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Profile of Serum Creatinine Levels with Creatinine Clearance Test (CCT) of Patients with Type 2 Diabetes Mellitus at Budhi Asih Hospital in 2021

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ABSTRACT
Diabetes Mellitus (DM) is a group of metabolic diseases with hyperglycemia characteristics that can lead to kidney complications. One of them is Diabetic Nephropathy which is a complication of microvascular damage and its monitoring is done by checking serum creatinine and creatinine clearance test (CCT). The purpose of this study was to determine the relationship between serum creatinine levels and creatinine clearance test (CCT) in patients with type 2 DM. Perform a serum creatinine examination which is used as the basis for calculating CCT. From 53 data on type 2 DM patients who had high serum creatinine levels, 49 (92.5%) people, 51 (96.2%) people with low CCT levels. The results of Spearman's correlation statistical test showed a correlation between serum creatinine levels and CCT. The strength of the correlation is moderate, and the correlation shows a negative direction with a correlation coefficient (r) of -0.389. It can be concluded that the higher the serum creatinine level, the lower the CCT value, so DM patients must control blood glucose regularly in order to prevent a decrease in kidney function that can lead to complications.
Keywords*: Creatinine, Creatinine Clearance Test (CCT), Type -2 Diabetes Melitus*

ABSTRAK
Diabetes Melitus (DM) merupakan suatu kelompok penyakit metabolik dengan karakteristik hiperglikemia dan dapat mengakibatkan komplikasi pada ginjal. Salah satunya adalah Nefropati Diabetik yang termasuk dalam komplikasi kerusakan mikrovaskuler dan monitoringnya dengan melakukan pemeriksaan kreatinin serum dan creatinine clearance test (CCT). Tujuan penelitian ini adalah untuk mengetahui hubungan kadar kreatinin serum dengan creatinine clearance test (CCT) pada penderita DM tipe 2. Jenis penelitian adalah observasional analitik dengan desain cross sectional dengan data sekunder sebanyak 53 data yang diperoleh dari rekam medik di RSUD Budhi Asih Jakarta Timur yang melakukan pemeriksaan kreatinin serum yang digunakan sebagai dasar perhitungan CCT. Dari 53 data penderita DM tipe 2 yang memiliki kadar kreatinin serum tinggi sebanyak 49 (92,5%) orang, kadar CCT rendah sebanyak 51 (96,2%) orang. Hasil uji statistik korelasi Spearman's menunjukkan adanya korelasi antara kadar kreatinin serum dengan CCT. Kekuatan korelasi sedang, dan korelasi menunjukkan arah negatif dengan koefisien korelasi (r) sebesar -0,389. Dapat disimpulkan bahwa semakin tinggi

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kadar kreatinin serum maka semakin rendah nilai CCT sehingga penderita DM harus melakukan kontrol glukosa darah secara rutin supaya mencegah terjadinya penurunan fungsi ginjal yang dapat mengarah pada kejadian komplikasi.
Kata Kunci: Kreatinin, Creatinine Clearance Test (CCT), Diabetes Melitus Tipe-2

INTRODUCTION

DM is a metabolic disease characterized by hyperglycemia with abnormalities in insulin secretion, insulin action, or both (Soelistijo, 2015). These disorders can be caused by the body's inability to produce the hormone insulin and the pancreas is not function (Joddy *et al.*, 2017). The number of cases and the prevalence of DM has increased over the last few decades. Data to the World Health Organization (WHO) globally in 2018 there were 422 million adults suffering from diabetes worldwide. Global prevalence has doubled from 4.7% in 1980 to 8.5% (WHO, 2018) . Risksesdas data in 2018 in every province of Indonesia there is a proportion of DM, especially the province of DKI Jakarta showing a prevalence of 3.4% the proportion of the population who has ever been diagnosed with DM by a doctor.

The classification of DM, according to the World Health Organization (WHO), is categorized as type 1 DM, type 2 DM and gestational type. The proportion of the incidence of type 2 DM is 95% of the world's population who suffer from DM and there are 5% of the number who suffer from type 1 DM (Bhatt et al., 2016) .

Complications can occur if DM is not treated properly. Complications in DM can be classified as microvascular and macrovascular. Microvascular complications include damage to the eye (diabetic retinopathy), damage to the kidneys (diabetic nephropathy), and damage to the nervous system (diabetic nephropathy). Macrovascular complications can occur in heart disease and peripheral vascular disease. (PERKENI, 2015).

One of the DM patients can cause complications in diabetic nephropathy. Diabetic nephropathy is a condition in which the kidneys have decreased function and damage to the blood filter membrane caused by high blood glucose levels. Kidney disease is the main cause of death in DM. Damage to the kidneys can be found when type 2 diabetes is diagnosed. There are 60% of hypertensive and DM patients in Asia suffer from diabetic nephropathy (Salman Alfarisi, Wiranto Basuki, 2012) . *American Journal of Kidney Disease* in 2018 diabetic nephropathy is characterized

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by the presence of microalbuminuria, namely the excretion of albumin protein into the urine of more than 30-300 mg, which can develop into microalbuminuria.

High blood glucose levels make the kidney filter too much blood and damage the blood vessels in the kidneys. High blood glucose can damage the blood vessels in the kidneys so that the blood vessels are damaged and do not work properly (Aditya et al., 2018). Parameters to determine the filter function and the degree of renal complications in DM patients were examined for serum creatinine and Creatinine Clearance Tests (CCT) (Verdiansyah, 2016). Serum creatinine examination is the result of the breakdown of muscle creatine phosphate, produced by the body constantly depending on muscle mass and produced in the same amount and excreted through urine every day (Martini et al., 2010). The decreased kidney filter function will make creatinine levels to increase in the blood (Indrasari, 2015). Diabetic nephropathy is characterized by damage to the glomeruli, tubules, interstitial and vascular tissues (Tangkelangi & Berelaku, 2019).

Examination of kidney function is not only chosen based from the value of creatinine but also must be assessed through other parameters. The parameter to determine kidney function and disease progression is to look at the CCT value, where a decrease in the CCT value will be followed by an increase in blood creatinine levels. Creatinine Clearance Test (CCT) is the volume of blood that is cleared of a substance by being excreted into the urine within 1 minute (Fera Sartika, Dwi Purbayanti, 2018). There are 10-40% of people with type 2 diabetes has kidney failure because the blood vessels in the kidneys are injured, the kidneys cannot clean the blood properly, so the body will retain more water and salt than in normal condition and can lead to weight gain and swelling of the ankles. One index that is good to detect and determine the severity of impaired kidney function, find the level of complications of DM and to determine the dose of drugs that should be given to patients (Dewi, 2015). To find out if the patient has kidney failure, it is necessary to calculate CCT, using several variables in the calculation, namely blood creatinine, 24-hour urine storage, age, gender, and weight. Using calculations based on the Cockroft-Gault formula (Sennang, 2005).

Research conducted by (Indriani et.al., 2017) proved that there was a relationship between urea levels, creatinine, and creatinine clearance with proteinuria in DM patients. Then, in another study conducted

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by (Samodro et.al., 2016) there was a significant relationship between creatinine clearance and type 2 DM patients, where the mean GFR was 54.33 ml/min/1.73 m2 showing a significant relationship. GFR decreased in patients with type 2 diabetes due to impaired kidney function. The difference from previous researchers is in terms of the type of examination.

Based on data from 2018, there were 503 patients suffering from DM at Budhi Asih Hospital, East Jakarta and 174 people suffering from DM with complications of kidney disease or diabetic nephropathy (Hardyati, 2019). Based on this description, the researcher wanted to know the relationship between serum creatinine levels and *Creatinine Clearance Test* (CCT) in patients with type 2 diabetes.

METHOD

The type of research used is an analytic observational study with a cross-sectional design because it emphasizes the time of measurement or observation of independent and dependent variable data only once at a time. The population in this study was data from patients with type 2 diabetes who qualified for the inclusion and exclusion criteria for the period of January 2018 – December 2020. The inclusion criteria in this study were age > 35 years, type 2 DM patients, and simultaneous creatinine and CCT examinations. Then for the exclusion criteria, namely age <35 years, not patients with type 2 DM, and not doing creatinine & CCT examinations. This study has shown the relationship between serum creatinine levels and creatinine clearance test (CCT) in patients with type 2 DM who has the Serum Creatinine and Creatinine Clearance Test (CCT).

The number of samples obtained using the Slovin formula. The data collected in this study is secondary data, by submitting a permit to collect data about patients with type 2 DM, selecting data for serum creatinine examination and Creatinine Clearance Test (CCT) along with other supports (examination number, gender, and age), record, recapitulate in tabular form, and process the data. Data processing and analysis were carried out using SPSS computer software from univariate to bivariate analysis.

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RESULTS AND DISCUSSION

Table 1. Frequency Distribution of Type 2 DM Patients by Gender in Budhi Asih Hospital

Gender	Frequency (n)	Percentage (%)
Man	25	47,2
Woman	28	52,8
Total	53	100

DM is a metabolic disease characterized by an increase in blood glucose resulting in a decrease in insulin secretion by pancreatic beta cells or impaired insulin function (insulin resistance) (Bhatt et al., 2016). In conditions of prolonged hyperglycemia in diabetes and uncontrolled blood glucose levels will increase the risk of microvascular complications such as complications in the kidneys (diabetic nephropathy) (Salman & Wiranto, 2012).

Based on the Slovin calculation formula, 53 medical record data were obtained for patients with Type 2 DM for the period of January 2018 - December 2020 at the Budhi Asih Hospital, East Jakarta, seen from table 4.1 shows that in Type 2 DM sufferers, the most suffered by women, namely 28 (52.8%) people, while for men there were 25 (47.2%) people. Data published by Riskesdas in 2018 showed that the female gender with DM in Indonesia had a greater proportion than the male gender. In the female gender, it was 1.78%, while the male gender was 1.21%. This can be caused by the occurrence of factors such as premenstrual syndrome, increased Body Mass Index (BMI) and menopause. When the estrogen hormone decreases, menopause is a factor that the female gender is more affected by type 2 diabetes. In estrogen and progesterone hormones can increase the insulin response in the blood during menopause, but the insulin response will decrease due to low estrogen and progesterone hormones (Meidikayanti & Wahyuni, 2017) . These results are in line with the research conducted (Trihartati, 2019), regarding complications in patients with type 2 DM of the 42 research subjects, 23 were female gender and 19 were male gender.

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Table 2. Distribution of Patients with Type 2 DM in Budhi Asih Hospital by Age

Characteristics (age)	Frequency (n)	Percentage (%)
35 – 44	5	9,4
45 – 54	6	11,3
55 – 65	17	32,1
>65	25	47,2
Total	53	100

Based on table 4, with the age variable, it was found that patients with Type 2 DM were most experienced by patients with the age group >65 years at 47.2%. At the age of >45 years, a person will be more often affected by DM because the level of insulin sensitivity begins to decrease so that blood glucose levels that should enter the cells but are in the bloodstream which will cause blood glucose levels to increase (Santosa et al., 2017). Based on that, the CCT level is increasing. These results are in line with research conducted by I Gusti Ayu in 2017 that most of the respondents who suffer from type 2 DM are aged 61-70 years, and there is an increase with increasing age.

Table 3. Distribution of Serum Creatinine Examination Results in Patients with Type 2 DM at Budhi Asih Hospital

Creatinine Level	Frequency (n)	Percentage (%)
Normal (0,1 – 1,2 mg/dL)	4	7,5
High (>1,2 mg/dL)	49	92,5
Total	53	100

Based on table 3, the results of the analysis of creatinine levels in patients with type 2 diabetes, the average creatinine level in patients with type 2 diabetes is 3.054 mg/dL. The highest creatinine level in patients with type 2 diabetes was 6.35 mg/dL. Normal levels on creatinine examination at Budhi Asih Hospital, the average respondent's creatinine level has a value above the normal value. The results showed that the average serum creatinine level was above the normal value. High creatinine levels in patients with type 2 diabetes indicate that they have decreased kidney function, which will lead to kidney failure. The kidneys filter most of the creatinine and excrete it in the urine. Creatinine levels will change in response to

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kidney dysfunction (DGA Suryawan, IAMS Arjani, 2016). In DM patients, there is a deficiency of insulin secretion or reduced insulin. As a result, glucose cannot be converted into glycogen. Based on that, blood glucose levels increase and hyperglycemia occurs. This condition will cause complications in the microvascular, namely small blood vessels in the kidneys, called diabetic nephropathy (Padma, 2017).

One of the functions of the kidneys is to excrete end products or waste products of the body's metabolism, such as urea, uric acid, and creatinine. If the rest of the body's metabolism is allowed to accumulate, these substances will become toxic to the body, especially the kidneys, and the results of metabolites such as creatinine will increase (Suryawan, 2016). This is supported by research conducted by Ahmad Syahlani, Nessy Anggun, and M. Syamsul Ma'arif in 2016 about the correlation between DM and creatinine urea levels, which showed that there was a significant relationship between creatinine levels in patients with type 2 diabetes.

Table 4. Distribution of CCT Examination Results in Patients with Type 2 DM at Budhi Asih Hospital

CCT	Frequency (n)	Percentage (%)
Normal	2	3,8
Low	51	96,2
Total	53	100

Based on table 4, the results of the distribution of CCT examinations showed that the average value of research subjects at Budhi Asih Hospital was 20,048 mL/minute with the lowest level of 5.52 mL/minute. This indicates the possibility of complications of diabetic nephropathy that most patients experience a decrease in CCT values and according to the stages of kidney disease determined by the *National Kidney Foundation* (2013), these results indicate stage four kidney damage with a severe decrease in CCT. From these results, it can be shown that most of the research subjects have poor glycemic control and may lead to diabetic nephropathy. Then, evaluation is necessary to prevent the situation does not worsen and complications in the kidneys. It is known that the kidney is an important organ that has an excretory function, regulates fluid body volume, maintains acid-base balance, regulates blood pressure, and maintains a balance of calcium and phosphorus (Nur, 2020). In a study (Purnamasari and Poerwantoro, 2011), it

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was found that the CCT value in DM patients was 28.38 mL/minute.

In DM patients, kidney damage begins with uncontrolled microalbuminuria and then develops into clinical proteinuria (Rivandi & Yonata, 2015). High blood glucose levels in the body can slowly damage the filtration membrane because glucose will react with proteins so as to change the structure and function of cells, including the glomerular basement membrane. A damaged protein barrier layer will result in leakage of protein into the urine, which can lead to impaired kidney function (Padma, 2017).

Table 5. Data Normality Test Results and Correlation Calculation Results between Serum Creatinine Levels and CCT at Budhi Asih Hospital

	Data Normality Test Kolmogrov-Smirnov		**Correlation Test Spearman's**		
Variable	N	Sig.	n	Sig.	Coefficient Correlation
Creatinine	53	0.033	53	0.004	-0.389
CCT	53	0.000	53		

Based on table 5, the results showed that there was a moderate correlation between serum creatinine and CCT with a correlation coefficient (r) of -0.389 at the 95% confidence level with a value of α0.05. The correlation shown is a negative correlation, which means that the higher the creatinine level, the lower the CCT level. In addition, there are studies that are in line with this study, which was (Indriani, et.al., 2017), which stated that there was a significant correlation between serum creatinine levels and CCT in DM patients, which showed similar results with the correlation coefficient of each are 0.298 and -0.382, respectively.

A correlation between serum creatinine levels and creatinine *clearance test* (CCT) in patients with type 2 diabetes. This can indicate that there are complications in type 2 DM patients with the kidneys or what is known as diabetic nephropathy. Diabetic nephropathy is a microvascular complication that causes kidney problems and will cause the patient to experience diabetes for a long time. According to (Restada, 2016), nephropathy ranks third in DM complications after retinopathy and neuropathy with 11 patients.

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Clinically, the disease in DM requires laboratory evaluation to determine the diagnosis, therapy, and control. To evaluate for possible complications, renal function tests such as serum creatinine and *creatinine clearance test* (CCT) were performed. The examination can be carried out periodically in accordance with the doctor's recommendations (American Diabetes Association, 2010).

The limitation of this study is that the researcher did not know the length of time the patient had diabetes and other variables, such as lifestyle, smoking, drug use, other illnesses, and other risk factors that could affect creatinine levels and CCT. Creatinine and CCT levels that can be influenced by lifestyle conditions require full control in preventing DM, control that can be carried out by people who may not have the opportunity in terms of laboratory examinations by carrying out routine controls at the public health center through simple actions such as POCT tests or blood pressure checks to anticipate complications of DM. In addition, there are limitations beyond control, and it turns out that CCT examinations are rarely carried out, and time constraints due to the COVID-19 pandemic condition have caused the number of samples to be unfulfilled.

CONCLUSION

Based on the research on the correlation between serum creatinine levels and creatinine clearance test (CCT) in patients with type 2 DM, which was analyzed from secondary data from medical records at Budhi Asih Hospital, it can be concluded that there is a significant correlation (p-value 0.004) on serum creatinine levels and CCT with the direction of the correlation is negative (r = -0,389) which means that the higher the creatinine level, the lower the CCT value. Based on the research that has been done, the researcher has a deficiency because it does not include several other risk factors such as lifestyle, smoking, drug use, congenital diseases, or complications that affect the condition of creatinine levels and CCT. It is hoped that further researchers can develop research mechanisms primarily with the aim of seeing the real condition of patients by looking at their lifestyle or diet and accompanying congenital diseases.

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