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Research Article

Association Between HbA1c Levels and Diabetic Nephropathy: A Clinical and Biochemical Assessment

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Abstract: Diabetic nephropathy is one of the most common microvascular complications of diabetes mellitus and a major cause of chronic kidney disease worldwide. Persistent hyperglycemia contributes to renal injury through various metabolic, hemodynamic and inflammatory mechanisms. Glycated hemoglobin (HbA1c) reflects average blood glucose levels over approximately two to three months and is widely used to assess long-term glycemic control. Elevated HbA1c levels may be associated with an increased risk of developing diabetic nephropathy. **Aim:** To evaluate the association between HbA1c levels and diabetic nephropathy and to assess the relationship between glycemic control and renal function parameters. **Materials and Methods:** A hospital-based observational analytical study is proposed involving patients diagnosed with type 2 diabetes mellitus. Demographic characteristics, duration of diabetes, HbA1c levels, serum creatinine, urinary albumin-to-creatinine ratio (UACR) and estimated Glomerular Filtration Rate (eGFR) are assessed. Patients are categorized according to HbA1c levels and the presence or absence of diabetic nephropathy. Statistical analysis includes descriptive statistics, independent-sample tests, correlation analysis and multivariable logistic regression. Results: In the illustrative dataset, patients with poor glycemic control (HbA1c ≥7%) demonstrate a higher proportion of diabetic nephropathy than patients with HbA1c below 7%. Increasing HbA1c levels are also associated with higher urinary albumin excretion and reduced eGFR. These findings illustrate a possible relationship between inadequate glycemic control and renal impairment. **Conclusion:** Poor glycemic control, as indicated by elevated HbA1c levels, may be associated with an increased prevalence and severity of diabetic nephropathy. Regular monitoring of HbA1c and renal parameters may help identify patients at increased risk of diabetic kidney disease.

Keywords: Diabetic Nephropathy, HbA1c, Type 2 Diabetes Mellitus, Glycemic Control, Renal Function, Urinary Albumin-to-Creatinine Ratio, Estimated Glomerular Filtration Rate (eGFR)

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or a combination of both. The prevalence of diabetes mellitus has increased considerably worldwide, making it a major public health concern. Long-standing diabetes can lead to several microvascular and macrovascular complications, including diabetic retinopathy, neuropathy, cardiovascular disease and diabetic nephropathy. Among these complications, diabetic nephropathy is particularly important because it can progressively impair renal function and ultimately lead to end-stage renal disease.

Diabetic nephropathy, also known as diabetic kidney disease, is characterized by structural and functional abnormalities of the kidneys associated with diabetes mellitus. It commonly presents with increased urinary albumin excretion, declining glomerular filtration rate and progressive renal impairment. The development of diabetic nephropathy is influenced by several factors, including duration of diabetes, poor glycemic control, hypertension, obesity, dyslipidemia, genetic susceptibility and smoking. The American Diabetes Association reports that chronic kidney disease occurs in approximately 20–40% of individuals with diabetes [1].

Hyperglycemia plays a central role in the pathogenesis of diabetic nephropathy. Persistent elevation of blood glucose produces several biochemical changes, including increased formation of advanced glycation end products (AGEs), activation of protein kinase C, increased oxidative stress and stimulation of inflammatory pathways. These mechanisms contribute to glomerular basement membrane thickening, mesangial expansion, podocyte injury and glomerulosclerosis. Progressive structural damage results in increased glomerular permeability, leading to urinary albumin leakage and subsequent deterioration of renal function.

Glycated hemoglobin (HbA1c) is an important biochemical marker used to assess long-term glycemic control. It is formed through the nonenzymatic attachment of glucose to hemoglobin in circulating red blood cells. Because red blood cells have an average lifespan of approximately 120 days, HbA1c reflects average blood glucose concentrations over the preceding two to three months. Unlike a single fasting or postprandial blood glucose measurement, HbA1c provides a more comprehensive assessment of glycemic exposure.

Several clinical studies have demonstrated that intensive glycemic control reduces the risk of microvascular complications in patients with diabetes mellitus. The Diabetes Control and Complications Trial demonstrated that improved glycemic control significantly reduced the development and progression of diabetic complications in patients with type 1 diabetes [2]. Similarly, the United Kingdom Prospective Diabetes Study established the importance of improved glycemic control in reducing microvascular complications among patients with type 2 diabetes [3].

The relationship between HbA1c and diabetic nephropathy is clinically significant because prolonged exposure to elevated blood glucose may accelerate renal microvascular damage. Patients with higher HbA1c levels may have a greater likelihood of developing albuminuria and declining eGFR. However, the relationship is influenced by other clinical variables, including blood pressure, duration of diabetes, age and treatment adherence. Furthermore, HbA1c measurements may become less reliable in advanced chronic kidney disease because of anemia, altered red blood cell survival and other hematological abnormalities [4,5].

The Kidney Disease

Improving Global Outcomes (KDIGO) guidelines recommend HbA1c monitoring in patients with diabetes and chronic kidney disease, while emphasizing individualized glycemic targets [4]. The assessment of urinary albumin-to-creatinine ratio and estimated glomerular filtration rate is also essential for identifying and monitoring diabetic kidney disease [1].

Therefore, the present study aims to investigate the association between HbA1c levels and diabetic nephropathy among patients with type 2 diabetes mellitus. It also evaluates the relationship between glycemic control and renal biochemical parameters, including serum creatinine, urinary albumin-to-creatinine ratio and estimated glomerular filtration rate [6,7].

MATERIALS AND METHODS

A hospital-based observational analytical study was designed to investigate the association between glycated hemoglobin levels and diabetic nephropathy among patients diagnosed with type 2 diabetes mellitus.

Study Setting and Duration

The study is proposed to be conducted in the Department of General Medicine and Department of Biochemistry at a tertiary care teaching hospital. The proposed study duration is six months following approval from the Institutional Ethics Committee.

Study Population

The study population consists of adult patients diagnosed with type 2 diabetes mellitus attending the outpatient and inpatient departments during the study period.

Sample Size

For the illustrative analysis, a sample size of 100 patients is considered. The final sample size for an actual research study should be calculated based on the expected prevalence of diabetic nephropathy or the anticipated difference in HbA1c between study groups, with an appropriate confidence level, statistical power and allowance for incomplete observations.

Inclusion Criteria

- Patients aged 30 years and above
- Patients diagnosed with type 2 diabetes mellitus
- Patients with a documented history of diabetes for at least one year
- Patients willing to participate in the study
- Patients providing written informed consent

Exclusion Criteria

- Patients diagnosed with type 1 diabetes mellitus
- Patients with known chronic kidney disease due to non-diabetic causes
- Patients with acute kidney injury
- Patients with active urinary tract infection
- Pregnant women
- Patients with recent blood transfusion or significant hemoglobin disorders that may interfere with HbA1c interpretation
- Patients with conditions causing significant alterations in red blood cell survival

Data Collection

Demographic and clinical information will be collected using a structured data collection proforma. The recorded parameters will include age, sex, duration of diabetes, family history of diabetes, hypertension status, body mass index, medication history and relevant clinical findings.

Blood samples will be collected under aseptic precautions for biochemical investigations. HbA1c will be estimated using a standardized laboratory method, preferably high-performance liquid chromatography (HPLC) or another NGSP-certified method.

Fasting blood glucose will be measured using an automated biochemical analyzer. Serum creatinine will be estimated using an enzymatic or standardized Jaffe method. Estimated glomerular filtration rate will be calculated using an appropriate validated CKD-EPI equation.

Urinary albumin excretion will be assessed using a spot urine albumin-to-creatinine ratio (UACR). According to established clinical criteria, albuminuria will be classified as follows:

- **Normal to Mildly Increased:** UACR below 30 mg/g
- **Moderately Increased:** UACR 30–300 mg/g
- **Severely Increased:** UACR above 300 mg/g [1]

For clinical confirmation of persistent albuminuria, repeated measurements should be obtained, as urinary albumin excretion can vary considerably.

Group Classification

Patients will be categorized according to their HbA1c levels:

- **Group I:** HbA1c below 7% (better glycemic control)
- **Group II:** HbA1c 7–8.9% (intermediate glycemic control)
- **Group III:** HbA1c 9% or above (poor glycemic control)

The presence of diabetic nephropathy will be evaluated using urinary albumin excretion and eGFR, considering the clinical history and exclusion of alternative renal diseases.

Statistical Analysis

The collected data will be entered into Microsoft Excel and analyzed using SPSS or an equivalent statistical software package. Continuous variables will be expressed as mean ± standard deviation or median with interquartile range, depending on their distribution. Categorical variables will be presented as frequencies and percentages.

The independent-sample t-test or Mann–Whitney U test will be used to compare continuous variables between groups. Chi-square or Fisher's exact test will be applied to assess associations between categorical variables. Pearson's or Spearman's correlation coefficient will be used to determine the relationship between HbA1c and renal parameters.

Multivariable logistic regression will be performed to evaluate whether HbA1c is independently associated with diabetic nephropathy after adjustment for potential confounders, including age, sex, duration of diabetes, hypertension and body mass index. A p-value below 0.05 will be considered statistically significant.

RESULTS

The majority of participants belonged to the 51–60-year age group (35%). Males constituted 58% of the study population, whereas females accounted for 42%. This distribution indicates a higher representation of male participants in the sample (Table 1).

Among the 100 illustrative participants, 40% had HbA1c levels below 7%, indicating relatively better glycemic control. Thirty-five percent had HbA1c levels between 7% and 8.9%, while 25% had HbA1c levels of 9% or above. Thus, 60% of the participants had HbA1c levels of 7% or higher, suggesting suboptimal glycemic control (Table 2).

Table 1: Distribution of Study Participants According to Age and Sex

Parameter	Number (n)	Percentage
Age group		
30–40 years	15	15
41–50 years	25	25
51–60 years	35	35
Above 60 years	25	25
Sex		
Male	58	58
Female	42	42
Total	100	100

Table 2: Distribution of Patients According to HbA1c Levels

HbA1c category	Number (n)	Percentage
Below 7%	40	40
7–8.9%	35	35
9% and above	25	25
Total	100	100

Table 3: Association between HbA1c Levels and Diabetic Nephropathy

HbA1c category	Patients with nephropathy (n)	Patients without nephropathy (n)	Total
Below 7%	8 (20%)	32 (80%)	40
7–8.9%	14 (40%)	21 (60%)	35
9% and above	18 (72%)	7 (28%)	25
Total	40	60	100

Table 4: Comparison of Renal Biochemical Parameters According to HbA1c Levels

Biochemical parameter	HbA1c below 7%	HbA1c 7–8.9%	HbA1c ≥9%
Mean HbA1c (%)	6.4	8.0	10.1
Serum creatinine (mg/dL)	0.9	1.2	1.8
UACR (mg/g)	18	85	420
eGFR (mL/min/1.73 m^2)	98	82	58

The illustrative findings demonstrate an increasing proportion of diabetic nephropathy with increasing HbA1c levels. Among patients with HbA1c below 7%, 20% had diabetic nephropathy. This proportion increased to 40% among patients with HbA1c between 7% and 8.9%. The highest proportion of diabetic nephropathy (72%) was observed among patients with HbA1c levels of 9% or above. These findings suggest a positive association between poor glycemic control and the occurrence of diabetic nephropathy (Table 3).

All values are hypothetical illustrative group means. UACR and eGFR values are included to demonstrate the presentation of renal parameters.

Patients with higher HbA1c levels demonstrated progressively higher serum creatinine and urinary albumin-to-creatinine ratio values. The mean serum creatinine increased from 0.9 mg/dL in the better-controlled group to 1.8 mg/dL in the group with HbA1c ≥9%.

Similarly, mean UACR increased from 18 mg/g to 420 mg/g across the three groups. In contrast, mean eGFR decreased from 98 to 58 mL/min/1.73 m^2. These findings illustrate a possible relationship between poor glycemic control, increased urinary albumin excretion and deterioration of renal function.

DISCUSSION

Diabetic nephropathy is a major complication of diabetes mellitus and contributes significantly to the burden of chronic kidney disease worldwide. Persistent hyperglycemia is considered one of the important modifiable risk factors involved in the development and progression of diabetic kidney disease. The present study is designed to investigate the association between HbA1c levels and diabetic nephropathy by evaluating glycemic control alongside renal biochemical parameters [8].

In the illustrative findings, a higher proportion of diabetic nephropathy was observed among patients with elevated HbA1c levels. The prevalence increased from 20% in patients with HbA1c below 7% to 72% in patients with HbA1c levels of 9% or above. This pattern suggests that prolonged exposure to hyperglycemia may be associated with an increased risk of renal complications. However, the relationship should be confirmed through statistical analysis of actual clinical observations.

The biological relationship between hyperglycemia and renal injury can be explained by several mechanisms. Chronic elevation of blood glucose promotes the formation of advanced glycation end products, increased oxidative stress, activation of inflammatory pathways and disturbances in intraglomerular hemodynamics. These changes contribute to glomerular basement membrane thickening, mesangial expansion and podocyte injury. Eventually, these structural abnormalities result in increased glomerular permeability and urinary albumin leakage.

The Diabetes Control and Complications Trial demonstrated that intensive glycemic management significantly reduced the risk of microvascular complications in individuals with type 1 diabetes [2]. Similarly, the United Kingdom Prospective Diabetes Study established that improved glycemic control reduced the risk of microvascular complications in patients with type 2 diabetes [3]. These landmark studies support the importance of maintaining adequate glycemic control to prevent long-term diabetic complications.

In the present illustrative analysis, increasing serum creatinine levels were observed with increasing HbA1c categories. Serum creatinine increased from 0.9 mg/dL in patients with HbA1c below 7% to 1.8 mg/dL in patients with HbA1c levels of 9% or above. This observation is consistent with the possibility that prolonged hyperglycemia contributes to progressive deterioration of renal filtration capacity.

Urinary albumin-to-creatinine ratio is an important early marker of kidney damage in patients with diabetes. In this illustrative dataset, mean UACR increased substantially across the HbA1c categories, indicating greater urinary albumin excretion among patients with poor glycemic control. According to the American Diabetes Association, UACR and eGFR should both be assessed for the diagnosis and monitoring of diabetic kidney disease [1].

Furthermore, the decrease in mean eGFR from 98 to 58 mL/min/1.73 m^2 across the HbA1c categories suggests a possible association between poor glycemic control and reduced renal function. However, HbA1c alone cannot establish the presence or severity of diabetic nephropathy. The duration of diabetes, hypertension, age, obesity, dyslipidemia and other comorbid conditions may independently influence renal outcomes.

The KDIGO 2022 guidelines emphasize individualized HbA1c targets in patients with diabetes and chronic kidney disease. Although improved glycemic control can reduce the risk of microvascular complications, excessively intensive treatment may increase the risk of hypoglycemia in certain patients. Furthermore, HbA1c reliability may decrease in advanced CKD due to altered red blood cell turnover and anemia [4].

An important clinical implication of the present research question is the need for regular monitoring of both glycemic and renal parameters. Measurement of HbA1c alone is insufficient for identifying all patients with diabetic kidney disease. Periodic assessment of UACR and eGFR enables earlier identification of renal abnormalities and appropriate clinical intervention.

The study also has potential limitations. A cross-sectional design can demonstrate an association but cannot establish a causal relationship between elevated HbA1c and diabetic nephropathy. Other confounding variables, such as duration of diabetes, hypertension, medication use and baseline renal function, may influence the findings. Additionally, a relatively small sample size and single-center setting may limit the generalizability of the results.

Overall, the proposed study highlights the clinical importance of HbA1c as a marker of long-term glycemic exposure and its potential relationship with diabetic nephropathy. A larger prospective study with repeated measurements of HbA1c, UACR and eGFR would provide stronger evidence regarding the relationship between glycemic control and renal disease progression.

CONCLUSION

HbA1c is therefore an important biochemical marker for monitoring long-term glycemic control and assessing the risk of diabetic complications. However, it should be interpreted alongside renal parameters, particularly serum creatinine, eGFR and urinary albumin-to-creatinine ratio. Early identification of poor glycemic control, regular renal function assessment, individualized diabetes management and appropriate intervention may help prevent or delay the progression of diabetic kidney disease.

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