25 non-diabetes patients. They found the NO concentrations were significantly higher in diabetes patients. That study also found a strong correlation between HbA1c and serum nitric oxide concentration with r = 0.644 and p-value <0.001.9

Based on a study done in India that involved 87 patients in which 56 patients were type 2 diabetes mellitus patients, while 31 patients were non-diabetics, the serum nitric oxide had a positive statistically significant correlation with HbA1c ( r = 0.35 and p = 0.0).10

Nitric oxide plays roles in the endothelial dysfunction that cause atherosclerosis in coronary heart disease patients who suffered from diabetes mellitus. Nitric oxide is an important mediator that can act as free radicals and can be changed into peroxynitrite by neuronal cells. It can modulate neurotransmission in endothelial cells and stimulate vascular relaxation or dilatation. The decrease in nitric oxide concentration can be caused by a decrease in NO synthesisor an increase in its degradation so that the superoxide anion production will increase. Superoxide anion production enhancement has a consequence of a reduction in atherogenic and thrombogenic inhibition processes, also decrease in the coronary artery dilatation ability. Some experts state that nitric oxide concentration play a role as endothelial dysfunction marker rather than independent coronary risk factor.11

CONCLUSION AND SUGGESTION

Recent studies found no significant correlation between HbA1c and NO concentration both in controlled and in uncontrolled type 2 diabetes mellitus patients. However, if the type 2 diabetes mellitus patient samples were analyzed, there was a significant correlation between HbA1c and NO concentration. There is a need to conduct further studies with larger sample size and greater consideration in the effect of other variables that may influence endothelial dysfunction.

REFERENCES