

The correlation between creatinine levels and estimated glomerular filtration rate (GFR) with blood glucose levels in diabetes mellitus type 2 patients

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Abstract

Diabetes mellitus (DM) was a group of metabolic diseases characterized by hyperglycemia. Measuring the blood creatinine level and calculating the estimated glomerular filtration rate (GFR) was crucial in determining if a person had impaired kidney

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Key words: blood glucose, creatinine, estimated GFR, Type 2 diabetes mellitus.

Contributions: AR, conceptualization, data curation, formal analysis, methodology, validation, visualization, writing – original draft, review & editing; RN, conceptualization, investigation, methodology, validation, and writing – original draft, review & editing; WW, conceptualization, methodology, formal analysis, validation, and writing – original draft, review and editing; NK, methodology, visualization, writing – review & editing; WR, review and editing.

Conflict of interest: the authors declare no conflict of interest.

Ethics approval and consent to participate: the research has obtained ethical approval from the Health Research Ethics Committee at Polytechnic of Health Bandung, as indicated by ethical certificate 40/KEPK/EC/XI/2021. Throughout the research, the researcher adhered to human principles, including obtaining informed consent, respecting human rights, ensuring beneficence, and avoiding harm (non-maleficence).

Patient consent for publication: written informed consent was obtained for anonymized patient information to be published in this article.

Funding: this research did not receive external funding.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

Received: 13 September 2023.
Accepted: 17 November 2023.
Early access: 15 December 2023.

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Licensee PAGEPress, Italy
Healthcare in Low-resource Settings 2024; 12:11790
doi:10.4081/hls.2023.11790

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function. These tests provided valuable insights into the progression of type 2 diabetes mellitus and its associated risk of kidney failure. The objective of this study was to investigate the correlation between average creatinine levels and GFR with blood glucose levels in type 2 DM patients. This correlative research used a cross-sectional approach and included samples from 30 patients with type 2 DM at a hospital in Bandung, Indonesia. The patients' blood glucose and blood creatinine levels were measured using GFR calculations and a Kenza Max photometer, respectively. The sampling method used was accidental sampling, with the sample criteria being type 2 DM patients who were willing to be respondents and did not have hypertension. The average creatinine levels and estimated GFR values were 0.97 mg/dL and 84.971 mL/min/1.73m². The results of the Pearson correlation test indicated non-significant correlations ($p > 0.05$, $p = 0.703$ and 0.819). This suggested that there was no significant relationship between creatinine levels and estimated GFR and blood glucose levels in type 2 DM patients. This study provided a foundational exploration of the link between blood glucose levels and kidney function, which could contribute to developing methods for examining kidney diseases in type 2 DM patients. This study's findings underscore the complexity of the relationship between metabolic control and renal function in type 2 diabetes mellitus patients, highlighting the need for individualized patient assessment and management strategies.

Introduction

One of the major global health concerns is non-communicable diseases (NCDs).¹ Diabetes mellitus is a non-communicable disease and poses a serious threat to global health.^{2,3} Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia, resulting from deficiencies in insulin secretion, insulin action, or a combination of both. Those with DM are at risk of dysfunction and failure in various organs, including the eyes, kidneys, nerves, heart, blood vessels and sexual dysfunction.^{4,5} The prevalence of diabetes has been steadily increasing worldwide in recent years.⁶ According to the International Diabetes Federation (IDF) in 2021, an estimated 537 million adults (aged 20-79) suffer from DM, and this number is projected to reach 783 million by 2045. It is estimated that over 6.7 million adults will die from diabetes-related causes in 2021.⁷ Indonesia is ranked as the country with the fifth-largest number of individuals having DM, with 19.47 million cases. The IDF notes that 80% of people with diabetes live in low and middle-income countries, and 45% of adults are estimated to remain undiagnosed.⁷ Generally, the diagnosis of DM is established based on the examination of blood glucose levels. DM has several categories, including type 1, type 2, maturity-

onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes resulting from endocrinopathies, steroid use, etc.⁸ In general, DM is divided into type I and type 2, with type 2 DM characterized by hyperglycemia due to insulin resistance accompanied by relative insulin deficiency.⁵ Early detection and treatment are beneficial in preventing or delaying the progression of chronic kidney disease (CKD).⁹ These initiatives encompass a range of strategies, including the provision of health promotion and education activities aimed at raising diabetes awareness.¹⁰ Typically, individuals with diabetes are advised to take anti-diabetic drugs to maintain controlled blood glucose levels, minimizing exposure to chronic hyperglycemia, which can lead to both macrovascular and microvascular complications.¹¹

One of the complications that often occurs in diabetic patients is diabetic nephropathy. Diabetic nephropathy is a diagnosis that refers to specific pathological structural and functional changes observed in the kidneys of patients with DM.¹² This complication arises through several mechanisms, such as alterations in renal hemodynamics and the accumulation of advanced glycation end products (AGEs), which can trigger structural kidney damage leading to Chronic Kidney Disease (CKD). CKD is a condition that can necessitate kidney replacement therapy in the form of hemodialysis or kidney transplantation.¹³ One of the manifestations of structural kidney damage is a decrease in the glomerular filtration rate (GFR).¹⁴ GFR represents the volume of plasma that the kidneys can clear entirely of specific compounds in one unit of time. Additionally, an indicator to assess kidney damage is a creatinine examination.¹⁵ Creatinine results from the endogenous metabolism of skeletal muscle and is excreted through glomerular filtration, ultimately being excreted in the urine without reabsorption by the kidney tubules. The creatinine level is closely related to the estimated GFR, which can be calculated by measuring the serum creatinine level of the suspected patient using the Modification of Diet in Renal Disease (MDRD) equation. Therefore, estimated GFR and blood creatinine levels are crucial indicators in determining whether a person has impaired kidney function.¹⁶ They serve as valuable tools to assess the progression of type 2 diabetes mellitus, which has the potential to lead to kidney failure, and as a means of monitoring kidney function in Type 2 DM patients who have experienced complications of kidney failure.¹⁴

The purpose of this study was to determine if there is a relationship between the average creatinine level and the estimated GFR with blood glucose levels in type 2 diabetes mellitus patients, by determining the average creatinine level and the estimated GFR value.

Materials and Methods

Study design

This study was a correlational study with a cross-sectional design aimed at determining the relationship between creatinine levels and estimated GFR on blood glucose levels in type 2 DM patients. The study was conducted at a hospital in Bandung, Indonesia, from October to November 2021.

Patients

The sampling technique used in this study was accidental sampling, wherein samples were collected from the serum of patients with type 2 DM who visited the hospital laboratory.

Inclusion criteria

Type 2 diabetic patients who are over 30 years old, have fasting blood glucose levels higher than 126 mg/dL, and have given their consent to participate in the study.

Exclusion criteria

Individuals with a history of hypertension and kidney failure were not included in the study.

Examination of blood glucose GOD-PAP methods

Glucose is oxidized by GOD to gluconic acid and hydrogen peroxide, which, in conjunction with POD, reacts with chloro-4-phenol and PAP to form a red quinoneimine. The absorbance of the colored complex, proportional to the concentration of glucose in the specimen, is measured at a 500 nm wavelength (Figure 1). GOD oxidizes glucose to gluconic acid and hydrogen peroxide, which, in conjunction with POD, reacts with chloro-4-phenol and PAP to form a red quinoneimine. The absorbance of the colored complex, proportional to the concentration of glucose in the specimen, is measured at a 500 nm wavelength. All measurements were conducted at room temperature.

Examination of creatinine serum Jaffe Reaction methods

The colorimetric reaction (Jaffe reaction) of creatinine with alkaline picrate was measured kinetically at 490-510 nm without any pre-treatment step. This reaction has been improved in terms of specificity, speed, and adaptability by developing an initial-rate method. The measurements were conducted at room temperature (Figure 2).

Reagent	1000 µL
Calibrator, Control, or Specimen	10 µL
Mix. Let stand for 10 minutes at 37°C or 20 minutes at room temperature. Read absorbance at 500 nm (460-560) against reagent blank. Coloration is stable for 15-20 minutes at 37°C and then slowly decreases.	

Figure 1. Procedure for quantitative determination of blood glucose GOD-PAP method.

Reagent	1000 µL
Calibrator, Control, or Specimen	100 µL
Mix. Let stand for 30 seconds at 25°C. Read the first absorbance at 490 nm (460-560) against the reagent blank. Exactly 2 minutes read the second absorbance. Coloration is stable for 15-20 minutes at 37°C and then slowly decreases.	

Figure 2. Procedure for quantitative determination of creatinine serum Jaffe Reaction method.

Estimation of GFR with Cockcroft-Gault formula based on SCR

The Cockcroft-Gault equation was used to estimate the GFR value from known variables such as serum creatinine (mg/dL), age (years), and body weight (kg) based on Equation 1 for males and Equation 2 for females.¹⁷

$$GFR (mL/min/1.73 m^2) = (140 - age) \times \frac{body\ weight}{serum\ creatinine} \times 72 \quad (eq. 1)$$

$$GFR (mL/min/1.73 m^2) = (140 - age) \times \frac{body\ weight}{serum\ creatinine} \times 72 \times 0.85 \quad (eq. 2)$$

Statistical analysis

The measured creatinine level, estimated GFR, and blood glucose level dataset were subjected to bivariate analysis, specifically the Pearson correlation test. The Pearson correlation coefficient provides a measure of the correlation between two variables, using a scale ranging from -1 to +1, where 0 indicates no linear or monotonic relationship. As the coefficient approaches an absolute value of 1, the association becomes stronger, moving closer to a straight line. It's important to note that the Pearson correlation coefficient should not be confused with linear regression. The Pearson correlation coefficient is used when both variables are observed values subject to natural random variation, such as in the accidental sampling method. Conversely, in linear regression, the values are dependent on a variable that is chosen and set as a constant in an experimental protocol. The basic decision-making process in the Pearson Correlation test is as follows: if the Significance (Sig) value is <0.05, then there is a correlation; if the Significance (Sig) value is >0.05, then there is no correlation

Results

Creatinine levels of the type 2 diabetes mellitus patients

Based on Table 1, the frequency distribution of 30 patients with Type 2 DM shows that two patients (6.7%) had low creatinine levels, 18 patients (60%) had normal creatinine levels, and ten patients (33.3%) had high creatinine levels. The average creatinine level in Type 2 DM patients was 0.97 mg/dL.

Table 2 presents the distribution of 30 patients with type 2 DM based on gender, age, and the duration of DM they have suffered. Among the female patients (70.0%), two patients (6.7%) had low creatinine levels, ten patients (33.3%) had normal creatinine levels, and nine patients (30.0%) had high creatinine levels. In contrast, among the male patients, nine (30%), eight (26.7%), and one (3.3%) had low, normal, and high creatinine levels, respectively.

The research conducted on 30 patients with Type 2 DM, aged 31-82 years, revealed three categories of results in serum creatinine levels: low, normal, and high. It was observed that ten individuals had high creatinine levels, predominantly in the age group of 60-69 years, with as many as eight patients (26.6%).

Furthermore, the study, conducted on 30 patients with type 2 DM, was mainly composed of patients who had suffered from type 2 DM for 6-10 years, totaling 17 patients. The examination of serum creatinine levels yielded three categories: low, normal, and high. It was found that one person (3.3%) had low creatinine levels, eight people (26.7%) had normal creatinine levels, and eight people (26.7%) had high creatinine levels. Eight patients had been living with DM for 0-5 years, while eight patients had been dealing with DM for more than 10 years.

Table 1. Frequency distribution of creatinine levels in type 2 diabetes mellitus patients.

Creatinine levels in type 2 diabetes mellitus patients (mg/dL)									
Variable	Low		Normal		High		Frequency		Mean
	N	%	N	%	N	%	N	%	
Creatinine levels in type 2 diabetes mellitus (mg/dL)	2	6.7	18	60	10	33.3	30	100	0.97

Table 2. Frequency distribution of creatinine levels in type 2 diabetes mellitus patients based on gender, age, and duration of diabetes mellitus.

Creatinine levels in type 2 diabetes mellitus patients (mg/dL)									
	Low		Normal		High		Frequency		
	N	%	N	%	N	%	N	%	
Gender									
Male	0	0	8	26.7	1	3.3	9	30.0	
Female	2	6.7	10	33.3	9	30	21	70.0	
Total	2	6.7	18	60.0	10	33.3	30	100	
Age									
30-39 years old	0	0	2	6.7	0	0	2	6.7	
40-49 years old	1	3.3	3	10.0	0	0	4	13.3	
50-59 years old	0	0	6	20.0	0	0	6	20.0	
60-69 years old	1	3.4	4	13.3	8	26.6	13	43.3	
>70 years old	0	0	3	10.0	2	6.7	5	16.7	
Total	2	6.7	18	60.0	10	33.3	30	100	
Duration of diabetes mellitus									
0-5 years	0	0	5	16.7	0	0	5	16.7	
6-10 years	1	3.3	8	26.7	8	26.7	17	56.7	
>10 years	1	3.4	5	16.6	2	6.6	8	26.6	
Total	2	6.7	18	60	2	33.3	30	100	

Estimation of glomerulus filtration rate of the type 2 diabetes mellitus patients

Based on Table 3, after analyzing the frequency distribution of 30 patients with type 2 diabetes mellitus, it was determined that normal GFR values were found in 15 patients with type 2 diabetes mellitus (50.0%), while an estimated mild GFR value was observed in nine patients (30.0%). The average estimated GFR value in type 2 diabetes mellitus patients was 84.971 mL/min/1.73m². Table 4 explains the frequency distribution of estimated GFR values for 30 patients with type 2 DM, the majority of whom were females (21 patients, 70%). Among the 21 female patients, nine (30%) had estimated GFR values in the normal category, six (20%) in the mild category, and the remaining six (20%) in the moderate category. For the males, there were nine patients (30%) with estimated GFR values in the normal category, six (20%) in the mild category, and six (10%) in the moderate category. After analyzing the frequency distribution of 30 patients with

Type 2 DM, within an age range of 31-82 years, it was observed that the age group of 60-69 years was the most dominant, comprising 13 patients (43.4%). Among these patients, 13 had estimated GFR values in the normal category, three (10.0%) in the mild category, and five (16.7%) had moderate GFR values. Among the 30 patients with type 2 DM, the analysis revealed that the majority had a long history of having type 2 DM for 6-10 years. Seventeen patients (56.6%) had estimated GFR values in the normal category, seven (23.4%) in the mild category, and five (16.6%) in the moderate category.

Pearson correlation test results

The results of the Pearson correlation analysis are tabulated in Table 5. The Pearson correlation between blood glucose levels and creatinine levels is of a negative value ($r = -0.730$), indicating an inversely linear relationship. However, the correlation between blood glucose levels and the estimated GFR values is 0.044, which is close to 0, suggesting no linear relationship.

Table 3. Frequency distribution of glomerulus filtration rate in type 2 diabetes mellitus patients.

Variable	Normal		Mild		Moderate		Severe		Chronic		Mean
	N	%	N	%	N	%	N	%	N	%	
	Estimation of GFR in type 2 diabetes mellitus (mL/min/1.73m ²)	15	50.0	9	30.0	6	20.0	0	0	0	

GFR, glomerulus filtration rate.

Table 4. Frequency distribution of glomerulus filtration rate in type 2 diabetes mellitus patients based on gender, age, and duration of DM diagnosis.

	Normal		Mild		Moderate		Severe		Chronic		Frequency	
	N	%	N	%	N	%	N	%	N	%	N	%
	Gender											
Male	6	20	3	10	0	0	0	0	0	0	9	30
Female	9	30	6	20	6	20	0	0	0	0	21	70
Total	15	50	9	30	6	20	0	0	0	0	30	100
Age												
30-39 years	2	6.7	0	0	0	0	0	0	0	0	2	6.7
40-49 years	3	10.0	1	3.3	0	0	0	0	0	0	4	13.3
50-59 years	4	13.3	2	6.7	0	0	0	0	0	0	6	20.0
60-69 years	3	10.0	5	16.7	5	16.7	0	0	0	0	13	43.4
70-82 years	3	10.0	1	3.3	1	3.3	0	0	0	0	5	16.6
Total	15	50.0	9	30.0	6	20.0	0	0	0	0	30	100
Duration of diabetes mellitus												
0-5 years	3	10	2	6.7	0	0	0	0	0	0	5	16.7
6-10 years	7	23.4	5	16.6	5	16.6	0	0	0	0	17	56.6
>10 years	5	16.6	2	6.7	1	3.4	0	0	0	0	8	26.7
Total	15	50.0	9	30.0	6	20.0	0	0	0	0	30	100

Table 5. The pearson correlation test results.

		Fasting glucose level	Creatinine level	Glomerulus filtration rate
Fasting glucose level	Pearson correlation (r)	1	- 0.073	0.044
	Sig. (2-tailed)	-	0.703	0.819
	N	30	30	30
Creatinine level	Pearson correlation (r)	-0.073	1	-0.863
	Sig. (2-tailed)	0.703	-	0.000
	N	30	30	30
Glomerulus filtration rate	Pearson correlation (r)	0.044	-0.863	1
	Sig. (2-tailed)	0.819	0.000	-
	N	30	30	30

Discussion

Among the 30 respondents with type 2 DM, more than half of them (60.0%) exhibited normal creatinine levels. Among the remaining respondents, 33.3% showed high creatinine levels, and 6.7% exhibited low creatinine levels. These results align with a study conducted by Dedi in 2020 on 174 type 2 DM patients, which found high creatinine levels in 40.2% of cases, normal creatinine levels in 44.2% of cases, and low creatinine levels in 15.5% of cases. Another study by Kurniawan reported that 55 type 2 DM patients had high creatinine levels in 83.6% of cases and normal creatinine levels in 16.4% of cases.^{18,19}

In this study, several cases of high glucose levels were followed by high creatinine values. In patients with type 2 diabetes mellitus, high glucose levels can damage the kidney filters over time, affecting kidney function and increasing blood creatinine levels. Several factors can lead to normal creatinine levels in type 2 DM patients in this study. One such factor is age. The study's age range was 31-82 years, with normal creatinine levels in 18 people (60.0%), most notably in the age range of 60-69 years. This indicates that the respondents' kidney function was still healthy and undamaged. Normal creatinine levels are generally maintained at a constant rate, and levels above the normal range indicate impaired kidney function.²⁰

Other factors that affect creatinine levels include blood glucose levels and the duration of type 2 DM. Elevated blood glucose levels weaken and make the blood vessel walls more brittle, leading to blockages in small blood vessels, resulting in microvascular complications such as nephropathy. Additionally, based on the estimated GFR value in type 2 DM patients, there were six individuals in the moderately reduced kidney function category, nine in the mildly decreased kidney function category, and 15 with normal kidney function. The estimation of GFR values in type 2 DM patients can be associated with several factors, including the duration of having type 2 DM, which is linked to the risk of DM complications. The main factor triggering complications in type 2 diabetes mellitus is not only the duration but also the severity of DM. However, when balanced with a healthy lifestyle, it can lead to a better quality of life that helps prevent complications.²¹

This aligns with the results of research that has shown that patients having type 2 DM for 6-10 years can have five individuals in the moderate category, indicating the beginning of kidney damage and decreased kidney function. In contrast, among other respondents with the same duration of DM, the average GFR was in the mild category, indicating indications of kidney damage but still maintaining normal kidney function. This illustrates that, among type 2 DM patients with a long duration of 6-10 years, many continue to lead a healthy lifestyle.

Another factor that can influence the GFR value is increased creatinine levels. Creatinine and GFR values are inversely proportional, where higher serum creatinine values correspond to lower GFR values. The results of this study indicate that GFR values can be used to monitor the progression of type 2 DM, which has the potential to lead to kidney problems (diabetic nephropathy).²²⁻²⁴ Bivariate analysis of the measured creatinine levels, estimated GFR, and blood glucose levels using Pearson correlation tests revealed that there was no significant relationship between creatinine levels (Sig. 0.703, $p > 0.05$) and estimated GFR (Sig. 0.819, $p > 0.05$) with blood glucose levels among the 30 type 2 DM patients.

Conclusions

This study indicates that high blood glucose levels do not necessarily correspond to high creatinine levels or low estimated GFR values. It also suggests that not all type 2 DM individuals with elevated blood glucose will experience kidney impairment. To strengthen this conclusion, additional research should incorporate HbA1C values, which serve as an indicator of well-managed blood sugar levels in type 2 DM patients.

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