

HbA1c Levels and Ureum Creatinine Levels Among T2DM Patients in Indonesia: A Systematic Review

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ABSTRAK

Pendahuluan: Diabetes mellitus tipe 2 (DMT2) merupakan penyebab utama penyakit ginjal kronis yang diakibatkan oleh hiperglikemia kronis, yang dapat menyebabkan kerusakan glomerulus. Tinjauan sistematis ini bertujuan untuk menganalisis hubungan antara kadar HbA1c dengan kadar ureum dan kreatinin pada pasien DMT2 di Indonesia. **Metode:** Tinjauan sistematis dilakukan sesuai dengan pedoman PRISMA 2020. Pencarian literatur dilakukan menggunakan Google Scholar, Garuda, PubMed, EBSCO, dan Scopus. Risiko bias dievaluasi menggunakan JBI *critical appraisal*. Data diekstraksi dan disintesis secara naratif. **Hasil:** Sebanyak sembilan studi potong lintang yang diterbitkan antara tahun 2020 dan 2025 memenuhi kriteria inklusi, melibatkan total 3.872 peserta. Kesembilan studi tersebut menunjukkan hasil yang bervariasi. Ada studi yang menganalisis kadar ureum saja dan ada pula yang menganalisis kadar ureum dan kreatinin secara bersamaan: 3 studi menunjukkan hubungan yang signifikan dengan kadar ureum. 5 studi menunjukkan hubungan yang signifikan dengan kreatinin. Namun, 4 studi tidak menunjukkan hubungan yang signifikan antara HbA1c dan kreatinin. **Kesimpulan:** Sebagian besar bukti menunjukkan adanya hubungan antara kontrol glikemik yang buruk dan perubahan parameter fungsi ginjal pada pasien dengan DM Tipe 2. Pemantauan HbA1c bersamaan dengan kadar ureum dan kreatinin berpotensi mendukung deteksi dini nefropati diabetik di Indonesia.

Kata kunci: HbA1c, ureum, kreatinin, diabetes melitus tipe 2

ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is the leading cause of chronic kidney disease resulting from chronic hyperglycemia, which can lead to glomerular damage. This systematic review aims to analyze the relationship between HbA1c levels and ureum and creatinine levels in T2DM patients in Indonesia. **Method:** A systematic review was conducted in accordance with the PRISMA 2020 guidelines. A literature search was conducted using Google Scholar, Garuda, PubMed, EBSCO, and Scopus. Risk of Bias was assessed using the JBI *critical appraisal*. Data were extracted and synthesized narratively. **Result:** A total of nine cross-sectional studies published between 2020 and 2025 met the inclusion criteria, involving a total of 3,872 participants. The nine studies showed varying results. There are studies that examine ureum levels alone and ureum and creatinine levels together: 3 studies show a significant association with ureum levels. 5 studies show a significant association with creatinine. However, 4 studies show no significant association between HbA1c and creatinine. **Conclusion:** Most evidence points to a link between poor glycemic control and changes in renal function parameters in patients with T2DM. Monitoring HbA1c along with ureum and creatinine has the potential to support the early detection of diabetic nephropathy in Indonesia

Keywords: HbA1c, ureum, creatinine, type 2 diabetes melitus

PENDAHULUAN

Type 2 Diabetes Mellitus (T2DM) is a chronic disease that has become a global health issue, with its prevalence continuing to rise each year. The International Diabetes Federation (IDF) reported in 2021 that 537 million adults aged 20–

79 worldwide are living with diabetes. Indonesia ranks among the top ten countries with the highest number of people with diabetes worldwide and is ranked fifth, with approximately 20.4 million cases in the adult population. The majority of diabetes cases are T2DM, which is closely linked to changes

in lifestyle, dietary patterns, and urbanization. The rising prevalence of T2DM also increases the risk of chronic complications, both macrovascular and microvascular. One of the most common and progressive microvascular complications is diabetic nephropathy, which is the leading cause of chronic kidney disease and end-stage kidney disease (ESRD) (PERKENI, 2024).

Poor glycemic control is a major risk factor for kidney damage in patients with T2DM. One of the parameters used to assess long-term glycemic control is the level of glycated hemoglobin (HbA1c), which is considered the gold standard for reflecting average blood glucose levels over the past 2–3 months. Chronic hyperglycemia in patients with T2DM causes a sustained increase in blood glucose, triggering the non-enzymatic glycation of proteins, lipids, and nucleic acids. This process results in the formation of Advanced Glycation End-products (AGEs), compounds that can accumulate in kidney tissue, particularly the glomerular basement membrane. Advanced Glycation End-products (AGEs) then bind to their receptor, the Receptor for Advanced Glycation End-products (RAGE), which activates various inflammatory and oxidative stress pathways. AGE–RAGE activation increases the production of reactive oxygen species (ROS), proinflammatory cytokines, and profibrotic factors such as transforming growth factor- β (TGF- β), which lead to thickening of the basement membrane, mesangial expansion, and renal fibrosis. The resulting progressive kidney damage subsequently causes elevated serum ureum and creatinine levels, which serve as markers of declining kidney function (Chen et al., 2024).

Kidney damage in patients with diabetes mellitus (DM) generally goes undetected in the early stages, making accurate and easily accessible kidney function parameters essential in clinical practice in Indonesia. Although glomerular filtration rate (GFR) or cystatin C are known to be more sensitive in detecting a decline in kidney function, their use remains limited due to cost constraints, more complex procedures, and uneven availability across healthcare facilities. On the other hand, ureum and creatinine tests are still more widely used because they are relatively inexpensive, simple, widely available, and routinely performed at most primary care facilities (FKTP) in Indonesia (PERKENI, 2021). Serum creatinine can reflect a decline in renal filtration function, while ureum is used as a supporting parameter in assessing renal excretory function and the patient's metabolic status (Muhammadiyah et al.,

2025; Purwanto & Listiawati, 2024). Therefore, the relationship between glycemic control, as assessed by HbA1c levels and elevated ureum and creatinine levels is important to examine as part of efforts to detect early signs of impaired kidney function in patients with diabetes mellitus (DM).

Although the relationship between HbA1c levels and elevated ureum and creatinine levels has been extensively studied in Indonesia, the research findings remain highly variable and inconsistent. A study conducted by (Pinky et al., 2023) in Bandar Lampung demonstrated a significant association between HbA1c levels and creatinine levels. Similar results were also reported by (Muhammadiyah et al., 2025) at the Bondowoso Regional Health Laboratory, indicating that high HbA1c levels are positively correlated with increased concentrations of creatinine, ureum, and microalbumin. However, (Nabila et al., 2022) reported different findings at the Pandanaran Gunungpati and Purwoyoso Community Health Centers, noting that there was no significant correlation between HbA1c and serum creatinine levels in patients with type 2 diabetes, as these results were influenced by the duration of diabetes, age, and the comorbidity of hypertension. Furthermore, in 2024, (Widayanti et al., 2024) also reported that HbA1c levels had no significant association with creatinine levels. There has not yet been a comprehensive literature review that integrates these local data to map the macro-level clinical profile of people with type 2 diabetes in Indonesia.

This systematic review was conducted to analyze and synthesize scientific evidence from various published studies in Indonesia on the relationship between HbA1c levels and ureum and/or creatinine levels in patients with type 2 diabetes mellitus. This systematic review is expected to provide an overview of the relationship between long-term glycemic control and changes in kidney function, as indicated by ureum and creatinine levels, in patients with type 2 diabetes mellitus. Additionally, this study is expected to provide a basis for clinical decision-making in efforts to detect kidney dysfunction early in Indonesia.

METODE

This systematic review was conducted in May 2026. The study was completed in accordance with the PRISMA checklist. This study used the PEO framework, in which the patient group consisted of individuals with type 2 diabetes

mellitus, the exposure involved levels HbA1c, and the outcome was ureum and creatinine levels

Search strategy

The literature search was conducted through Google Scholar, Garuda, PubMed, EBSCO, and Scopus using a combination of keywords and Boolean operators. The search for articles on Google Scholar and Garuda used the following keywords: (“Type 2 Diabetes Mellitus” OR “diabetes mellitus”) AND (“HbA1c” OR “Glycated Hemoglobin”) AND (ureum OR Creatinine OR creatine) AND “Indonesia”. Search for articles in PubMed using the keywords ((“Diabetes Mellitus, Type 2”[MeSH Terms] OR “Type 2 Diabetes”[Title/Abstract])) AND ((“HbA1c”[Title/Abstract])) AND ((“ureum”[MeSH Terms] OR “Ureum”[Title/Abstract] OR “Blood ureum Nitrogen”[Title/Abstract] OR (“Creatinine”[MeSH Terms] OR “Kreatinin”[Title/Abstract] OR (“Glomerular Filtration Rate”[MeSH Terms] OR “eGFR”[Title/Abstract])) AND (“Indonesia”[Title/Abstract] OR “Indonesia”[MeSH Terms])). The article search via EBSCO used the keywords (“Type 2 Diabetes”) AND (“HbA1c”) AND (“ureum” OR “Creatinine” OR “Glomerular Filtration Rate”) AND (“Indonesia**”). Meanwhile, the search on Scopus used the TITLE-ABS-KEY keywords (“Type 2 Diabetes” OR “T2DM”) AND TITLE-ABS-KEY (“HbA1c”) AND TITLE-ABS-KEY (“ureum” OR “Ureum” OR “Creatinine” OR “Kreatinin” OR “GFR” OR “eGFR” OR “LFG”) AND TITLE-ABS-KEY (“Indonesia”).

In selecting articles, we applied inclusion and exclusion criteria. The inclusion criteria for this study are articles published between 2020 and 2025 that discussed the relationship between HbA1c levels and ureum and/or creatinine levels in patients with type 2 diabetes mellitus in Indonesia; articles written in Indonesian or English; and observational studies. The exclusion criteria applied were grey literature, conference abstracts,

letters to the editor, articles that were not fully accessible, studies not conducted on humans, and review articles.

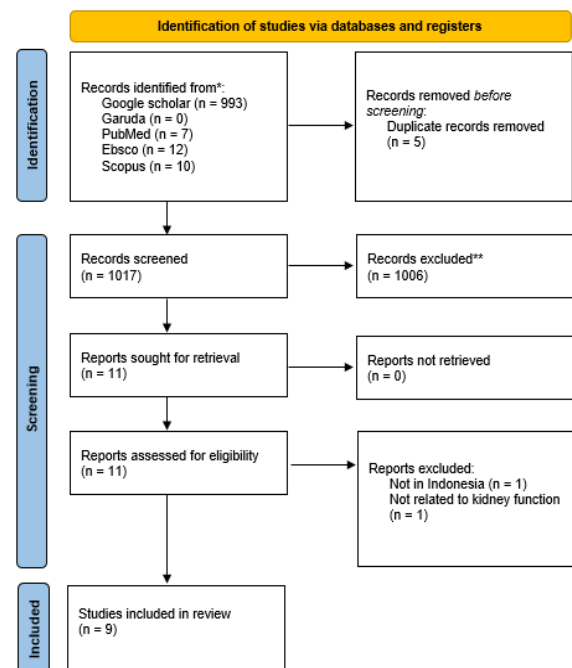
Risk of bias, data extraction, synthesis

Risk of bias was assessed using the Joanna Briggs Institute’s 8-item checklist for cross-sectional studies. A low risk (+) is assigned a score of 1, an unclear risk (?) is assigned a score of 0.5, and a high risk (-) is assigned a score of 0. The scores are totaled; a score of <4 indicates high risk, 4–6 indicates moderate risk, and 6.5–8 indicates low risk of bias.

Data extraction include authors, year of publication, type of study, type of analysis, sample, location, and result.

Synthesis and analysis

Data were synthesized and analyzed narratively.



Gambar 1. PRISMA flowchart

HASIL

Tabel 1
Study characteristics

Authors and year	Type of study	analysis	Sample	Location	Result
(Anggrina et al., 2022)	Cross sectional	Spearman test	107	Internal Medicine Outpatient Clinic at Karangasem Regional General Hospital	-The HbA1c level has a correlation with ureum of -0.215 (p=0.026) -HbA1c levels have a correlation with creatinine of -0.254

(p=0.008)						
(Cahyani et al., 2020)	Cross sectional	Spearman test	24	Gamping Community Center	1 Health	There is no relationship between HbA1c and creatinine levels (p=0.961; r=-0.006)
(Hertanti & Indanah, 2025)	Cross sectional	Pearson	48	Cahaya Husada Clinic		-There is a significant association between HbA1c and ureum levels (p=0,006; r=0.393) -There is no significant association between HbA1c and creatinine levels (p=0,352; r=-0.137)
(Nabila et al., 2022)	Cross sectional	Spearman's correlation test	36	Pandanaran, Gunungpati, Purwoyoso Community Centers	and Health	There was no significant correlation between HbA1c and serum creatinine levels in patients with type 2 diabetes in Java (r=-0,206; p=0,228).
(Pinky et al., 2023)	Cross sectional	Spearman's correlation test	30	Pertamina Amin Laboratory, Lampung	Bintang Hospital Bandar	-There is a significant association between HbA1c levels and creatinine levels (p=0,004; r=-0,511) -There is a significant association between HbA1c levels and ureum levels (p=0,000; r=-0,636)
(Muhammadiyah et al., 2025)	Cross sectional	Chi Square	3432	Bondowoso Regional Health Laboratory		High HbA1c levels are positively correlated with increased creatinine concentrations (p = 0,020)
(Purwanto & Listiawati, 2024)	Cross sectional	Pearson correlation test	41	Krakatau Hospital, Cilegon	Medika	HbA1c and creatinine levels have a positive correlation with a r value of 0.337 and a statistically significant relationship (p = 0,031)
(Widyayanti et al., 2024)	Cross sectional	Chi Square	106	Sinar Kasih Hospital, Purwokerto	General	HbA1c levels are not significantly associated with creatinine levels (p=0.066). There is no correlation coefficient value
(Zulfian et al., 2020)	Cross sectional	Spearman test	48	Hospital Pertamina Amin, Lampung	Bintang Bandar	HbA1c levels correlate with creatinine levels, with an r value of 0.333 (p=0.021)

Some studies show a significant association with increased ureum levels (Hertanti & Indanah, 2025) and decreased ureum levels (Anggrina et al., 2022; Pinky et al., 2023). Additionally, some studies show a significant

association with creatinine, an increase in creatinine (Muhammadiyah et al., 2025; Purwanto & Listiawati, 2024; Zulfian et al., 2020), and a decrease in creatinine (Anggrina et al., 2022; Pinky et al., 2023). However, four studies show no

significant association between HbA1c and creatinine (Cahyani et al., 2020; Hertanti &

Indanah, 2025; Nabila et al., 2022; Widyayanti et al., 2024).

Tabel 2
Risk of bias

Authors, year	1	2	3	4	5	6	7	8	Bias
Anggrina et al 2022	+	+	+	?	+	-	?	+	Moderate
Cahyani et al 2020	-	+	+	?	+	-	+	+	Moderate
Hertanti & Indanah 2025	-	+	+	?	+	-	?	+	Moderate
Nabila et al 2022	+	+	+	?	+	-	+	+	Low
Pinky et al 2023	-	+	+	?	-	-	?	+	Moderate
Muhammadiyah et al 2025	+	+	+	+	+	-	+	-	Moderate
Purwanto & Listiawati 2024	?	+	+	?	+	-	+	+	Moderate
Widyayanti et al 2024	-	+	+	?	-	-	+	+	Moderate
Zulfian et al 2020	+	?	+	?	-	-	?	+	Moderate

PEMBAHASAN

The significant association between rising HbA1c levels and increased creatinine and ureum levels is due to the patient’s poor lifestyle and the close relationship between diabetes mellitus and kidney function. Patients who do not follow dietary recommendations, lack physical activity, and do not get enough sleep will experience elevated blood sugar levels, which lead to increased HbA1c. As a result, in the long term, this will damage the kidneys, disrupting their filtration function and leading to increased levels of creatinine (Muhammadiyah et al., 2025) and ureum (Hertanti & Indanah, 2025). In terms of kidney damage, high HbA1c levels contribute to atherosclerosis, which in turn causes a reduced blood supply to the kidneys. As a result of this reduced blood supply, the kidneys become hypoxic (Zulfian et al., 2020).

However, different results were found in a study by (Widyayanti et al., 2024), which showed no significant association. This may be due to differences in the sample, methods, or instruments used in the examination. Different results were also reported by (Pinky et al., 2023) and (Anggrina et al., 2022) Although these two studies showed significant results, the relationship was inverse. If HbA1c rises, both ureum and creatinine levels will decrease. This can occur for two reasons. First, it is possible that the complications arising are not in the kidneys but in other organs. Second, even though HbA1c has increased, the rise may not yet

be sufficient to elevate ureum and creatinine levels (Anggrina et al., 2022; Pinky et al., 2023).

Findings regarding the relationship between glycemic control and renal function parameters, such as ureum and creatinine, highlight the importance of monitoring renal function in patients with type 2 diabetes mellitus as a means of early detection of kidney disease. In the context of healthcare in Indonesia, these findings are relevant to the Chronic Disease Management Program (Prolanis), a healthcare program with a proactive approach that involves participants, healthcare facilities, and the Social Health Insurance Agency (BPJS Kesehatan) in maintaining the health of patients with chronic diseases. Through this program, periodic ureum and creatinine testing can be implemented as part of routine monitoring for patients with type 2 diabetes mellitus. (Badan Penyelenggara Jaminan Sosial Kesehatan, 2024)

Regular screening has the potential to identify early-stage kidney function decline, allowing for appropriate intervention before the condition progresses to advanced-stage chronic kidney disease (Badan Penyelenggara Jaminan Sosial Kesehatan, 2024). In addition to providing clinical benefits such as preventing or slowing the progression of kidney complications, this approach also has the potential to be cost-effective, particularly in terms of healthcare financing. The cost of routine laboratory tests is relatively lower than the cost of managing end-stage kidney disease, such as hemodialysis or kidney

transplantation (Nuswantoro et al., 2022). Without an effective preventive strategy, patients may progress to end-stage renal failure and require hemodialysis, which currently represents one of the largest financial burdens for BPJS.

The findings indicate the benefits of measuring ureum and creatinine levels in patients with type 2 diabetes mellitus for the early detection of kidney dysfunction; however, this literature review still has several limitations that need to be considered. The studies reviewed in this literature review mostly employed observational designs, particularly cross-sectional studies, which limits the ability to establish a causal relationship between glycemic control and changes in kidney function. In addition, differences in subject characteristics, sample size, adherence to diabetes medication, and the presence of comorbidities influenced the study results. Therefore, further research with a more uniform and robust methodology is needed to confirm the existing findings regarding the relationship between HbA1c and ureum and/or creatinine levels in patients with type 2 diabetes mellitus in Indonesia.

SIMPULAN

In patients diagnosed with type 2 diabetes mellitus, a clear correlation has been found between long-term glycemic control (HbA1c) and changes in ureum and creatinine levels resulting from uncontrolled, chronic hyperglycemia, which exacerbates glomerular damage. ureum and creatinine levels, as key indicators, reflect a decrease in renal excretion and the progression of diabetic nephropathy, despite significant variations in individual characteristics and treatment regimens. Therefore, healthcare facilities are encouraged to maximize regular renal monitoring in patients with diabetes as a means of early detection of potential complications, to reduce morbidity rates, and to alleviate the future economic burden associated with hemodialysis.

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