Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/23638
DOI URL: http://dx.doi.org/10.21474/IJAR01/23638

RESEARCH ARTICLE

CORRELATION BETWEEN HBA1C AND MICROALBUMINURIA IN TYPE II DIABETES MELLITUS: IMPACT OF DISEASE DURATION

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Manuscript Info

Manuscript History
Received: 8 April 2026
Final Accepted: 10 May 2026
Published: June 2026

Key words:-
Type 2 diabetes mellitus; HbA1c; microalbuminuria; albumin-to-creatinine ratio; diabetic nephropathy; disease duration; glycaemic control

Abstract

Background: Type 2 diabetes mellitus (T2DM) is a leading cause of chronic kidney disease worldwide, with microalbuminuria serving as the earliest detectable marker of diabetic nephropathy. Glycated haemo globin (HbA1c) reflects long-term glycaemic control and is postulated to correlate with renal microvascular injury. However, the modulating role of disease duration on this relationship remains incompletely characterised.

Objectives: To compare HbA1c and microalbuminuria (urine albumin-to-creatinine ratio, ACR) between T2DM patients with disease duration <5 years and >5 years, and to assess the correlation between HbA1c and ACR within each group.

Methods: A cross-sectional observational study was conducted on 121 diagnosed T2DM patients (59 with disease duration <5 years and 62 with >5 years) attending a tertiary care hospital. HbA1c was measured by HPLC, and microalbuminuria was quantified as spot urine albumin-to-creatinine ratio (ACR). Pearson's correlation coefficient and independent samples t-test were used for statistical analysis.

Results: The mean HbA1c was significantly higher in the >5 years group (10.26 ± 1.70%) compared to the <5 years group (6.82 ± 0.80%; p<0.0001). Mean ACR was also significantly elevated (56.41 ± 38.15 vs 23.87 ± 26.58 mg/g; p<0.0001). In the >5 years group, HbA1c showed a significant positive correlation with microalbumin (r=0.444, p=0.0003) and ACR (r=0.591, p<0.0001). In the <5 years group, the correlation was significant only for ACR (r=0.489, p=0.0001) but not for urine microalbumin (r=0.156, p=0.237). Among patients with HbA1c >10%, 89.2% had microalbuminuria.

Conclusion: Disease duration significantly amplifies the correlation between HbA1c and microalbuminuria in T2DM. The ACR is a sensitive marker even in early disease. Regular HbA1c monitoring and ACR screening should be initiated at diagnosis to prevent progression to overt nephropathy.

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Introduction:-

Type 2 diabetes mellitus (T2DM) is a major global health burden, with an estimated 537 million adults affected worldwide in 2021, projected to reach 783 million by 2045 [1]. India alone accounts for approximately 77 million diabetic individuals, making it the second largest diabetic population globally [2]. Among the chronic complications of T2DM, diabetic nephropathy (DN) is the leading cause of end-stage renal disease (ESRD), affecting 20-40% of patients over their lifetime [3].

Microalbuminuria, defined as a urinary albumin-to-creatinine ratio (ACR) of 30-300 mg/g creatinine, represents the earliest detectable stage of diabetic nephropathy, preceding overt proteinuria by several years [4]. Early identification of microalbuminuria is critical, as timely interventions including strict glycaemic control and renin-angiotensin system blockade can retard renal progression and reduce cardiovascular risk [5].

Glycated haemoglobin (HbA1c) is the gold standard biomarker for long-term glycaemic control, reflecting mean blood glucose levels over the preceding 2-3 months [6]. Hyperglycaemia drives renal microvascular injury through multiple pathways including advanced glycation end-product (AGE) accumulation, activation of the polyol pathway, protein kinase C activation, and oxidative stress, collectively promoting glomerular hyperfiltration, podocyte injury, and mesangial matrix expansion [7,8].

While the association between poor glycaemic control and nephropathy is well established, the modulating effect of disease duration on the HbA1c-microalbuminuria relationship has received comparatively less attention, particularly in the Indian population. Understanding this relationship is essential for stratifying nephropathy risk and tailoring screening protocols.

The present study was designed to compare HbA1c and ACR between T2DM patients with disease duration <5 years and >5 years, and examine the correlation between HbA1c and ACR in each subgroup, to clarify whether disease duration modulates this relationship.

Material and Methods:-

Study Design and Setting:-

This was a hospital-based cross-sectional observational study conducted at a tertiary care teaching hospital in Chhatrapati Sambhajinagar, Maharashtra, India. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants.

Study Population:-

A total of 121 patients with established Type 2 diabetes mellitus were enrolled. Patients were categorised into two groups based on disease duration: Group A (<5 years, n=59) and Group B (>5 years, n=62). Inclusion criteria were: age 18-65 years; confirmed T2DM as per ADA 2023 criteria [9]; willingness to participate. Exclusion criteria included: known primary renal disease; urinary tract infection at the time of sampling; haematuria; pregnancy; haemoglobinopathies affecting HbA1c accuracy; severe hepatic or cardiac failure.

Clinical and Laboratory Parameters:-

All patients underwent a detailed clinical evaluation including history of diabetes duration, smoking status, and residence (rural/urban). Blood samples were collected after overnight fasting. HbA1c was measured by high-performance liquid chromatography (HPLC) using a standardisedanalyser. A fresh spot urine sample was collected for urine microalbumin and urine creatinine estimation. Urinary ACR was calculated as urine albumin (mg/dL) / urine creatinine (g/dL). Additional biochemical parameters including serum electrolytes, kidney function tests (serum urea and creatinine), and fasting lipid profile (total cholesterol, HDL, LDL, TG, VLDL) were measured by standard enzymatic methods.

Statistical Analysis:-

Data were entered in Microsoft Excel and analysed using SPSS version 23. Continuous variables are expressed as mean ± standard deviation (SD). Between-group comparisons were performed using the independent samples t-test. Pearson's correlation coefficient (r) was used to assess the linear relationship between HbA1c and microalbumin/ACR. A p-value of <0.05 was considered statistically significant.

Results and Observations:-

Demographic Profile:-

The study enrolled 121 T2DM patients: 59 in Group A (disease duration <5 years) and 62 in Group B (>5 years). The mean age of the entire cohort was 48.1 ± 8.0 years (range 28-60 years). The sex distribution was 59 males and 62 females. Demographic parameters were comparable between the two groups with no statistically significant differences (Table 1).

Table 1: Demographic Profile of Study Groups

Parameter	<5 Years (n=59)	>5 Years (n=62)	p-value	Significance
Age (years), Mean±SD	47.9 ± 8.1	48.3 ± 8.0	0.794	NS
Sex: Male/Female	31M / 28F	28M / 34F	0.391	NS
Urban : Rural	46 : 13	51 : 11	0.511	NS
Smoker / Ex-smoker / Non-smoker	5 / 10 / 44	12 / 12 / 38	0.212	NS

Comparison of HbA1c and Renal Parameters:-

Patients with disease duration >5 years had significantly higher mean HbA1c (10.26 ± 1.70%) compared to those with <5 years (6.82 ± 0.80%; p<0.0001). Similarly, mean urine microalbumin and ACR were significantly elevated in Group B (Table 2). Mean ACR in the >5 years group (56.41 ± 38.15 mg/g) was more than double that of the <5 years group (23.87 ± 26.58 mg/g), indicating a substantially greater burden of early renal injury with increasing disease duration.

Table 2: Comparison of HbA1c and Renal Parameters between Groups

Parameter	<5 Years (n=59)	>5 Years (n=62)	t-value	p-value
HbA1c (%)	6.82 ± 0.80	10.26 ± 1.70	-14.13	<0.0001*
Urine Microalbumin (mg/dL)	3.70 ± 8.90	6.63 ± 4.52	-2.30	0.0233*
ACR (mg/g creatinine)	23.87 ± 26.58	56.41 ± 38.15	-5.42	<0.0001*

***Statistically significant (p<0.05). NS = Not Significant.**

Correlation between HbA1c and Microalbuminuria:-

Pearson's correlation analysis revealed that in Group B (>5 years), HbA1c showed a statistically significant positive correlation with both urine microalbumin (r=0.444, p=0.0003) and ACR (r=0.591, p<0.0001). In Group A (<5 years), the correlation between HbA1c and urine microalbumin was not statistically significant (r=0.156, p=0.237), but the correlation with ACR was significant (r=0.489, p=0.0001). In the overall cohort, both correlations were significant. These findings demonstrate that disease duration substantially strengthens the HbA1c-microalbuminuria relationship (Table 3).

Table 3: Correlation of HbA1c vs Microalbumin and ACR

Group	r (HbA1c vs Microalbumin)	p-value	r (HbA1c vs ACR)	p-value
<5 Years	0.156	0.2372 (NS)	0.489	0.0001*
>5 Years	0.444	0.0003*	0.591	<0.0001*
Overall (n=121)	0.309	0.0006*	0.658	<0.0001*

***Statistically significant (p<0.05). NS = Not Significant. ACR = Albumin-to-Creatinine Ratio.**

HbA1c Category and Microalbuminuria Prevalence:-

When patients were stratified by HbA1c category, a progressive increase in the prevalence of microalbuminuria (ACR 30-300 mg/g) was observed. Only 3.3% of patients with well-controlled HbA1c (<6.5%) had microalbuminuria, compared to 32.3% in the moderate control group (6.5-8%), 69.6% in the uncontrolled group (8-10%), and 89.2% in the severely uncontrolled group (>10%), demonstrating a strong dose-response relationship (Table 4).

Table 4: HbA1c Categories and Microalbuminuria Prevalence

HbA1c Category	n	Microalbuminuria (ACR 30-300)	Normal ACR (<30)	%MA
<6.5% (Well controlled)	30	1	29	3.3
6.5-8.0% (Moderate)	31	10	21	32.3
8.0-10% (Uncontrolled)	23	16	7	69.6
>10% (Severely Uncontrolled)	37	33	4	89.2

MA = Microalbuminuria; ACR = Albumin-to-Creatinine Ratio.

Discussion:-

The present study demonstrates that disease duration is a significant modifier of the HbA1c-microalbuminuria relationship in T2DM. The most striking finding was the marked elevation in both HbA1c and ACR in patients with longer diabetes duration, corroborating the concept that cumulative glycaemic exposure drives progressive renal microvascular damage.

Our finding that mean HbA1c is significantly higher in the >5 years group (10.26%) compared to the <5 years group (6.82%) is consistent with the natural history of T2DM, wherein progressive beta-cell failure leads to worsening glycaemia over time. The UKPDS study demonstrated that HbA1c rises approximately 1% per decade even with conventional treatment, reflecting relentless disease progression [9,10].

The observation that HbA1c significantly correlates with urine microalbumin only in the >5 years group ($r=0.444$, $p=0.0003$) while no such correlation exists in the <5 years group ($r=0.156$, $p=0.237$) is clinically significant. This suggests that early in the disease course, renal changes are still subclinical and intermittent hyperglycaemia may not yet have produced a measurable albumin response. After 5 years of cumulative hyperglycaemic exposure, the glomerular basement membrane thickening, mesangial expansion, and podocyte injury are sufficiently advanced that any further glycaemic worsening is accompanied by a measurable increase in microalbuminuria [11,12].

Interestingly, ACR correlated significantly with HbA1c even in the <5 years group ($r=0.489$, $p=0.0001$), suggesting that ACR is a more sensitive renal biomarker than spot urine microalbumin alone. This finding aligns with current clinical guidelines recommending ACR over spot microalbumin as the preferred screening tool for early diabetic nephropathy [13].

The dose-response relationship between HbA1c categories and microalbuminuria prevalence (3.3% at HbA1c <6.5% rising to 89.2% at HbA1c >10%) is consistent with the findings of Ohkubo et al. and the ADVANCE trial, which demonstrated a linear relationship between glycaemic control and renal outcomes [14,15]. This pattern strongly supports intensive glycaemic management to preserve renal function.

Our findings are comparable to those of Dabla et al. [16] who reported a significant positive correlation between HbA1c and microalbuminuria in T2DM patients, and to those of Yalagudri et al. [17] who demonstrated that prolonged hyperglycaemia is the key determinant of early nephropathy. However, by stratifying patients by disease duration, the present study adds the clinically important insight that the HbA1c-microalbuminuria correlation strengthens with disease chronicity.[18,19,20,21]

A notable limitation is the cross-sectional design, which precludes causal inference. The relatively small sample size and single-centre nature also limit generalisability. Prospective longitudinal studies with annual ACR measurements are needed to delineate the temporal sequence of glycaemic deterioration and renal injury.

Conclusion:-

Disease duration significantly modulates the correlation between HbA1c and microalbuminuria in Type 2 diabetes mellitus. The relationship is stronger in patients with diabetes duration exceeding 5 years, while ACR serves as a sensitive early marker even in short-duration disease. The prevalence of microalbuminuria rises sharply with worsening glycaemic control. These findings underscore the importance of achieving and maintaining HbA1c targets from the earliest stage of T2DM and implementing ACR screening at the time of diagnosis to detect subclinical renal injury before it progresses to overt nephropathy.

Limitations:-

The cross-sectional design limits causal inference between glycaemic exposure and renal injury.Single-spot urine ACR measurement may be affected by diurnal variation; a first-morning void specimen or 24-hour urine collection would have improved accuracy.The study does not account for the duration or type of antidiabetic treatment, which may independently influence both HbA1c and renal outcomes.Blood pressure measurements and antihypertensive therapy were not systematically recorded, despite hypertension being a major cofactor for nephropathy progression.Single-centre hospital-based recruitment may introduce selection bias and limit community-level generalisability.

Future Directions:-

Longitudinal cohort studies with serial HbA1c and ACR measurements (annual) are needed to establish the temporal sequence of glycaemic deterioration and microalbuminuria onset.Community-based screening programmes targeting rural diabetic populations where both glycaemic control and renal function surveillance are often suboptimal.Investigation of the role of epigenetic modifications and metabolic memory in perpetuating renal injury even after glycaemic correction.

References:-

1. International Diabetes Federation. IDF Diabetes Atlas, 10th ed. Brussels, Belgium: IDF; 2021. Available from: https://www.diabetesatlas.org
2. Anjana RM, Pradeepa R, Deepa M, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol. 2017;5(8):585-596.
3. Koye DN, Magliano DJ, Nelson RG, Pavkov ME. The global epidemiology of diabetes and kidney disease. Adv Chronic Kidney Dis. 2018;25(2):121-132.
4. American Diabetes Association Professional Practice Committee. Standards of Medical Care in Diabetes—2023. Diabetes Care. 2023;46(Suppl 1):S1-S291.
5. Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020;383(15):1436-1446.
6. Nathan DM, Kuenen J, Borg R, et al. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008;31(8):1473-1478.
7. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. Diabetes. 2005;54(6):1615-1625.
8. Forbes JM, Cooper ME. Mechanisms of diabetic complications. Physiol Rev. 2013;93(1):137-188.
9. ElSayed NA, Aleppo G, Aroda VR, et al. 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2023. Diabetes Care. 2023;46(Suppl 1):S19-S40.
10. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359(15):1577-1589.
11. Hivre M, Holkar S, Vaishnav D, Surkar P. Beyond HbA1c: alternative glycemic biomarkers in hemoglobinopathies, malignancy, and special clinical populations - a review. Int J Drug Deliv Technol. 2026;16(7s): 303-327
12. Wolf G, Ziyadeh FN. Molecular mechanisms of diabetic renal hypertrophy. Kidney Int. 1999;56(2):393-405.
13. Bonventre JV. Can we target tubular damage to prevent renal insufficiency? Nephrol Dial Transplant. 2014;29(Suppl 1):i62-i68.
14. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102(5S):S1-S127.
15. Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res Clin Pract. 1995;28(2):103-117.

16. ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008;358(24):2560-2572.
17. Dabla PK, Kumar R, Sharma TK, Singh B, Ganguly NK. Prevalence of microalbuminuria and its correlation with glycaemic control and other cardiovascular risk factors in patients with type 2 diabetes. Biochem Res Int. 2012;2012:1-7.
18. Yalagudri S, Nagarajan A, Basha PM, Kumaravel R. Correlation of HbA1c levels with microalbuminuria in type 2 diabetes mellitus. Int J Res Med Sci. 2017;5(5):2073-2077.
19. Viberti GC, Hill RD, Jarrett RJ, Argyropoulos A, Mahmud U, Keen H. Microalbuminuria as a predictor of clinical nephropathy in insulin-dependent diabetes mellitus. Lancet. 1982;1(8287):1430-1432.
20. Mogensen CE, Christensen CK, Vittinghus E. The stages in diabetic renal disease. With emphasis on the stage of incipient diabetic nephropathy. Diabetes. 1983;32(Suppl 2):64-78.
21. Tuttle KR, Bakris GL, Bilous RW, et al. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes Care. 2014;37(10):2864-2883.