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Association Between HbA1c Level and Renal Function Markers in Patients with Diabetes Mellitus

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Abstract

Background: Diabetes mellitus (DM) is a major contributor to kidney failure worldwide. Glycated haemoglobin (HbA1c) is widely recognised as a marker for glycemic regulation, yet its association with renal function decline is not fully clarified. *Objective:* This study investigates the association between HbA1c levels and renal function indicators, namely creatinine, urea, and microalbumin, in individuals with DM. *Materials and Methods:* A cross-sectional approach was utilised, analysing retrospective data collected from the medical records of DM patients participating in the Prolanis program in Bondowoso Regency during 2024. Correlation tests and linear regression were used to determine the relationship between HbA1c and the selected renal parameters, with a statistical significance threshold of $p < 0.05$. *Results:* Most patients exhibited HbA1c levels and renal parameters within normal limits. Nonetheless, a statistically significant positive correlation was identified between elevated HbA1c levels and increased concentrations of creatinine ($p = 0.020$), urea ($p = 0.01$), and microalbumin ($p = 0.01$). *Conclusion:* Higher HbA1c levels are associated with deteriorating kidney function among DM patients. However, HbA1c should not be solely relied upon as a standalone marker for renal impairment. Further investigations are necessary to elucidate the biological pathways involved and to evaluate the potential of HbA1c control in mitigating kidney disease progression.

Keywords

Creatinine, Diabetes mellitus, Microalbuminuria, Urea nitrogen

1. Introduction

Diabetes mellitus is a chronic metabolic disorder characterised by the body's inability to effectively utilise glucose due to insufficient insulin secretion, impaired insulin action, or both. This results in persistent hyperglycemia, typically defined as a fasting blood glucose (FBG) level of ≥126 mg/dL or a 2-hour postprandial glucose (2h-PPG) level of ≥200 mg/dL (American Diabetes Association, 2025). Globally, an estimated 589 million adults (11.1% of the population aged 20–79 years) were living with diabetes in 2024, a figure projected

to rise to 853 million (13.0%) by 2050. In Indonesia, the number of adults with diabetes was approximately 20.4 million in 2024 and is expected to increase to 28.6 million by 2050 (International Diabetes Federation, 2025). This escalating prevalence contributes substantially to morbidity, mortality, and healthcare costs, highlighting the urgent need for reliable biomarkers to monitor disease progression and predict long-term complications.

Glycated haemoglobin (HbA1c) is one of the most widely recognised indicators of long-term glycemic control. HbA1c reflects average blood glucose levels over the preceding three months and is formed through a non-enzymatic glycation process when glucose binds to haemoglobin (Hempe & Hsia, 2022). Due to its stability and reproducibility, HbA1c is routinely used for diagnosis and monitoring of treatment outcomes in patients with diabetes mellitus. Nevertheless, its predictive value for diabetes-related complications remains an area of ongoing investigation, particularly in relation to end-organ damage.

Renal impairment is among the most serious complications of diabetes mellitus, affecting approximately 30–40% of patients who eventually progress to chronic kidney disease (CKD). Globally, the incidence of diabetes related CKD increased by 74% between 1990 and 2017 (Meda E.Pavkov, 2023). In Indonesia, the prevalence of CKD has shown a marked increase, from 0.38% in 2018 to 0.94% in 2023, with North Kalimantan consistently reporting the highest burden (0.64% to 1.61%) and the lowest shifting from West Sulawesi (0.18%) to Southwest Papua (0.41%) (Hidayangsih et al., 2023; Badan Pendidikan dan Pelatihan Kesehatan, 2023). This parallel between global and national trends underscores the urgency of refining risk stratification particularly by clarifying the extent to which HbA1c reflects early renal dysfunction to enable timely, context-specific interventions and delay progression toward end-stage renal disease.

Most studies linking HbA1c with renal outcomes have focused solely on albuminuria. For instance, Lian *et al.*, in 2021 demonstrated a significant association between HbA1c and urinary albumin excretion; however, their findings are limited in scope, as non-albuminuric diabetic kidney disease is increasingly recognised as a distinct clinical phenotype (Marco et al., 2022). A broader evaluation is therefore warranted. Serum creatinine, blood urea, and urinary microalbumin collectively capture glomerular filtration, nitrogen excretion, and early glomerular injury, providing a more comprehensive picture of renal function. Recent guidelines recommend using both

albuminuria and eGFR from serum creatinine for early CKD detection (KDIGO, 2022). while clinical evidence supports combining microalbuminuria with traditional serum biomarkers to improve the identification of incipient nephropathy (Kiconco et al., 2019). Establishing the association between HbA1c and this biomarker panel may thus clarify its predictive role in early kidney dysfunction and strengthen its clinical value in diabetes management.

2. Materials and Methods

This research adopted an analytical cross-sectional study to examine the association between glycated haemoglobin (HbA1c) concentrations and renal function indicators, specifically creatinine, urea, and microalbumin, among patients enrolled in the 2024 Prolanis Diabetes Mellitus program in Bondowoso Regency.

2.1. Study Population and Sampling

The study population comprised individuals diagnosed with diabetes mellitus registered under the Prolanis program, and laboratory evaluations were documented at the Bondowoso District Health Laboratory (Labkesda). A census sampling strategy was employed, wherein all participants meeting the eligibility criteria were included by the predefined inclusion and exclusion parameters.

Inclusion criteria were as follows: a confirmed clinical diagnosis of diabetes mellitus; and Complete laboratory data encompassing HbA1c, creatinine, urea, and microalbumin measurements. Exclusion criteria included: incomplete laboratory profiles; and absence or unavailability of corresponding medical record documentation.

2.2. Data Collection

This study utilised retrospective data from the electronic medical records maintained by the Bondowoso District Health Laboratory (Labkesda). The dataset encompassed laboratory findings collected between January and December 2024, including individual patient measurements of glycated haemoglobin (HbA1c), serum creatinine, blood urea, and microalbumin concentrations.

2.3. Data Analysis

Descriptive statistics were used to summarise the distribution of HbA1c and renal function parameters (serum creatinine, blood urea, and urinary microalbumin). The Shapiro–Wilk test was applied to assess data normality. For continuous variables, correlations were examined using Pearson's test (parametric) or Spearman's test (non-parametric). To facilitate categorical

comparisons, HbA1c was classified as normal (<5.7%), intermediate (5.7–6.4%), and high (≥6.5%), while serum creatinine, blood urea, and microalbumin were categorised according to established clinical reference ranges. Associations between categorical variables were analysed using the Chi-square test. Linear regression analyses were performed to evaluate the magnitude and direction of the relationship between HbA1c and renal markers. All analyses were conducted using IBM SPSS Statistics, version 27 (IBM Corp., Armonk, NY, USA), with statistical significance set at $p < 0.05$.

2.4. Ethical Clearence

Ethical approval for this study was obtained from the Health Research Ethics Committee, Faculty of Dentistry, University of Jember (Approval No. 2978/UN25.8/KEPK/DL/2025). As the study involved retrospective analysis of anonymised electronic medical records, the requirement for individual informed consent was waived by the committee.

3. Results and Discussion

3.1. Characteristics of Respondent Data Variables

A total of 3,432 patients were included in this study. The primary variables analysed comprised serum creatinine, blood urea, urinary microalbumin, and glycated haemoglobin (HbA1c). Each variable was categorised based on standard clinical reference ranges, as presented in Table 1.

Table 1. Characteristics of Respondents (n = 3,432)

No	Variabel	Category	n (% ± SD)	Reference range
1	Creatinine	Normal	3,402 (99.1±0.93)	≤1.2 mg/dL
		High	30 (0.9±0.93)	>1.2 mg/dL
2	Urea (% ± SD)	Normal	1,020 (29.7± 0.46)	10–50 mg/dL
		High	2,412 (70.3±0.46)	>50 mg/dL
3	Microalbumin (% ± SD)	Normal	2,103 (61.3±0.56)	<30 mg/g
		Intermediate	1,211 (35.3±0.56)	30–300 mg/g
		High	118 (3.4±0.56)	>300 mg/g
4	HbA1c (% ± SD)	Normal	1,248 (36.4±0.8)	<5.7%
		Intermediate	1,190 (34.7±0.8)	5.7–6.4%
		High	994 (29.0±0.8)	≥6.5%

As shown in Table 1, the majority of participants had values within the normal range for serum creatinine and microalbumin, while a substantial proportion exhibited elevated blood urea and HbA1c levels.

3.2. Effect of HbA1c on Kidney Function Parameters

The statistical analysis revealed that elevated HbA1c levels were positively associated with increased serum creatinine concentrations in 15 cases; 746 samples correlated with high HbA1c levels and elevated blood urea levels. In addition, 77 samples showed a corresponding rise in microalbumin concentrations with increased HbA1c values. These findings indicate a statistically significant association between poor glycemic control and impaired renal function. Detailed results of the analyses are presented in Tables 2, 3, and 4.

Table 2. Effect of HbA1c on Creatinine

		Creatinine			p-value	Upper	Lower
		Normal	High	Total			
HbA1c	Normal	1243	5	1248	0.020	26.7	0.40
	Intermediate	1180	10	1190			
	High	979	15	994			
Total		3402	30	3432			

Table 3. Effect of HbA1c on Urea

		Urea			p-Value	Upper	Lower
		Normal	High	Total			
HbA1c	Normal	432	816	1248	0.01	188.8	9.50
	Intermediate	340	850	1190			
	High	248	746	994			
Total		1020	2412	3432			

Table 4. Effect of HbA1c on Microalbumin

		Microalbumin			Total	p-Value	Upper	Lower
		Normal	Intermediate	High				
HBA1C	Normal	886	346	16	1248	0.01	326	1.3
	Intermediate	781	384	25	1190			
	High	436	481	77	994			
Total		2103	1211	118	3432			

3.3. Discussion

The present analysis revealed that most HbA1c, serum urea, microalbumin, and creatinine measurements remained within clinically accepted reference intervals, posing limitations in establishing a robust and conclusive correlation between hyperglycemia and renal function decline. Although the proportion of samples exhibiting abnormal values was relatively modest, statistically significant associations were observed between elevated HbA1c levels and increases in all three renal biomarkers assessed. These initial findings suggest that even modest abnormalities may have clinical importance.

However, it is increasingly recognised that even modest elevations within these ranges may carry prognostic value. Longitudinal studies have demonstrated that low-grade albuminuria, even below the conventional microalbuminuria threshold of 30 mg/g, is associated with a significantly higher risk of chronic kidney disease progression and cardiovascular events (Choi et al., 2022; Tang et al., 2022). Similarly, long-term cohort analyses indicate that fluctuations and borderline elevations in HbA1c contribute to renal decline independent of mean glycemic levels (Xu et al., 2023). These observations underscore the clinical importance of detecting and monitoring subtle deviations in glycemic and renal parameters, as they may represent early indicators of adverse outcomes in patients with diabetes.

Recent evidence further supports these findings. A study conducted in Pakistan reported significantly elevated serum urea and creatinine levels among diabetic patients, suggesting impaired renal clearance associated with poor glycemic control (Ullah et al., 2023). Similarly, Octaviani et al., (2025) found a strong correlation between HbA1c ≥7% and increased serum creatinine in Indonesian patients with type 2 diabetes, indicating that HbA1c can serve as a proxy marker of early renal dysfunction. In contrast, some

studies have reported non-significant associations, such as Cahyani et al., (2020), who observed no relationship between HbA1c and creatinine in a small cohort, highlighting that sample size and disease stage may influence observed correlations. This variability across studies underscores the complexity of interpreting HbA1c as a renal predictor.

Other biomarkers of kidney function have also been explored. A cross-sectional study from Tulungagung, Indonesia, demonstrated a significant inverse association between HbA1c and estimated glomerular filtration rate (eGFR), underscoring the importance of monitoring renal clearance alongside traditional biomarkers (Syaifuddin et al., 2023). Conversely, a study from North Sulawesi found no significant correlation between HbA1c and eGFR, reinforcing the heterogeneity of findings across populations and methodologies (Gahung et al., 2016). The inconsistency of results highlights the potential impact of methodological heterogeneity and population-specific characteristics on the observed relationship between HbA1c and renal outcomes.

Collectively, these results indicate that while HbA1c is not universally predictive of renal impairment, integration with creatinine, urea, and microalbumin measurements may enhance its clinical utility. Our findings therefore align with and extend the existing literature by demonstrating consistent associations across multiple renal markers in a large Indonesian cohort. However, these findings do not provide sufficient empirical support to advocate for HbA1c as an independent or definitive predictor of renal dysfunction among individuals with diabetes mellitus. In light of the escalating burden of non-communicable disease risk factors globally, the insights gained from this study may offer valuable contributions to formulating proactive, evidence-based strategies to delay or prevent the onset and progression of diabetic kidney disease.

From a clinical perspective, these findings highlight the importance of incorporating renal biomarkers into routine diabetes care. Integrating glycemic monitoring with serum creatinine, urea, and urinary microalbumin assessment at the primary care level may provide a more effective strategy for the early detection of diabetic kidney disease. Such integration would not only enable timely interventions to prevent progression to chronic kidney disease, but also align with international recommendations advocating multidisciplinary approaches in managing diabetes related complications. Implementing this combined screening protocol in community health settings, particularly in resource-limited regions, could therefore enhance patient outcomes by facilitating earlier

identification of individuals at high risk for renal impairment.

This study was conducted among individuals diagnosed with diabetes mellitus receiving treatment at primary healthcare centers in Bondowoso Regency, to investigate the association between glycated haemoglobin (HbA1c) levels and renal function parameters, including serum urea, creatinine, and microalbumin. The findings revealed that elevated HbA1c levels were significantly associated with increased concentrations of creatinine (n = 15), urea (n = 746), and microalbumin (n = 77). Despite these statistically significant associations, further investigation—particularly through rigorously designed clinical trials is warranted to determine whether targeted reduction of HbA1c levels can effectively lower the risk or incidence of kidney failure among high-risk diabetic populations.

This study's findings align with the well-established pathophysiological framework regarding hyperglycemia-induced renal impairment in patients with diabetes mellitus. Chronic hyperglycemia precipitates glomerular hyperfiltration and intraglomerular hypertension, which disrupts nitric oxide (NO) bioavailability and induces vasoconstriction and renal hypoxia. These conditions promote the overproduction of reactive oxygen species (ROS), leading to oxidative stress and direct damage to the glomerular endothelium. This cascade ultimately accelerates nephron loss through extracellular matrix accumulation and tubulointerstitial fibrosis (Mora-Fernández *et al.*, 2014; Yu and Bonventre, 2018). Moreover, prolonged hyperglycemia activates a range of pro-inflammatory signalling pathways. Elevated levels of cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-18 (IL-18) have been implicated in promoting renal inflammation and fibrosis. These cytokines enhance mesangial matrix expansion and stimulate profibrotic processes, contributing to kidney structural and functional deterioration (Tuttle et al., 2022). In parallel, serum urea concentrations also increase due to reduced renal clearance of nitrogenous waste products. Elevated urea itself may exacerbate renal damage by enhancing oxidative stress and endothelial dysfunction within the microvasculature of the kidney. Notably, microalbuminuria is recognised as an early clinical manifestation of diabetic nephropathy. Albumin in urine is primarily attributed to increased glomerular permeability caused by podocyte effacement and inflammation. Persistent albuminuria is not only a hallmark of early kidney injury but also a robust predictor of progression to chronic kidney disease (CKD) and eventual end-stage renal disease (ESRD) (Monseu et al., 2015). Collectively, these mechanisms

underscore the critical role of glycemic control in mitigating renal complications in individuals with diabetes mellitus. Our findings reinforce the necessity of comprehensive monitoring of renal biomarkers—such as serum creatinine, urea, and urinary microalbumin in conjunction with glycemic indices like HbA1c, to facilitate early detection and targeted interventions to preserve renal function.

This study had several limitations. First, its cross-sectional design precludes the ability to infer causal relationships between glycemic control and renal function biomarkers; the observed associations should therefore be interpreted as correlational rather than causal. Second, detailed information on patients' pharmacological history, duration since diabetes diagnosis, and comorbidities such as hypertension or cardiovascular disease was not available. These variables are known to significantly influence the trajectory of diabetic nephropathy and may confound the observed associations. Third, potential variability in laboratory measurements cannot be excluded if internal or external quality assurance procedures were not consistently standardized across all assays. Such variability may have introduced measurement bias that could attenuate or exaggerate the observed associations. Collectively, these limitations may restrict the robustness and generalizability of our findings. Future studies employing longitudinal or prospective designs, incorporating standardized laboratory procedures, and using more comprehensive clinical datasets are warranted to provide a clearer understanding of the causal pathways linking HbA1c and renal outcomes in this population.

4. Conclusions

This study identified significant associations between elevated HbA1c levels and increased concentrations of serum creatinine, urea, and urinary microalbumin among patients with diabetes mellitus in Bondowoso Regency. While HbA1c remains a valuable indicator of long-term glycemic control, it should not be interpreted as a standalone predictor of renal dysfunction. Instead, its clinical utility is strengthened when interpreted in combination with renal biomarkers, enabling a more comprehensive assessment of early kidney injury. Integrating HbA1c monitoring with routine renal function testing at the primary care level may enhance risk stratification, facilitate timely interventions, and reduce the progression of diabetic kidney disease.

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