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The Relationship of Glycated Albumin Levels and Estimated Glomerular Filtration Rate (eGFR) in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Diabetes Mellitus (DM) is a chronic condition associated with increased blood glucose levels exceeding the normal limit. Type 2 Diabetes Mellitus (T2DM) is the most frequent type of DM. Glycaemic status control in DM patients can prevent complications of DM, for instance measuring glycated albumin (GA) levels. A decline in renal function is one of the most often complications due to DM. In clinical practice, renal function decline can be evaluated by estimated glomerular filtration rate (eGFR) formulas, such as Cockcroft-Gault (CG), Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Aim: To analyze the association between GA levels and eGFR calculated with CG, MDRD, and CKD-EPI formula in patients with T2DM. Methods: This study was an observational analytical study with a cross-sectional design conducted on 67 subjects from February – October 2021. The data obtained for this research was secondary data from the medical records of T2DM patients at Diponegoro National Hospital. The independent variable in this research was GA levels and the dependent variable was eGFR. The correlation analysis was done using Pearson test. Results: The Pearson's correlation test results between GA levels and eGFR calculated with CG, MDRD, and CKD-EPI formula in patients with type 2 DM were p=0,081and r=0,215; p=0,060 and r=0,231; p=0,062 and r=0,229, respectively. **Conclusion**: There was no significant association between GA levels and eGFR in patients with type 2 DM.

Keywords: [Type 2 diabetes mellitus, glycated albumin, eGFR]

INTRODUCTION

Diabetes Mellitus (DM) is defined as a chronic condition associated with abnormally high blood glucose levels in the body. Type 2 Diabetes Mellitus (DM) is the most common type of diabetes, which is characterized by hyperglycemia, insulin resistance, and relative insulin deficiency.[1,2] Referring to data generated by the International Diabetes Federation (IDF) in 2019, Indonesia was determined as the 7th country with the most DM sufferers (10.7 million people) in the age range of 20-79 years.[3] Health Department of Semarang reported that type 2 DM was the 5th most common disease in Semarang with 44,492 cases in 2020.[4]

DM may lead to various complications and contribute to a significant increase in morbidity and mortality. The onset and worsening of DM complications can be prevented by controlling the glycemic status of the patient. Glycated albumin (GA) has been suggested as one of the more sensitive glycemic indexes in evaluating short-term glucose fluctuations, in about 2-4 weeks. GA testing is also considered to be more stable than HbA1c, because GA levels are not affected by haematological disorders, hemoglobin metabolism, and pregnancy.[5]

DM disease that is not treated properly may result in impaired kidney function, which is characterized by a decrease in the glomerular filtration rate (GFR). Glomerular filtration rate can be evaluated through direct examination by injecting exogenous markers into the body. However, this examination is very complicated to be conducted and requires relatively high costs. Therefore, various estimated glomerular filtration rate (eGFR) formulas have been designed to estimate GFR by measuring levels of endogenous markers, such as serum creatinine and cystatin C.[6]

Several eGFR formulas are still widely used by far for clinical purposes in evaluating kidney function, particularly Cockcroft-Gault (CG), Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Research that analyzes the relationship between GA and the value of eGFR is still not commonly carried out. Thus, the researcher was intended to evaluate the relationship of GA as a relatively more stable glycemic index with eGFR values calculated by means of various formulas, including CG, MDRD, and CKD-EPI formulas, specifically in patients with type 2 DM.

MATERIALS & METHODS

This research was successfully carried out in February – October 2021 at Medical Record Installation of Diponegoro National Hospital (RSND) in Semarang. The method utilized in this research was observational analytic with a crosssectional approach. This research was conducted to evaluate the relationship between GA levels and eGFR values measured by using the CG, MDRD, and CKD-EPI formulas in patients with type 2 DM.

67 outpatients with type 2 DM at Diponegoro National Hospital were determined as samples of this research based on inclusion and exclusion criteria. Inclusion criteria in this research consisted of patients with type 2 diabetes over 18 years of age with medical records from laboratory results of serum creatinine and GA levels, and had a normal body temperature. (± 36,5^{o}C) and a history of hypertension, while the exclusion criteria in this research consisted of patients with thyroid disorders, nephrotic syndrome, and patients who were treated with glucocorticoid therapy. The samples were successfully selected through consecutive sampling from medical record data of patients with type 2 DM that met the inclusion and exclusion criteria of this research.

In this research, GA levels were determined as the independent variable, and eGFR values were determined as the dependent variable. GA levels were measured by means of the enzymatic method with a normal value of 12% to 16%, while the eGFR values were calculated based on serum creatinine levels, body weight, height, gender, and ethnicity factors by using an online calculator.[7]

The normality test was carried out by utilizing the Kolmogorov-Smirnov test, because the number of research samples was >50 patients. A significance value of more than 0.05 ($p>0.05$) indicated a normal data distribution. Data transformation with Log 10 was carried out on data that were not normally distributed. In addition, the relationship between GA and eGFR was evaluated through hypothesis testing with Pearson's test, because the data were normally distributed. This research was performed after obtaining ethical clearance from the Health Research Ethics

Commission (KEPK) of the Faculty of Medicine at Diponegoro University with No. 253/EC/KEPK/FK-UNDIP/VII/2021. The identity of the subjects would be kept strictly confidential and would not be published for any other purpose. The research costs were fully borne by the researcher.

RESULT

Descriptive analysis was conducted by identifying the frequency and distribution of data from each variable. Regarding to data derived from the subjects, the characteristics of the research subjects were successfully obtained as follows:

Table 1. Characteristics of Research Subjects

Variable	F	%	Mean ± SE	Median (min-max)
Sex				
Male	32	47,76		
Female	35	52,24		
Age (years)			58,7 ± 10,99	60 (34 – 84)
31-40	6	9		
41-50	8	11,9		
51-60	21	31,3		
61-70	25	37,3		
71-80	6	9		
80-90	1	1,5		
Body mass index (kg/m^2)			25,25 ± 2,69	25,3 (19,3 – 29,8)
18,5-24,9	28	41,8		
25-29.9	39	58,2		
Blood pressure (mmHg)				
Systole			133,1 ± 12,04	132 (110 – 157)
Diastole			82,8 ± 6,68	80 (65 – 97)
Fasting Blood Glucose (mg/dL)			148,45± 73,73	124 (40 –369)
Controlled	37	55,2		
Uncontrolled	30	44,8		
GA (mg/dL)			22,19 ± 7,93	20,3 (11,2 – 50,3)
Decreased	1	1,5		
Normal	17	25,4		
Increased	49	73,1		
Creatinine serum (mg/dL)			1,12 ± 0,39	1,03 (0,52 – 2,32)
Decreased	2	3		
Normal	48	71,6		
Increased	17	25,4		
eGFR				
CG (ml/min)			64,88 ± 24,37	64 (26 – 118)
MDRD (ml/min/1,73 m^2)			65,82 ± 22,81	64 (24 – 132)
CKD-EPI (ml/min/1,73 m^2)			72,78 ± 23,40	73 (26 – 122)

Table 1 shows the characteristics of the subjects, which include gender, age, BMI, blood pressure, FBS levels, GA levels, serum creatinine levels, and eGFR values calculated by using the CG, MDRD, and CKD-EPI formulas.

Correlative Test

Pearson correlation test on the correlation of GA levels to eGFR values by utilizing the CG, MDRD, and CKD-EPI formulas showed the following results: p=0.081 and r=0.215; p=0.060 and r=0.231; p=0.062 and r=0.229. The results of this test indicated that there was no significant relationship between GA levels and eGFR values based on calculations by means of 3 formulas: CG, MDRD, and CKD-EPI in type 2 DM patients.

Table 2. Correlation Test Result

eGFR	GA	
	p	r
CG	0,081	0,215
MDRD	0,060	0,231
CKD-EPI	0,062	0,229

DISCUSSION

Characteristics of Research Subjects

Having regard to the sex distribution of the research subjects, there were 32 samples (47.76%) with male sex and 35 samples (52.24%) with female sex. The age distribution of the research subjects was in the range of 34-84 years.

The average blood pressure of research subjects was amounted to 133/83 mmHg, and classified as prehypertension according to the division of the Joint National Committee (JNC) VIII. The data obtained in this research were in line with the determined inclusion criteria, which included patients with a history of hypertension. Furthermore, the distribution of FBS levels in research subjects was found in the range of 40 mg/dL to 369 mg/dL with a mean value of 148.45 mg/dL.

Moreover, the distribution of GA levels of research subjects was found to be in the range of 11.2% to 50.3% with a mean value of 22.19%, and the majority of subjects (73.1%) had elevated GA levels. The mean value of serum creatinine level was in the amount od 1.12 mg/dL. The lowest creatinine level was found at 0.52 mg/dL and the highest creatinine level was amounted to 2.32 mg/dL.

After obtaining secondary data, eGFR values were calculated by using three formulas, namely CG, MDRD, and CKDEPI. Subsequently, the calculation results were grouped based on five stages of classification of ND disease. The mean values of eGFR calculated by means of the CG, MDRD, and CKD-EPI formulas were amounted to 64.88 ml/min, 65.82 ml/min/1.73 m^2 and 72.78 ml/min/1.73 m^2.

Relationship between GA Levels and eGFR values in Patients with Type 2 DM

The significance values of GA levels on eGFR calculated by utilizing the CG, MDRD and CKD-EPI formulas were amounted to p=0.081 and r=0.215; p=0.060 and r=0.231; p=0.062 and r=0.229. This shows that there was no significant relationship between GA levels and eGFR values. These results are consistent with a research conducted by Kim et al (2015), which reported that no significant relationship was found between eGFR and GA values in patients with type 1 and 2 DM, because the p value was > 0.05 (p = 0.358).[8] The results of this research are also in line with a research carried out by Ma et al (2011), which showed that there was no significant relationship between GA levels and decreased kidney function as measured by eGFR, because p was > 0.05 (p=0.39).[9]

However, the results of this research were found to be different from previous research by Raghav et al (2018), which reported an increase in GA levels in type 2 DM patients who experienced decreased kidney function with eGFR values that remained more than or equal to 30 ml/min/1.73m^2.[10] The difference results in the research of Raghav et al (2018) with this research may be influenced by differences in the research flow. Raghav et al (2018) used GA level data in a number of measurements, while this research used GA data obtained in one measurement.

Another factor that may influence the results of this research is the factor of obesity status. Body mass index is known to have a negative association with GA levels. Overweight or obese individuals are likely to experience a microinflammatory process that can suppress albumin synthesis and increase aluminum catabolism, thereby reducing the GA levels.[11] A similar mechanism was also found in individual smokers. GA levels in individual smokers are significantly lower than in nonsmokers.[12]

In addition, another factor that may also influence the results of this research is serum creatinine levels, one of the endogenous substances used in the calculation of eGFR. Renal tubular creatinine secretion will likely increase as the GFR decreases, thereby causing the estimated renal function to be higher than normal. Moreover, creatinine can be metabolized or excreted via extrarenal pathways, particularly in the gastrointestinal

tract by normal flora, which will also lead to higher-than-normal estimates of GFR values. Serum creatinine levels are also related to muscle mass, because creatinine is formed in muscle. Therefore, serum creatinine levels may be inaccurate in elderly individuals and female sex, because older individuals and females have relatively lower muscle mass.[13]

Physical activity is also capable of increasing serum creatinine levels. Research conducted by Baxmann et al (2008) submitted that serum creatinine was found to be elevated in individuals with moderate to vigorous physical activity. However, no increase in cystatin-C levels was found.[14]

This research only obtained data on GA levels from one examination and did not exclude subjects with overweight nutritional status. Moreover, this research did not include other variables, such as smoking history, muscle mass, and physical activity, which may indicate the insignificant relationship between GA levels and eGFR values.

CONCLUSION

In this research, no significant relationship was found between GA levels and eGFR values in patients with type 2 diabetes. Consequently, further research may be conducted by obtaining data on GA levels through more than one examination and considering other variables, such as overweight and obesity nutritional status, smoking history, muscle mass, physical activity, and cystatin-C levels, thus proving the relationship between GA levels and eGFR values in patients with type 2 DM.

Declaration by Authors

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