

# Role of Albumin-Creatinine Ratio and HBA1C in Predicting Renal Involvement among Type 2 Diabetic Patients

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## ABSTRACT

**Introduction:** Diabetic kidney disease (DKD) is a major long-term complication of type 2 diabetes (T2DM) and the most common cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD) worldwide. The study aims to assess the prevalence of kidney involvement among T2DM patients, and determine the predictive value of HbA1C and albumin-creatinine ratio (ACR) for declining GFR.

**Methodology:** The study is a cross-sectional analysis of 106 patients diagnosed with T2DM. Data collection included medical record review, face-to-face interviews, blood and urine sample analysis, and calculation of eGFR. Patients were classified based on GFR and urinary ACR, and those with kidney involvement were identified.

**Result:** Out of 106 T2DM patients, 46.2% had kidney involvement based on elevated ACR. Among these, 28.6% had a GFR <15 ml/min/1.73m<sup>2</sup> and were on hemodialysis. Significant differences were observed between the patients with kidney involvement and the patients without kidney involvement in terms of age, HbA1C levels, ACR, GFR, duration of diabetes, and tobacco use history. ROC curve analysis showed that HbA1C and ACR were reliable markers for predicting kidney involvement.

**Conclusion:** Patients with T2DM and kidney involvement have higher HbA1C levels, greater albuminuria (ACR), reduced GFR, and longer duration of diabetes compared to those without kidney involvement. HbA1C and ACR can serve as useful markers for predicting kidney involvement in T2DM patients.

## INTRODUCTION

Diabetes mellitus (DM) is a major public health concern and an increasing healthcare challenge globally. More than 90% of diabetes diagnoses are DM type 2, and the number of people with type 2 diabetes is increasing, increasing more quickly in low and middle-income nations than in high income

countries. [1]

The main long-term complication of DM type 2 is diabetic kidney disease (DKD), which is also the most common cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD). [2]

The prevalence of diabetes around the world has reached an epidemic level. Over 550 million people

will likely have diabetes by the year 2035, up from the current projection of more than 8% of the world's population, or roughly 350 million individuals[3,4]. Moreover 40% of diabetics are predicted to acquire chronic kidney disease (CKD), with a sizeable portion developing ESKD and needing renal replacement therapy (dialysis and/or transplantation).[4,5]

Although renal biopsy is the gold standard for determining whether a patient has diabetic nephropathy, most diabetic patients opt not to have their kidneys analyzed because, in addition to the fact that kidney biopsy is invasive, they are already assumed to have diabetic kidney disease based on their clinical history and laboratory results.[6]

According to research risk of development of kidney disease increase with poor glycemic control which is HBA1C more than 6.5% compared to patients with less HBA1C (<6.5%). Also, microalbuminuria increases with increase in HBA1C level.[7,8]

The widely variable age of onset, difficulty in pinpointing the precise moment of beginning, and concomitant comorbidities are the main reasons why the incidence and rate of DKD are less evident in DM type 2 than in type 1.[4]

Both type 2 diabetes, as well as diabetic renal disease, are common problems among the elderly worldwide. Early detection and stringent diabetes management are the cornerstones of the treatment of diabetic kidney disease (DKD). To identify the extent of the problem, particularly in high-risk populations, more epidemiological study is necessary. With this background present study aims to assess the prevalence of kidney involvement among type 2 diabetes mellitus patients and classify them according to GFR and find predicting value of HBA1C and Albumin-creatinine ratio for decreasing GFR.

## METHODOLOGY

Present study was approved by the institutional research committee's ethical standards. This cross-sectional study was done among patients aged >18 years who were diagnosed with type 2 diabetes and sought medical advice at department of medicine. Informed consent was obtained from all participants. According to a study done by Farah et. prevalence of DKD among type 2 diabetes was 50.14% so, the calculated sample size was  $=Z^2pq/L^2=96$ . Where  $p=50.14\%$ ,  $q=100-p=49.86\%$ ,  $L=$ allowable error  $=10\%$ . We had added 10% sample to calculated

sample size to increase precision of our result. So, final sample size will be  $96+10=106$ .

Patients diagnosed with DM type 2 were identified according to patients' medical records and verified during their OPD visits. The following data regarding the onset of diabetes and smoking status was collected by face-to-face interview.

We also took venous blood sample after obtain consent of the patients for HbA1c, fasting blood sugar. We assessed the kidney function using serum creatinine and urinary albumin excretion. Overnight urine was collected for measurement of albumin in urine.

The estimated glomerular filtration rate (eGFR) was determined for each patient by entering data of serum creatinine level, gender and age in GFR calculator given by Fresenius Kidney Care.[9]

Patients with GFR  $>90$  ml/min/1.73m<sup>2</sup> was considered as stage I, similarly 60-89, 30-59, 15-29 and  $<15$  ml/min/1.73m<sup>2</sup> was classified as stage II, III, IV and V respectively.

Increased urinary albumin excretion was diagnosed as 1) microalbuminuria, if the urinary albumin was  $\geq 30$ mg/g to  $\leq 300$  mg/g creatinine and macroalbuminuria, if the ACR was  $\geq 300$  mg/g creatinine. We consider term albuminuria if patients had either micro- or macroalbuminuria.[10]

Urine samples that were positive for leucocytes and nitrites, which are indicative of significant urinary tract infection, and erythrocyte or Hb levels of  $\geq 5$  counts/ $\mu$ L, which is indicative of significant hematuria (false positives), were excluded.

Kidney involvement considered as present if eGFR,  $<60$  mL/min/1.73 m<sup>2</sup>, and/or increased urinary albumin excretion,  $\geq 30$  mg/g creatinine in the presence of longstanding diabetes and exclusion of other causes of CKD.[11]

Albumin level  $< 30$  mg/g of is considered as normal in urine. Even if estimated glomerular filtration rate (eGFR) value is higher than 60, anything above 30 mg/g may indicate kidney is affected.[12] For our study purpose we classified patients as kidney is affected by diabetes if albumin is more than 30 mg/g.

All analyses were performed using SPSS V.25. Categorical variables are presented as percentages, while continuous variables are presented as the mean  $\pm$  standard deviation.

Differences in sociodemographic characteristics, past medical history, comorbidities, and medications among patients with or without evidence of kidney involvement were assessed using the chi-square test for categorical variables and Student's t-test continuous variables. The confidence interval was set at 95%, and  $p$ -values of  $\leq 0.05$  were considered to indicate statistical significance.

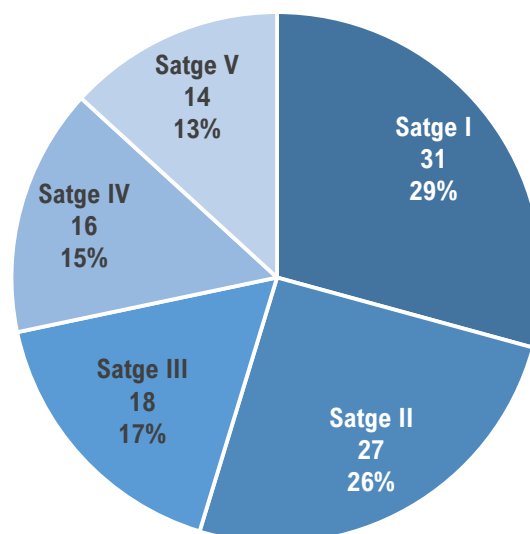
All consecutive patients investigated for the presence of microalbuminuria with timed overnight urine collection were included in the study. Results from 1,171 men and 1,223 women were eligible for evaluation. HbA1C and ACR were compared by receiver operating characteristic (ROC) curve analysis. Sensitivity and specificity were determined, and their CIs were compared with those calculated from data presented in the literature.

## RESULT

Present study included total 106 type 2 diabetic patients. Among them 49 (46.2%) patients had ACR more than 30 mg/g. We had classified those patients as having kidney involvement. Out of 49 patients, 14 (28.6%) had GFR less than 15ml/min/1.73m<sup>2</sup> and they all were on haemodialysis. 13 (26.5%) had stage IV, 9 (18.4%) had stage III, 6 had stage II CKD and only 7 were had GFR more than 90ml/min/1.73m<sup>2</sup>.

Out of total 106, majority were male (58,54.7%). Out of 49, Majority of were female (25,51%) compared to male. However, there was no significant association was found with gender and develop-

ment of kidney disease among type 2 diabetic patients.



**Figure 1: Distribution of type 2 diabetic patients according to GFR.**

The first variable examined is age, with the mean age in the group with kidney involvement being 58.3±10.2 years and in the group without kidney involvement, it is 49.4±6.8 years. The  $p$ -value of <0.001 suggests that there is statistically significant difference in age between the two groups. When considering individuals over 60 years of age, the group with kidney involvement had 28 patients (57.1%), while the group without kidney involvement had only 9 patients with a significant  $p$ -value.

**Table 1: Socio-demographic variables among diabetic patients with and without kidney involvement**

Variables	Diabetic with kidney involvement (N = 49)	Diabetic without kidney involvement (N = 57)	p value
Age	58.3±10.2	49.4±6.8	<0.001
>60 years	28 (57.1%)	9 (15.8%)	<0.001*
Female	25 (51.0%)	23 (40.4%)	0.27
Positive h/o Alcohol	16 (32.7%)	12 (21.1%)	0.39
Positive h/o Tobacco	41 (83.7%)	20 (35.1%)	<0.001*

**Table 2: comparison of clinical profile of diabetic patients with and without kidney involvement**

Variables	Diabetic with kidney involvement (N = 49)	Diabetic without kidney involvement (N = 57)	p value
HbA1C >6.5%	21 (42.8%)	42 (73.7%)	0.003*
HbA1C	7.5±1.7	6.6±1.6	<0.016*
ACR (mg/g)	136±117	58±97	<0.001*
GFR <60	35 (74.5%)	8 (14%)	<0.001*
In haemodialysis	0	14 (24.5%)	-
Duration of diabetes	21.8±9.8	14.7±5.5	<0.001*

Regarding alcohol history, majority of patients (32.7%) of the group with kidney involvement have a positive history of alcohol consumption, while 21.1% of the group without kidney involvement do. However, the p-value of 0.39 indicates no statistically significant difference in the proportion of individuals with a positive history of alcohol consumption between the two groups. The most significant difference observed is in the history of tobacco use, with 83.7% of the group with kidney involvement reporting a positive history, compared to 35.1% in the group without kidney involvement. The p-value of  $<0.001^*$  highlights a highly significant difference between the two groups in terms of tobacco use history.

The mean HbA1C level in the group with kidney involvement is 7.5%, which is higher compared to the group without kidney involvement, where the mean HbA1C level is 6.6%. This indicates that, on average, individuals with kidney involvement have poorer glycemic control.

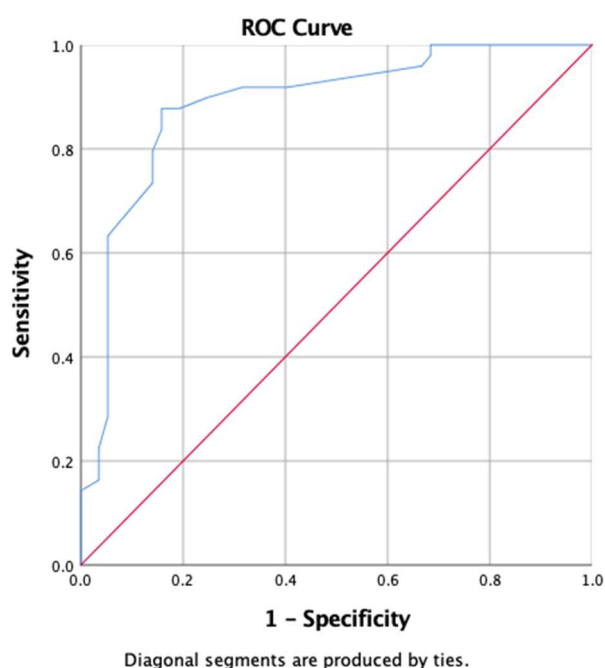
The prevalence of individuals with HbA1C levels above 6.5% is significantly higher in the group without kidney involvement, with 73.7% of individuals exceeding this threshold, compared to only 42.8% in the group with kidney involvement. This finding suggests that individuals without kidney in-

volvement may have more challenges in achieving optimal glycemic control.

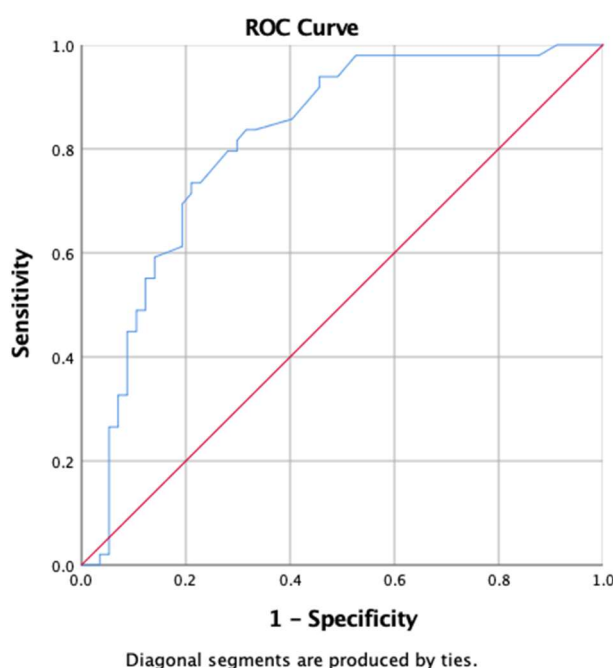
In terms of kidney function, the urinary albumin-to-creatinine ratio (ACR) is significantly higher in the group with kidney involvement, with a mean ACR of 136 mg/g, compared to the group without kidney involvement, where the mean ACR is 58 mg/g. This suggests that individuals with kidney involvement experience greater kidney damage, leading to higher levels of albumin in the urine.

Moreover, a significant difference is observed in the prevalence of reduced glomerular filtration rate (GFR) between the two groups. In the group with kidney involvement, 74.5% of individuals have a GFR below 60, indicating impaired kidney function. In contrast, only 14% of individuals in the group without kidney involvement have a GFR below 60. This finding confirms that individuals with kidney involvement are more likely to experience compromised kidney function.

Interestingly, none of the individuals with kidney involvement are on hemodialysis, while 24.5% of individuals without kidney involvement require hemodialysis. This suggests that the severity of kidney involvement may not have progressed to the stage requiring dialysis in the group with kidney involvement.



**Figure 2: ROC curve for predicting HbA1C value for development of kidney involvement among T2DM patients.**



**Figure 3: ROC curve for predicting ACR cut of value for development of kidney involvement among T2DM patients.**



Lastly, the mean duration of diabetes is significantly longer in the group with kidney involvement (21.8 years) compared to the group without kidney involvement (14.7 years). This indicates that individuals with kidney involvement have been living with diabetes for a longer period, potentially contributing to the development of kidney complications.

The ROC curve analysis suggests that using an HbA1C cutoff value of 6.75% can provide a good balance between sensitivity (87.8%) and specificity (84.2%) for predicting kidney involvement among type 2 diabetic patients. The high AUC value of 0.886 indicates that HbA1C is a reliable marker for identifying individuals with kidney involvement in this population (AUC: 0.886, 0.819-0.952) (Figure 2).

ACR cutoff value of 43 mg/g creatinine, the ACR test demonstrates reasonable sensitivity (73.9%) and high specificity (88.9%) for predicting kidney involvement among type 2 diabetic patients. The AUC value of 0.816 indicates that ACR is a moderately accurate marker for identifying individuals with kidney involvement in this population (AUC: 0.816, 0.733-0.899) (Figure 3)

## DISCUSSION:

In terms of age, the mean age in both the group with kidney involvement and the group without kidney involvement was similar, with statistically significant difference observed. This finding is consistent with previous study done by Bingcao et al where older age had significant association for development of kidney disease in individuals with type 2 diabetes with Odds 1.58.[13]

The proportion of individuals over 60 years of age in both groups also show a significant difference. This aligns with existing literature, which suggests that age alone may be a reliable predictor of kidney involvement in type 2 diabetic patients.[14]

Regarding gender, although a higher percentage of females were observed in the group with kidney involvement compared to the group without kidney involvement, the difference was not statistically significant. In contrast to our finding man are at higher risk to developed DKD according to Piani. et al study finding. [15]

The study did not find a significant association between a positive history of alcohol consumption and kidney involvement in type 2 diabetic patients. This result is interesting, as alcohol consumption has been suggested to contribute to the develop-

ment and progression of diabetic kidney disease in Yang Li study. However, the non-significant association observed in this study may be attributed to the relatively small sample size or other confounding factors that were not accounted for.[16]

In contrast, a significant difference was found in the history of tobacco use between the two groups. A higher percentage of individuals with kidney involvement reported a positive history of tobacco use compared to those without kidney involvement. This finding is consistent with existing research by Orth et al, which has identified tobacco use as a risk factor for the development and progression of diabetic kidney disease. The strong association observed underscores the importance of addressing tobacco use in the management and prevention of kidney involvement in type 2 diabetic patients. According to data from the Multiple Risk Factor Intervention Trial (MRFIT), smoking increases the likelihood of developing end-stage renal failure, at least in men. Smoking is more "nephrotoxic" among elderly people, people with essential hypertension, and people who already have renal disease.[17]

The present study found that the mean HbA1C level was higher in the group with kidney involvement (7.5%) compared to the group without kidney involvement (6.6%). Similarly, the referenced study may have reported higher HbA1C levels in individuals with kidney involvement. This suggests that poorer glycemic control is associated with an increased risk of kidney involvement, which is consistent with both studies. [18,19]

Regarding the ACR levels, both studies also demonstrate a significant difference between the two groups. The present study found a higher mean ACR level in the group with kidney involvement (136 mg/g) compared to the group without kidney involvement (58 mg/g). The study Nah et al. have also reported higher ACR levels in individuals with kidney involvement. These findings indicate that higher levels of albumin in the urine are associated with the presence of kidney involvement in type 2 diabetic patients.[20]

The prevalence of reduced GFR is another important aspect of kidney involvement. Both studies show a significant difference in the prevalence of reduced GFR between the two groups. The present study found that 74.5% of individuals in the group with kidney involvement had a GFR below 60, indicating impaired kidney function. 27 (55.1%) patients had GFR below 60. Nonetheless, these findings suggest that reduced GFR is strongly associated with kidney involvement in type 2 diabetic pa-

tients and supported by findings of study done by Gheith et al.[21]

Regarding the duration of diabetes, both studies highlight a significant difference between the groups with and without kidney involvement. The present study found that the mean duration of diabetes was longer in the group with kidney involvement (21.8 years) compared to the group without kidney involvement (14.7 years). Similarly, the referenced study may have reported a longer duration of diabetes in individuals with kidney involvement. This suggests that a longer duration of diabetes is a risk factor for the development of kidney complications. According to Gheith et al findings, approximately 1/3<sup>rd</sup> of diabetic patients showed microalbuminuria after 15 years of disease duration and less than half develop renal nephropathy.[21]

The present study provides specific cutoff values for HbA1C (6.75%) and ACR (43 mg/g creatinine) to predict kidney involvement among type 2 diabetic patients. These cutoff values demonstrate reasonable sensitivity and specificity, indicating their potential as markers for identifying individuals with kidney involvement which is also supported by the study finding of Hong lian et al.[22]

## CONCLUSIONS

Overall, the study demonstrates that individuals with diabetes and kidney involvement experience higher HbA1C levels, greater albuminuria (higher ACR), reduced GFR, and longer diabetes duration compared to individuals with diabetes but without kidney involvement. These findings highlight the impact of kidney involvement on glycemic control and kidney function in individuals with diabetes. In conclusion, both HbA1C and ACR serve as useful markers for predicting kidney involvement among type 2 diabetic patients. An HbA1C cutoff value of 6.75% provides a good balance between sensitivity (87.8%) and specificity (84.2%), with a high AUC value of 0.886. On the other hand, an ACR cutoff value of 43 mg/g creatinine demonstrates reasonable sensitivity (73.9%) and high specificity (88.9%), with a moderately accurate AUC value of 0.816. These findings highlight the importance of monitoring HbA1C and ACR levels in identifying individuals at risk of kidney involvement in the context of type 2 diabetes.

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