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RESEARCH ARTICLES

Profile of Glomerular Filtration Rate Estimation Using the CKD-EPI Method in Type 2 Diabetes Mellitus Patients: Assessing the Risk of Kidney Complications

Profile Estimasi Glomerular Filtration Rate dengan Metode CKD-EPI pada Pasien DM Tipe 2: Menilai Risiko Komplikasi Ginjal

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Abstract

Diabetes mellitus is a metabolic disease that occurs due to the body's inability to produce and/or use insulin effectively, resulting in high blood sugar levels. Type 2 diabetes mellitus (DM) accounts for 90% of all diabetes cases globally, with significant contributing factors such as obesity, sedentary lifestyles, and poor dietary habits. In 2019, Indonesia ranked seventh in the world for the number of diabetes cases, with 10.7 million individuals affected. This research used a retrospective, observational, descriptive-analytic approach to assess kidney dysfunction in newly diagnosed type 2 diabetes mellitus patients, using the CKD-EPI equation to estimate eGFR.. The eGFR analysis revealed that most patients had eGFR values below the normal threshold of <90 mL/min/1.73 m², with an average of 77.5 ± 28.51 mL/min/1.73 m², indicating kidney impairment at the early stage. The largest group (45%) showed normal kidney function, while 21% had mild dysfunction. Patients with kidney impairment (eGFR < 90 mL/ min/ 1.73m²) had a higher average fasting blood glucose level (240 ± 82.9 mg/dL) compared to those without kidney impairment. These findings emphasized the importance of early detection and intervention for managing both blood glucose levels and kidney function effectively. Early detection of kidney impairment in type 2 diabetes mellitus patients is crucial in preventing further complications and preserving kidney health.

Keywords: CKD-EPI, eGFR, type 2 diabetes mellitus

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Abstrak

Diabetes melitus merupakan penyakit metabolik yang terjadi akibat ketidakmampuan tubuh dalam memproduksi dan/atau menggunakan insulin secara efektif, sehingga mengakibatkan tingginya kadar gula darah. Diabetes tipe 2 menyumbang 90% dari seluruh kasus diabetes di dunia, dengan faktor penyumbang utama seperti obesitas, gaya hidup sedentari, dan pola makan yang tidak sehat. Pada tahun 2019, Indonesia menduduki peringkat ketujuh dunia dalam jumlah kasus diabetes, dengan 10,7 juta penderita. Penelitian ini menggunakan pendekatan retrospektif, observasional, deskriptif-analitik untuk menilai gangguan ginjal pada pasien DM tipe 2 yang baru didiagnosis, dengan menghitung eGFR berdasarkan rumus CKD-EPI. Hasil analisis eGFR menunjukkan bahwa sebagian besar pasien memiliki nilai eGFR di bawah ambang normal (<90 mL/menit/1,73 m²), dengan rata-rata 77,5 ± 28,51 mL/menit/1,73 m², yang menunjukkan adanya gangguan ginjal pada tahap awal. Kelompok terbesar (45%) menunjukkan fungsi ginjal normal, sedangkan 21% mengalami gangguan ringan. Pasien dengan gangguan ginjal (eGFR < 90 mL/menit/1,73 m²) memiliki rata-rata kadar gula darah puasa lebih tinggi (240 ± 82,9 mg/dL) dibandingkan dengan yang tidak mengalami gangguan ginjal. Temuan ini menegaskan pentingnya pemantauan dini untuk mengidentifikasi komplikasi ginjal pada pasien DM tipe 2. Deteksi dini dan intervensi yang tepat sangat penting untuk mengelola kadar gula darah dan fungsi ginjal guna mencegah kerusakan lebih lanjut.

Kata Kunci: *diabetes mellitus tipe 2, eGFR, CKD-EPI*

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Highlight:

- A significant portion of newly diagnosed type 2 diabetes mellitus patients exhibits a decline in renal function (eGFR) below the normal threshold, indicating the presence of kidney impairment from the early stages of diagnosis.
- There are significant differences in fasting blood glucose levels and serum creatinine between type 2 DM patients with renal impairment and those with normal renal function.
- These findings emphasize the urgent need for early kidney function monitoring using the CKD-EPI formula to prevent the progression of diabetic nephropathy complications and the risk of end-stage renal disease.

INTRODUCTION

Diabetes mellitus is a metabolic disease that occurs due to the body's inability to produce and/or use insulin effectively, resulting in high blood sugar levels that disrupt the metabolism of fats, carbohydrates, and proteins (Kazi and Blonde, 2019; Varghese and Jialal, 2023). It encompasses four primary types: type 1 diabetes, type 2 diabetes, gestational diabetes, and specific types linked to other causes. The International Diabetes Federation (IDF) has consistently reported a significant increase in the prevalence of diabetes worldwide since 2000, particularly in developing countries. This global trend is largely driven by population growth, urbanization, and the rapid adoption of unhealthy lifestyles, which include poor dietary habits and reduced physical activity.

As a result, diabetes has become one of the most pressing public health challenges globally, with its associated complications, such as cardiovascular disease, neuropathy, diabetic nephropathy, and diabetic retinopathy, causing a huge burden on healthcare systems. (Widhyasih et al., 2021; Magliano et al., 2021).

It is estimated that approximately 285 million people worldwide were living with type 1 and type 2 diabetes mellitus in 2009. This number has increased significantly globally over the years to 366 million people in 2011, then increased to 382 million in 2013, and reached 425 million sufferers in 2017. Type 2 diabetes mellitus now accounts for about 90% of all diabetes cases, driven largely by two primary factors: the aging population and lifestyle changes (Saeedi et al., 2019). In 2019, Indonesia recorded 10.7 million individuals with type 2 diabetes, placing the country seventh globally in terms of the highest number of diabetes cases. As a country in Southeast Asia, Indonesia plays a significant role in contributing to the increase in diabetes mellitus cases in the region, especially type 2 diabetes. The rising prevalence of type 2 diabetes in Indonesia is influenced by various complex factors, including population growth, urbanization, and significant changes in dietary patterns and lifestyle (Mihardja et al., 2018).

Type 2 diabetes mellitus is one of the main causes of kidney disease besides hypertension, because this condition requires long-term medical management to control blood glucose levels and reduce the risk of complications, including impaired kidney function. Chronic kidney failure due to diabetes mellitus is the leading cause of end-stage renal disease (ESRD) in individuals with type 2 diabetes mellitus worldwide. This phenomenon highlights the importance of more holistic preventive strategies and integrated management to mitigate the long-term impact of diabetes, particularly concerning progressive kidney damage, which significantly affects the quality of life for patients and adds a burden to global healthcare systems (KDIGO, 2023).

According to the KDIGO guidelines, chronic kidney disease is identified when the glomerular filtration rate (GFR) decreases to less than 60 mL/min/1.73 m² for at least three months, regardless of the underlying cause. GFR is a crucial parameter used to evaluate kidney function, as it reflects how well the kidneys are filtering blood. There are two primary methods for measuring GFR: using endogenous markers and exogenous markers. Endogenous markers, such as creatinine, are naturally present in the body, while exogenous markers like inulin, iothalamate, and chromium 51 ethylenediamine tetraacetate (51 Cr-EDTA) need to be administered externally (KDIGO, 2023).

The gold standard for measuring GFR involves the use of exogenous markers, particularly inulin clearance, which directly measures how well the kidneys are filtering a substance that is freely filtered and not reabsorbed or secreted by the kidneys. However, the use of inulin as a marker is not commonly employed in clinical practice due to several limitations, including the high cost of the procedure, the time required for measurement, and the fact that it is not available in many healthcare settings. Given these challenges, measuring GFR with endogenous markers, particularly creatinine, has become a widely accepted and practical alternative. The estimation of GFR using creatinine-based formulas is a standard method employed in clinical practice, as it is less expensive and easier to perform. These formulas use serum creatinine levels, along with factors such as age, sex, and race, to estimate kidney function. The use of GFR estimation formulas is endorsed by various healthcare organizations, including the UK National Renal Service Framework, which recommends annual GFR assessments for all patients with diabetes. Regular monitoring of kidney function in diabetes patients is

essential, as diabetes is one of the leading causes of chronic kidney disease (CKD) and can lead to kidney failure if not managed properly (Nazzal et al., 2020).

The Modification of Diet in Renal Disease (MDRD) formula and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula are two of the most commonly used methods for estimating glomerular filtration rate (eGFR) in clinical practice. Both of these formulas have been extensively validated. Both of these formulas have been extensively validated and are widely accepted for clinical use. They provide a reliable estimate of kidney function, enabling healthcare providers to monitor and detect early signs of kidney damage, which is particularly important in diabetic patients who are at a higher risk for developing CKD. Early detection accompanied by appropriate intervention plays an important role in preventing or slowing the progression of kidney disease, thus contributing to improving clinical outcomes and quality of life in patients with diabetes mellitus.

In summary, while the gold standard for measuring GFR is based on exogenous markers like inulin clearance, practical limitations have led to the widespread use of creatinine-based estimation formulas such as the MDRD and CKD-EPI equations. The estimated glomerular filtration rate (eGFR) formula is an important instrument in clinical practice, especially in the management of patients with diabetes mellitus, because it allows early detection and more effective monitoring of the progression of chronic kidney disease (Nazzal et al., 2020).

The CKD-EPI equation is widely recognized as providing a more accurate and reliable estimation of the glomerular filtration rate (eGFR) than the MDRD and Cockcroft-Gault equations, particularly for assessing kidney function across diverse populations. Owing to its improved accuracy, the CKD-EPI equation has become one of the recommended methods for estimating kidney function in clinical practice.

Based on this rationale, the present study aims to explore the use of the CKD-EPI equation to estimate eGFR as an indicator of kidney function in newly diagnosed patients with type 2 diabetes mellitus at the Internal Medicine Outpatient Clinic of PKU Muhammadiyah Sampangan Hospital, Semanggi, Surakarta. This study seeks to evaluate the applicability of the CKD-EPI equation in assessing kidney function in this specific patient population, thereby contributing to a better understanding of renal health among individuals with newly diagnosed type 2 diabetes. The findings are expected to support more accurate and individualized management of diabetic nephropathy, one of the major complications of type 2 diabetes mellitus.

METHODS

This research employed a descriptive, analytical, observational, and retrospective approach to evaluate the profile of kidney impairment in newly diagnosed type 2 diabetes mellitus patients, with the estimated glomerular filtration rate (GFR) based on CKD-EPI formula. The data were sourced from the medical records of new type 2 DM patients who received treatment at the Outpatient Internal Medicine Polyclinic of PKU Muhammadiyah Sampangan Semanggi Surakarta Hospital for one year, namely the period from January 1 to December 31, 2020. A total sampling approach was used, including 56 patients who met both the inclusion and exclusion criteria for the study. Ethical approval was obtained from for granted through clearance letter no. 5086/C.2/KEPK-FKUMS/IX/2-23. This research aimed to provide a comprehensive overview of kidney function in the early stages of type 2 diabetes, shedding light on potential renal complications and the importance of early monitoring and intervention.

The participants in this study were chosen based on defined inclusion and exclusion criteria to maintain the integrity and relevance of the results. The inclusion criteria were: individuals newly diagnosed with type 2 diabetes mellitus (DM), aged 18 years or older, and those who had available creatinine test data from the PKU Muhammadiyah Sampangan Semanggi Surakarta Hospital Laboratory. This ensures that the data used to calculate eGFR were both current and directly applicable to the condition being investigated.

The exclusion criteria included patients who have been diagnosed with kidney failure before the study began, as this would confound the results by introducing factors unrelated to the impact of type 2 DM on kidney function. Patients with kidney diseases prior to the diagnosis of DM could skew the analysis of eGFR, making it difficult to isolate the effects of diabetes alone on kidney function.

For the eligible patients, the eGFR was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) method. This widely utilized approach in clinical settings provides a reliable estimation of kidney function by incorporating factors such as serum creatinine levels, age, gender, and ethnicity. The CKD-EPI formula offers a more accurate prediction of glomerular filtration rate, making it a preferred tool for evaluating kidney health. The specific formula used for calculating eGFR is as follows:

$$GFR = 141 \times \min(S_{cr}/k,1)^{\alpha} \times \max(S_{cr}/k,1)^{-1.209} \times 0.993^{age} \times 1.018\ (\text{Female}) \times 1.159\ (\text{Black skin})$$

Using the CKD-EPI method to estimate eGFR, this research aims to evaluate the extent of kidney function in newly diagnosed type 2 diabetes mellitus (DM) patients and to detect early signs of kidney damage that may have already begun. This is essential to provide a deeper understanding of how diabetic nephropathy develops in patients with type 2 diabetes mellitus and to identify potential kidney complications that may impact the patient's quality of life if not addressed promptly. Thus, this study is expected to provide useful information for early management and prevention of further kidney damage in diabetes patients.

Table 1. Stratification of Glomerular Filtration Rate (eGFR)

Stratification code	Terminology	eGFR (ml/min/1.73 m^2)
G1	Normal	≥90
G2	Light	60-89
G3a	Light-medium	45-59
G3b	Medium-severe	30-44
G4	Heavy	15-29
G5	Terminal	<15

Source: KDIGO, 2023

The eGFR results were categorized based on kidney function impairment and calculated from serum creatinine levels. The stratification of glomerular filtration rate is presented in Table 1. Serum creatinine levels were measured in 2020 using samples obtained from the study subjects, which were centrifuged and analyzed with a chemistry

analyzer using the Jaffe method. Data analysis was performed using the chi-square test to evaluate the variations in the proportions of eGFR results among newly diagnosed type 2 DM patients. This statistical method allowed for the comparison of categorical variables and the assessment of significant differences in kidney function across different patient groups. This approach helps to identify correlations between kidney function and diabetes-related complications, enabling early intervention strategies to prevent further kidney deterioration.

RESULTS AND DISCUSSIONS

This study focused on newly diagnosed type 2 diabetes mellitus (DM) patients, finding an average age of 63 ± 7.58 years. It also revealed a higher proportion of female patients (64.3%) compared to male patients (35.7%) within a sample of 56 individuals. This demographic information highlights the importance of focusing on older adults, especially male, who are at a higher risk for developing type 2 DM and the related complications, emphasizing the need for targeted interventions and monitoring in these high-risk groups.

The kidney function evaluation in this study revealed an average eGFR of 77.5 ± 28.51 mL/min/1.73 m², which is below the normal threshold. This indicates that many patients in this cohort were already experiencing some degree of kidney dysfunction at the time of their diabetes diagnosis. Since eGFR is a vital marker for assessing kidney function, these findings suggest an early onset of diabetic nephropathy or other renal complications, which are commonly seen in individuals with type 2 DM.

Considering that kidney damage in diabetes often progresses without noticeable symptoms, the study underscores the importance of early screening for kidney dysfunction in type 2 DM patients. Detecting kidney impairment at an early stage can prevent further deterioration and reduce the risk of developing end-stage renal disease, a severe and common complication of diabetes. Early interventions, such as better glycemic control, managing blood pressure, and adopting lifestyle modifications, can significantly lower the risk of kidney failure and improve the prognosis for patients with diabetes.

Table 2. Demographic profile of study participants

Variable[a]	Mean ±SD	Frequency N(%)
Age (years)	63 ± 7.58	-
Creatinine (mg/dL)	1.1 ± 0.80	-
eGFR (ml/min/1,73 m^2)	77.5 ± 28.51	-
Fasting Blood Glucose (mg/dL)	212.3 ± 88.5	-
Gender		20 (35.7%) Male 36 (64.3%) Women

Note: mg= milligram; dl =deciliter; eGFR = estimated Glomerular Filtration Rate

This study focused on detecting complications of diabetes mellitus at early diagnosis, particularly kidney dysfunction, through assessment of eGFR using the CKD-EPI formula, classified into six categories based on the 2013 KDIGO guidelines, revealing important insights. The results presented in Table 3 show that the majority of respondents (55%) exhibited kidney impairment with an eGFR below normal, while 45% maintained normal kidney function. These findings highlight the high prevalence of kidney impairment in diabetic patients, emphasizing the need for early detection of

kidney impairment to prevent further complications. They also suggest that regular kidney function monitoring is essential for diabetes patients, especially considering that kidney dysfunction can develop silently and progressively without overt symptoms.

Table 3. Distribution of eGFR stages in type 2 DM Patients

Proportion of Classification eGFR	Impaired Kidney Function	Frequency N (%)
Normal	No	25 (45%)
Light	Yes	12 (21%)
Light-Medium	Yes	9 (16%)
Medium-Heavy	Yes	5 (8%)
Heavy	Yes	2 (3%)
Terminal	Yes	2 (3%)

Sources: Primary data, 2020

Table 4 shows that age and gender do not exhibit significant differences between type 2 DM patients with and without kidney disorders. However, the parameters of creatinine and fasting blood sugar in patients with impaired kidney function (eGFR < 90 ml/min/1.73 m²) show significant differences with a *p-value* < 0.05 when compared to patients without kidney impairment, with an average creatinine level of 1.4 ± 0.9 and fasting blood glucose of 240.8 ± 82.9 mg/dL.

Table 4. Variation in characteristics according to kidney function in type 2 DM patients

Parameter Characteristics	Without Impaired Renal Function (%)	With Impaired Renal Function (%)	*p-value*
Age (Years)	61.8 ±7.3	64.0±7.7	0.27
Gender			
Man	8 (40%)	12 (60%)	0.23
Woman	18 (50%)	18 (50%)	
Fasting Blood Glucose (mg/dL)	179.3±84.7	240.8±82.9	<0.01*
Creatinine (mg/dL)	0.63±0.13	1.4±0.9	<0.01*

Note: mg = milligram, dl = deciliter, chi-square test, signifikan if p-value < 0.05

Among individuals with diabetes mellitus, diabetic nephropathy stands as one of the most prevalent complications, impacting approximately 40% of patients and constituting the primary cause of kidney disease in this group. This condition is characterized by the presence of microalbuminuria (30 mg/day), which occurs even in the absence of clear kidney abnormalities, along with a gradual decline in GFR. Over time, if not properly managed, diabetic nephropathy can worsen, eventually progressing to end-stage renal failure. Early detection and effective management, including tight blood sugar control and blood pressure regulation, are essential to prevent or slow the progression of kidney impairment and support long-term well-being for patients with this condition (Gembillo et al., 2021). As diabetic nephropathy often develops silently, the early detection of changes in kidney function is crucial for preventing further damage. The glomerular filtration rate is considered the most reliable marker of renal

function, as it reflects the kidneys' ability to filter blood, process waste, and excrete the products through urine. GFR is influenced by several factors, including age, gender, and serum creatinine levels. A normal GFR typically ranges from 100-150 mL/min, and a reduction in this rate indicates a decline in kidney function. To assess kidney function, the two most commonly used methods are creatinine clearance and estimated GFR, both of which provide valuable insights into the extent of kidney impairment. These methods have become essential tools in clinical practice, allowing for early identification of diabetic nephropathy and timely intervention, which is vital in managing the progression of renal disease in diabetic patients (Pottel et al., 2020; Noronha et al., 2022).

Glomerular filtration rate is influenced by several factors, both physiological and pathological. The CKD-EPI formula is considered the most accurate eGFR equation, having been extensively evaluated across large and diverse populations, making it highly applicable for general clinical use. Given this, the current study utilizes the CKD-EPI equation to calculate eGFR. Despite being one of the most commonly used and practical methods for estimating eGFR and evaluating kidney function, the CKD-EPI equation does have certain limitations, particularly when applied to specific patient populations and clinical conditions. To mitigate potential bias, it is often necessary to adjust the formula, incorporate additional markers such as cystatin C, and combine it with albuminuria testing. Furthermore, it is essential to consider the patient's overall clinical context when interpreting eGFR results to ensure accurate assessments.

In this research, half of the newly diagnosed (incident) type 2 diabetes mellitus (DM) patients exhibited various levels of kidney dysfunction, ranging from mild impairment to advanced stages of kidney failure. More specifically, patients with stage 3 kidney dysfunction, defined by an eGFR <60 mL/min/1.73 m^2, were found to face a mortality risk up to 10 times higher compared to those with end-stage renal disease (Nichols et al., 2020). These findings emphasize the critical importance of closely monitoring kidney function from the moment of diagnosis in type 2 DM patients. Early detection of kidney dysfunction can prevent its development into further complications, namely diabetic nephropathy, a serious and potentially life-threatening complication. (Thomas, 2019).

The development of diabetic kidney disease is a complex, multifactorial process influenced by a combination of genetic susceptibility and environmental factors, all of which interact to accelerate kidney damage in individuals with diabetes. Unmodifiable risk factors include family history, genetics, sex, the age at which diabetes is diagnosed, and the duration of the condition. On the other hand, modifiable risk factors such as maintaining optimal blood sugar control, managing blood pressure, quitting smoking, reducing alcohol consumption, exercising regularly, and following a balanced diet can play an important role in slowing the progression of the disease. This highlights the importance of not only early diagnosis but also long-term management of type 2 diabetes to prevent or delay the onset of kidney-related complications. Effective interventions can dramatically reduce the incidence of diabetic nephropathy and improve patient outcomes, underscoring the need for continued vigilance and proactive management in the care of individuals with type 2 DM (Ismail et al., 2021; Roy et al., 2021). These factors underscore the importance of early intervention and lifestyle changes in inhibiting and/or preventing the progression of diabetic nephropathy.

Kidney dysfunction in diabetes mellitus (DM) is primarily caused by hyperglycemia, which leads to nephron loss and hyperfiltration. This condition triggers a series of changes in which oxidative stress and hypoxia play an important role, namely

inflammatory, metabolic, hemodynamic, hormonal, and epigenetic changes. The main mechanisms underlying kidney injury in diabetic nephropathy include glomerular hypertrophy, inflammation in the glomerular and tubulointerstitial areas, and cellular apoptosis with alterations in the extracellular matrix. This process leads to glomerular basement membrane thickening, podocyte depletion, mesangial matrix expansion, and tubular injury. These structural changes result in glomerulosclerosis, vascular remodeling, endothelial dysfunction, and tubulointerstitial fibrosis, all of which impair kidney function. As the disease progresses, this damage can lead to reduced kidney filtration capacity and complications such as proteinuria and eventual kidney failure. Early interventions, including tight glycemic control, blood pressure management, and renoprotective therapies, are crucial in slowing the progression of diabetic nephropathy and improving patient outcomes (DeFronzo et al., 2021; Gembillo et al., 2021).

CONCLUSIONS

In this study, it was found that approximately half of the patients newly diagnosed with type 2 diabetes mellitus (DM) experience varying degrees of kidney dysfunction, ranging from mild impairment to advanced stages of kidney failure. Patients with stage 3 renal impairment, characterized by an eGFR <60 mL/min/1.73 m², face a significantly higher mortality risk up to 10 times greater than those progressing to end-stage renal failure. This underscores the importance of closely monitoring kidney complications from the initial diagnosis to prevent the development of diabetic nephropathy, which can lead to severe complications. The United States Renal Data System (USRDS) also highlights that the progression of diabetic nephropathy not only accelerates the decline in kidney function but also increases the risk of mortality in patients with chronic kidney disease (CKD), compared to other causes of CKD. The progression of diabetic kidney disease is a complex, multifactorial process influenced by a combination of genetic susceptibility and environmental factors. Unmodifiable risk factors include family history, genetics, gender, the age at diagnosis, and the duration of diabetes. Meanwhile, modifiable risk factors include maintaining a healthy lifestyle through controlling blood glucose, blood pressure, quitting smoking, reducing alcohol consumption, engaging in physical activity, and maintaining a balanced diet. Therefore, it is crucial to perform early detection through regular monitoring of kidney function in type 2 diabetes patients to prevent complications like diabetic nephropathy from developing at an early stage, and to control disease progression.

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