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Correlation of glycemic control and proteinuria markers with renal complications in diabetes

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Abstract

Background: Diabetes mellitus is a major global health concern with significant microvascular complications, including diabetic nephropathy, which necessitates early detection of renal involvement using reliable biochemical markers. This study aimed to evaluate glycosylated haemoglobin levels and urinary protein-to-creatinine ratio (UPCR) in diabetic subjects and controls, and to assess the correlation between UPCR in random urine samples and 24-hour urinary protein excretion.

Materials and methods: A total of 103 subjects were included in the study, comprising 62 diabetic and 41 non-diabetic individuals. Detailed medical histories were obtained, and relevant clinical examinations were performed. Biochemical parameters assessed included fasting blood sugar, glycosylated haemoglobin (HbA1c), serum creatinine, urine creatinine, urine protein, UPCR, and 24-hour urinary protein excretion.

Results: Diabetic subjects showed significantly higher mean levels of fasting blood sugar, serum creatinine, HbA1c, 24-hour urinary protein, and UPCR compared to non-diabetic controls ($P < 0.001$). A strong positive correlation was observed between fasting blood sugar, HbA1c, 24-hour urinary protein, and the protein-to-creatinine ratio. Additionally, serum creatinine levels were significantly elevated in diabetic patients with a protein-to-creatinine ratio (UPCR) ≥0.2, suggesting significant renal involvement ($P < 0.001$).

Conclusion: Glycosylated haemoglobin serves as a reliable marker for glycemic control, while the protein-to-creatinine ratio in random urine samples provides a practical and effective tool for early detection of renal involvement in diabetic patients.

Keywords: diabetes; glycosylated haemoglobin; serum creatinine; 24-hour urinary protein; protein-to-creatinine ratio

Introduction

Diabetic nephropathy (DN) is the most prevalent and serious complication of diabetes mellitus (DM), significantly contributing to increased morbidity and mortality rates [1]. It is a clinical syndrome characterized by persistent albuminuria and progressive decline in renal function, affecting up to 50% of individuals with diabetes [2]. Diabetes-related kidney disease is a leading cause of end-stage kidney disease (ESKD) worldwide. Additionally, DN is frequently associated with hypertension and elevated cardiovascular risk [1]. The incidence of DN is expected to rise with the increasing global prevalence of diabetes [1, 2].

Improving glycemic control can delay the onset of diabetes-related complications, reduce the risk of myocardial infarction and cardiovascular death, and improve survival in dialysis-dependent diabetic patients. Glycosylated hemoglobin (HbA1c) is a crucial marker for monitoring long-term blood glucose levels [3].

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Proteinuria, an indicator of kidney damage, is one of the key markers for assessing renal involvement in diabetic patients [4]. The protein-to-creatinine ratio (PCR) in a random urine sample has been shown to correlate effectively with 24-hour urinary protein levels in patients with diabetes and overt nephropathy. This ratio can serve as a valuable and practical tool for detecting proteinuria or estimating its severity in such patients [5]. Alternatively, the PCR from spot urine samples offers a more convenient method for estimating proteinuria [6]. The protein-to-creatinine ratio in random urine samples has been found to correlate with 24-hour urinary protein concentration, making it useful for screening and as a convenient outpatient procedure [7].

This study aimed to evaluate glycosylated hemoglobin as an indicator of glycemic control and the urinary protein-to-creatinine ratio in diabetic patients and controls. Additionally, it aimed to assess renal involvement in relation to the duration of diabetes and to determine the correlation between the protein-to-creatinine ratio in random urine samples and 24-hour urine protein levels.

Materials and Methods

This study was conducted on 103 patients (55 male and 48 female participants), including 62 diabetic patients and 41 non-diabetic controls, who attended the outpatient department at Shridevi Institute of Medical Sciences and Research Hospital, from January 2024 to February 2025. The mean age of participants was 47.5 years (range: 20–82 years). Informed consent was obtained from all participants, and the study was approved by the institutional ethics and research committee.

Patients clinically diagnosed with diabetes mellitus (including both insulin-dependent and non-insulin-dependent diabetes mellitus) were included in the study. Patients with chronic renal failure, glomerulonephritis due to other systemic conditions, and those with hypertension were excluded.

Biochemical parameters were analyzed using the Ciba Corning Analyzer. The parameters assessed included fasting blood glucose, glycosylated haemoglobin (HbA1c), serum creatinine, urine creatinine, urine protein, protein-to-creatinine ratio (PCR), and 24-hour urinary protein.

Measurement of protein and creatinine in urine

Fasting blood glucose was measured using the glucose oxidase method. HbA1c was estimated by the cation-exchange resin method. Serum and urine creatinine levels were determined using the modified Jaffe method. Urine protein concentration was measured using the dye-binding method. The protein-to-creatinine (UPCR) ratio in random urine samples was calculated and expressed as a ratio.

Statistical analysis

All data were expressed as mean ± standard deviation (SD) and range values. Comparisons between two groups were performed using the Student's *t*-test. Correlation between the spot UPCR ratio and 24-hour urinary total protein was assessed using Pearson's correlation coefficient. The sensitivity, specificity, and predictive values of the random urine UPCR at various cut-off levels were evaluated using the 24-hour urinary total protein as the gold standard. Categorical data were analyzed using the Chi-square test. Diagnostic validity tests were performed to evaluate the usefulness of various parameters as indicators of renal involvement. A *P*-value ≤ 0.05 was considered statistically significant.

Results

Table 1 presents a comparison of key biochemical parameters between diabetic subjects and non-diabetic controls. The mean levels of fasting blood sugar (FBS), serum creatinine, HbA1c, 24-hour urinary protein, and the protein-to-creatinine (UPCR) ratio in random urine samples were significantly higher in the diabetic group. These differences were highly significant ($P < 0.001$), indicating a clear association between diabetes and elevated markers of renal involvement.

Table 1: Comparison of various parameters in controls and diabetic patients.

Parameters	*Study population*		*Case v/s Controls*	
	Control (n=41) Mean±SD	*Case (n=62) Mean±SD*	*t-value*	*P-value*
FBG, mg /dL	92.0 ± 12.9	199.0 ± 91.5	> 0.43	< 0.001
Serum creatinine, mg/dL	0.85 ± 0.25	1.17 ± 0.56	3.48	< 0.01
HbA1C, %	6.28 ± 0.62	7.95 ± 1.49	6.80	< 0.001
24-hr urinary protein concentration, g /day	0.10 ± 0.09	1.09 ± 1.79	3.63	< 0.001
UPCR in random sample	0.09 ± 0.09	1.18 ± 1.80	3.86	< 0.001

Abbreviations: FBG: fasting blood glucose; HbA1C: glycosylated haemoglobin, UPCR: Urinary protein creatinine ratio.

As shown in Table 2, the mean serum creatinine level in diabetic patients with a UPCR ≥0.2 was 1.31 ± 0.60 mg/dL. In contrast, diabetic patients with a UPCR <0.2 had a mean serum creatinine level of 0.82 ± 0.16 mg/dL. This difference was statistically significant ($P < 0.001$), suggesting that a higher UPCR is associated with more pronounced renal impairment in diabetic patients.

Table 2: Comparison of FBS, serum creatinine, HbA1C, 24 hr urinary protein, and protein to creatine ratio in diabetic subjects with protein to creatine ratio 0.2 as a cut-off value.

	FBG, mg /dL	*Serum creatinine, mg/dL*	*HbA1C, %*	*24-hr urinary protein concentration, g /day*	*UPCR in random sample*
UPCR ratio in random sample ≥ 0.2 (n=44)	203.8 ± 100.4	1.31 ± 0.60	8.08 ± 1.71	1.51 ± 1.92	1.65 ± 1.97
UPCR ratio in random sample < 0.2 (n=18)	181.8 ± 64.0	0.82 ± 0.16	7.61 ± 0.64	0.09 ± 0.06	0.08 ± 0.05
P-value	0.55	< 0.001	0.48	< 0.001	< 0.01

Abbreviations: FBG: fasting blood glucose; HbA1C: glycosylated haemoglobin, UPCR: Urinary protein creatinine ratio.

Table 3 illustrates the relationship between the duration of diabetes and renal parameters. Diabetic patients with a disease duration of more than five years showed significantly higher mean values of 24-hour urinary protein and UPCR in random urine samples compared to those with diabetes for less than five years ($P < 0.05$). These findings indicate that the duration of diabetes has a direct impact on the progression of renal involvement, with longer disease duration correlating with worsening proteinuria and kidney function.

Table 3: Comparison of 24-hour urinary protein concentration and UPCR in random urine sample level in diabetic subjects based on duration of diabetes.

Duration	*24-hr urinary protein concentration, g /day*	*UPCR in random sample*
< 5 years, Mean±SD (n=29)	0.76 ± 1.33	0.81 ± 1.44
> 5 years, Mean±SD (n=33)	1.37 ± 2.00	1.50 ± 2.04

Abbreviations: UPCR: Urinary protein creatinine ratio.

There was a strong positive correlation observed between fasting blood glucose, glycosylated hemoglobin, 24-hour urinary protein, and the protein-to-creatinine ratio in random urine samples. These associations suggest that poor glycemic control is closely linked to early renal dysfunction in diabetic individuals. Additionally, serum creatinine levels also showed a highly significant positive correlation with both 24-hour urinary protein and the UPCR ($P < 0.001$), further emphasizing their value as indicators of renal involvement.

Table 4 demonstrates the diagnostic validity of using a 24-hour urinary protein level and UPCR (cut-off value: 0.20) to detect renal involvement in diabetic patients. Both parameters exhibited comparable accuracy, sensitivity, specificity, and predictive values, supporting the clinical utility of the UPCR in random urine samples as a practical alternative to 24-hour urine collection, especially in outpatient settings.

Table 4: Validity of 24 hours urinary protein and UPCR to detect renal involvement with cut-off value of 0.20.

	24-hr urinary protein concentration, %	*UPCR in random sample, %*
Sensitivity	71	74
Specificity	93	90
Positive predictive value	94	92
Negative predictive value	68	70
Accuracy	80	81

Abbreviations: UPCR: Urinary protein creatinine ratio.

Pearson's correlation coefficient (r) values confirm that fasting blood glucose, HbA1c, 24-hour urinary protein, and the UPCR are positively correlated. Furthermore, the correlation between serum creatinine and both 24-hour urinary protein and the UPCR was highly significant ($P < 0.001$), reinforcing the relevance of these markers in the early detection and monitoring of renal complications in diabetic patients.

Discussion

This study aimed to explore the correlation between HbA1c and the UPCR in random urine samples with 24-hour urinary protein excretion in diabetic patients. The findings demonstrate that higher levels of HbA1c are positively correlated with increased protein-to-creatinine ratio and 24-hour urinary protein excretion, suggesting that poor glycemic control is associated with greater renal impairment. The observed correlation between elevated HbA1c levels and increased risk of diabetic nephropathy is consistent with previous

research, emphasizing the importance of stringent blood glucose monitoring to prevent long-term complications [8].

Guidelines from the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO) 2022 underscore the importance of integrated care—incorporating lifestyle modifications, regular monitoring, and pharmacotherapy—to improve kidney and cardiovascular outcomes in diabetic patients [9]. The highly significant correlation observed between serum creatinine and both 24-hour urinary protein excretion and UPCR further supports the clinical utility of these markers in assessing renal function in patients with diabetes. These results are consistent with prior studies indicating that persistent hyperglycemia can cause progressive glomerular damage, increased renal permeability, and subsequent proteinuria [10, 11].

Interestingly, while positive correlations were observed between fasting blood glucose, HbA1c, and urinary protein markers, although not all correlations reached statistical significance. This discrepancy could be attributed to variability in glycemic control among the study participants, differences in disease duration, or the sample size. These findings highlight the need for continuous monitoring and personalized treatment plans to mitigate renal complications in diabetes [12].

The high sensitivity, specificity, and predictive values of both the 24-hour urinary protein concentration and the UPCR underscore their clinical value in detecting renal involvement. Given the ease of obtaining a random urine sample, UPCR presents a practical and reliable alternative to the 24-hour urine collection, which is often cumbersome for patients and difficult to implement in routine clinical practice [13].

Moreover, the study's focus on urinary protein excretion as a marker of renal involvement is supported by emerging evidence on novel biomarkers. Recent research has identified urinary pyruvate kinase M2 (PKM2) as a potential early diagnostic marker for diabetic nephropathy, indicating that the landscape of renal biomarkers is evolving toward more sensitive and specific tools [14,15]. Despite this, 24-hour urinary protein measurement continues to provide a more comprehensive assessment of kidney function in many clinical settings, as demonstrated in recent clinical trials [16].

Limitations: This study was conducted in a single tertiary care center with a limited number of participants, which may not fully represent the broader diabetic population. A multicenter study with a larger sample size would provide more robust and generalizable findings.

Conclusion

The present study highlights the value of estimating glycosylated hemoglobin as an indicator of glycemic control and measuring the protein-to-creatinine ratio in random urine samples to detect renal involvement in diabetic patients. This approach offers a practical, efficient, and non-invasive tool for early diagnosis and timely intervention. Furthermore, maintaining optimal long-term glycemic control is critical for preventing and delaying the progression of diabetic nephropathy. These findings underscore the importance of proactive monitoring and early therapeutic strategies to improve clinical outcomes and preserve renal function in diabetic care.

Conflicts of interest

Authors declare no conflicts of interest.

References

[1] Samsu N. Diabetic nephropathy: challenges in pathogenesis, diagnosis, and treatment. Biomed Res Int. 2021; 2021:1497449.

[2] Selby NM, Taal MW. An updated overview of diabetic nephropathy: Diagnosis, prognosis, treatment goals and latest guidelines. Diabetes Obes Metab. 2020; 22:3–15.

[3] Rhee JJ, Ding VY, Rehkopf DH, Arce CM, Winkelmayer WC. Correlates of poor glycemic control among patients with diabetes initiating hemodialysis for end-stage renal disease. BMC Nephrol. 2015; 16:204.

[4] Haider MZ, Aslam A. Proteinuria. 2023; In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.

[5] Rodby RA, Rohde RD, Sharon Z, Pohl MA, Bain RP, et al. The urine protein to creatinine ratio as a predictor of 24-hour urine protein excretion in type 1 diabetic patients with nephropathy. The Collaborative Study Group. Am J Kidney Dis. 1995; 26:904–909.

[6] Kamińska J, Piekarska VD, Tomaszewska J, Karna JM, Lenkiewicz OMK. Diagnostic utility of protein to creatinine ratio (P/C ratio) in spot urine sample within routine clinical practice. Crit Rev Clin Lab Sci. 2020; 57:345–364.

[7] Olayinka L, Garnett E, Burnett B, Devaraj S. Comparison of random urine protein/creatinine ratio with 24-hour urine protein in suspected pre-eclampsia. Pract Lab Med. 2023; 36:00316.

[8] Aati IK, Mohammed HJ, Mohammed MM, Rasool RN. High HbA1C and glycemic control as diabetic nephropathy etiology. J Angiotherapy. 2024; 8:1–6.

[9] De Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, et al. Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 2022; 45:3075–3090.

[10] Huang L, He L, Luo X, Zhou X. Association of haemoglobin glycation index with all-cause and cardiovascular disease mortality in diabetic kidney disease: a cohort study. Diabetol Metab Syndr. 2024; 16:221.

[11] Ikramov A, Mukhtarova S, Trigulova R, Alimova D, Abdullaeva S. Prediction of glycosylated hemoglobin level in patients with cardiovascular diseases and type 2 diabetes mellitus with respect to anti-diabetic medication. Front Endocrinol (Lausanne). 2024; 15:1305640.

[12] American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021; 44:15–33.

[13] Peredo GBG, Castellón IM, Peredo AJG, Lopes MB, Tapioca FPM, et al. The urine protein/creatinine ratio as a reliable indicator of 24-h urine protein excretion across different levels of renal function and proteinuria: the TUNARI prospective study. BMC Nephrol. 2024; 25:418.

[14] Wang C, Li C, Gong W, Lou T. New urinary biomarkers for diabetic kidney disease. Biomark Res. 2013; 1:1–4.

[15] Park YS, Han JH, Park JH, Choi JS, Kim SH, et al. Pyruvate kinase M2: a new biomarker for the early detection of diabetes-induced nephropathy. Int J Mol Sci. 2023; 24:2683.

[16] Chawla R, Garg A. Editorial: Advancements and insights into diabetic nephropathy. Int J Diabetes Dev Ctries 44, 2024; 44:633–634 .