# Correlation between HbA1C and Serum Creatinine Levels of Javanese Ethnicity Type 2 Diabetes Mellitus Patients

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**ABSTRACT**
Javanese people had genetic polymorphisms that made them susceptible to type 2 diabetes mellitus. The complication of diabetes was diabetic nephropathy, the most common etiology of end-stage renal disease. Hyperglycemia could interfere with the glomerular filtration and cause an increase in serum creatinine. HbA1c test and serum creatinine were used to monitor diabetes patients. This research analyzed the correlation between HbA1c and serum creatinine in Javanese ethnicity type 2 DM patients. It was observational analytic research using the cross-sectional approach. The subject were 36 Javanese type 2 DM patients at Pandanaran, Gunungpati, and Purwoyoso Community Health Center. The primary data was obtained through a questionnaire. HbA1c and serum creatinine were from the medical record. The analysis was Spearman's correlation test, which showed significance if p<0,05. The average age of the subject was 59,67±5,5 years and most of them had hypertension (69,4%). The average level of HbA1c was above normal (8,04±2,09%), while the serum creatinine level was normal (0,79±0,31 mg/dL). There was no significant correlation between HbA1c and serum creatinine levels (p=0,228; r=-0,206). HbA1c as the glycemic control parameter of DM patients was not correlated to the serum creatinine as the renal function parameter.

**Keywords** : Type 2 diabetes mellitus, HbA1c, glycemic control, serum creatinine

## INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a metabolic disease indicated by hyperglycemia due to insulin resistance.[1] It causes microangiopathic complications, such as diabetic nephropathy.[1] Diabetic nephropathy is indicated by the increase of albumin excretion in urine due to the glomerular change.[2] In a certain period, this condition could lead to end-stage renal disease.[2]

In 2017, 462 million people were estimated to be global T2DM patients.[3] According to Indonesian Basic Health research, the prevalence of DM in Indonesia was 1,5% during 2013, and 2% during 2018.[4] Diabetic nephropathies occur in every one-fifth of DM patients and could greatly affect patients' social and economic condition.[5] In Indonesia, this DM complication is the second most common complication after hypertension, etiology diagnose as stage 5 Chronic Kidney Disease (CKD).[6]

Chronic hyperglycemia is indicated by the increase of HbA1c, representing bad glycemic control.[7] Hyperglycemia is a risk factor of diabetic nephropathy where the glomerular change mechanism involves mesangial matrix expansion, sclerosis, basal membrane thickening, tubular epithelium flattening, and lumen widening.[2] The kidney function marker such as serum creatinine indicates kidney damage.[8] Decreased clearance by the kidneys results in increased creatinine levels.[8] The glycemic control is related to the last diabetic complication.[9] The glycemic control is tested using the HbA1c test, which represented the average glycemic level for the last three months.[10] Target of 7% HbA1c value is recommended to slower microvascular complication.[11]

Chutani *et al.'s study showed* an increase in serum urea and creatinine on type 1 and 2 DM subjects compared to the non-DM subjects.[12] Widyatmojo *et al.'s study showed* no correlation between the two variables.[7] However, Zulfian *et al.'s study* showed a significant correlation between HbA1c and creatinine with moderate positive correlation

strength.[13] This study focused on subjects like Javanese T2DM patients with certain genetic polymorphisms that make them susceptible to T2DM.[14] The authors were interested in investigating any significant correlation between HbA1c level and serum creatinine level in Javanese T2DM patients, considering the risk factors they had.

## METHOD

This study was conducted after the ethical clearance was issued by the Health Research Ethics Committee Faculty of Medicine Universitas Muhammadiyah Semarang Number 106/EC/FK/2021. This study was conducted on December 2021 at Pandanaran, Gunungpati, and Purwoyoso Community Health Center. It was observational analytic study using a cross-sectional approach. The subject was 36 T2DM patients who met the inclusion criteria: agreed to be the respondent, suffered from T2DM, came from Javanese ethnicity up to two generations away, 30 – 70 years old. Patients with gestational diabetes and kidney disease were excluded.

The sampling technique used was purposive sampling. From the subject, 89 questionnaire data were obtained as the primary data. Besides, secondary data was obtained from the medical record which included HbA1c level and serum creatinine level data of 103 patients. The medical record data were matched with the patients when they completed the questionnaire. From the process above, 36 subjects matched with the criteria were obtained. HbA1c and serum creatinine level were then analyzed using Spearman's correlation test and was significant if $p<0,05$. Before that, ratio scale data were obtained using the Shapiro Wilk normality test to decide between parametric or non-parametric tests. *P*-value >0,05 shows normal distribution.

## RESULTS

Table 1 showed that the patients' age data were normally distributed (p=0,343), the period of DM was not normally distributed (p=0,000), and HbA1c and serum creatinine level data were not normally distributed (p=0,018; p=0,000). Therefore, it could be concluded that the next analysis employed Spearman's correlation.

Table 2 showed that most of the subjects were female (86,1%). The average age of the participants was 59,67±5,5 years old. The average DM period of the patients was 8,33±9,17 years old. T2DM patients with hypertension were 25 people (69,4%). The average HbA1c level was 8,04±2,09%, with 5,0%. The average serum creatinine level of the subject was 0,79±0,31 mg/dL.

Based on table 3, there was no significant correlation between HbA1c and serum creatinine levels in Javanese T2DM patients (r=-0,206; p=0,228).

*Table 1. Test of normality*

| Data | Significance (*p*) |
|---|---|
| Patients' age | 0,343 |
| Period of DM | 0,000 |
| HbA1c (%) | 0,018 |
| Serum creatinine (mg/dL) | 0,000 |

*Table 2. Characteristics of patients*

| Characteristics (n=36) | Frequencies | Mean± SD | Min | Max |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 5 (13,9%) | | | |
| Female | 31 (85,1%) | | | |

| | | | | |
|---|---|---|---|---|
| Total | 36 (100%) | | | |
| **Age (year)** | - | 59,67 ± 5,50 | 49 | 69 |
| **Period of DM (year)** | - | 8,33±9,17 | 1 | 53 |
| **History of hypertension** | | | | |
| Yes | 25 (69,4%) | | | |
| No | 11 (30,6%) | | | |
| Total | 36 (100%) | | | |
| **HbA1c (%)** | - | 8,04±2,09 | 5,0 | 13,3 |
| **Serum creatinine (mg/dL)** | - | 0,79±0,31 | 0,38 | 1,54 |
| **Community health center** | | | | |
| Pandanaran | 13 (36,1%) | | | |
| Gunungpati | 9 (25%) | | | |
| Purwoyoso | 14 (38,9%) | | | |
| Total | 36 (100%) | | | |

*Table 3. The correlation between HbA1c level and serum creatinine level*

| Variable | Correlation coefficient (r) | p value |
|---|---|---|
| HbA1c (%)<br>Serum creatinine (mg/dL) | -0,206 | 0,228 |

*Spearman correlation test, p<0,05 significant difference

## DISCUSSION

The average age of the subject was more than 40 years old. The effect of aging in DM pathophysiology is the β cell function degradation which leads to the decrease of insulin secretion.[15] In this study, the female subject was more than the male. A study stated that estradiol improves insulin sensitivity and acts as a shield for age-related disease.[16] Most of the research subjects were also diagnosed with hypertension. A study on Goto Kakizaki (GK) rats showed that DM and hypertension have synergic effects for kidney failure, albuminuria, endoplasmic reticulum stress, oxidative stress, and glomerular damage.[17] The DM duration also affects the possibility of complication, of which diabetic nephropathy might appear in ten years after the diagnosis of T2DM.[18]

The characteristics of serum creatinine and HbA1c level found in the study were varied. The HbA1c level of the research subject was considered normal and increasing, which represented the glycemic control of the DM patient. Following the previous research, the average HbA1c level of the uncontrolled glucose group was higher than the controlled glucose group.[19] The HbA1c ≥6,5% in the first year of DM could increase the risk of microvascular and macrovascular complications.[9] Meanwhile, the HbA1c ≥8% could lead to microvascular complications and even death.[9] The average HbA1c level based on this research was above normal but the average level of serum creatinine was normal.

DM is caused by some factors, such as genetic factors, diet, physical activities, and other diseases. The previous study on a genetic factor of DM patients found the 16S rRNA and ND1 gene mutation, which affected the NADH dehydrogenase subunit 1, the mitochondrial OXPHOS complex 1 component, and caused type 2 DM.[20] Javanese with 2R/3R and 3R/3R CAPN10 SNP-19 genotype are susceptible to

T2DM.[14] Besides, meta-analytic research showed that T2DM could be caused by unhealthy diets such as high-sugar food and beverage, processed meat, red meat, and other low-fiber food.[21] Physical activities are also one of the risk factors for T2DM. The regular physical activities intervention could improve T2DM patient condition, such as controlling the glycemic index, weight loss, and preventing further complications.[22]

HbA1c is the parameter for patients' glycemic control, while serum creatinine is the indicator for kidney function. The correlation test showed no significant correlation between HbA1c and serum creatinine level in Javanese ethnicity T2DM patients. Widyatmojo *et al.* and Rokim's study also concluded that HbA1c is not correlated to serum creatinine.[7,23] A study conducted in a certain hospital with T2DM patients also concluded no correlation between both variables.[24] However, the result was contrary to Zulfian *et al.'s study,* which showed a significant correlation between HbA1c and creatinine with moderate positive correlation strength.[13] The finding is also different from the study of Sivasubramanian *et al.* that showed that there was a significant positive correlation between HbA1c with albumin ration and serum creatinine of T2DM patients in Southern India.[25] Subramanyam et al. described the positive correlation between those variables, yet the subjects were patients with chronic kidney disease stage three, four, and five, in which the kidney indicated a decrease in function.[26]

The similarity and difference of the finding could be caused by the different character of the subject, such as gender, the regularity of taking DM medication, and the hypertension history. The difference could also be affected by the variable-affecting factors such as anemia, transfusion history, the regularity in taking medicine, muscle mass, or the high protein diet. The anti-diabetic medicine mostly used in the study were *Metformin* and *Sulfonylurea*.[27] In this case, the HbA1c level of patients with regular medication was lower than those who took the medicine irregularly.[27] The study showed that the HbA1c level of DM patients with iron deficiency anemia was lower than the HbA1c level of DM patients without anemia, which could contribute to false results during the monitoring as the condition also reduced the HbA1c level.[28]

Hyperglycemia could affect kidney structure.[2] The mechanism of kidney failure caused by hyperglycemia was described in an experimental study.[29] In rats with type 2 DM, the kidney structure indicated reduced glomerulus, widened kidney capsule and tubulin, and thickened basal membrane.[29] The serum creatinine and urea level could be normal in the early stage of kidney disease with glomerular changes such as widened basal membrane and mesangial matrix accumulation.[25] A study focusing on DM patients showed that the serum creatinine of patients diagnosed with DM for more than 5 years did not increase as they were not diagnosed with diabetic nephropathy.[23] The early intervention, detection, and monitoring of T2DM patients with estimated serum creatinine and HbA1c are recommended to control the glomerular damage progressivity due to high blood sugar levels.[12]

This research has some limitations, such as the limited research subject and the other unobservable factors related to the HbA1c and serum creatinine level. Some of the affecting factors are anemia, blood transfusion history, the regularity in taking anti-diabetic medicine, diet, physical activities, muscle mass, high protein diet, and other medicines that could affect HbA1c and serum creatinine level at the time of data collection.

## CONCLUSION

Based on the analysis, the average HbA1c level of Javanese T2DM patients was 8,04±2,09% (above normal), and the serum creatinine of Javanese ethnicity T2DM patients was 0,79±0,31 mg/dL (normal). There was no significant correlation between HbA1c and serum creatinine level in Javanese T2DM patients. Although, good glycemic control is necessary to prevent later complications in diabetes mellitus patients.

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