



**PROSPECT OF GLYCATED ALBUMIN AS PREDICTOR OF GFR IN T2DM PATIENT  
WITH CHRONIC KIDNEY DISEASE**

**Prof. R. Ramesh<sup>1\*</sup>, Dr. R. Reeta<sup>2</sup>, V. Kuzhandai Velu<sup>3</sup>, Dr. Kulkarni Sweta<sup>4</sup>, Swathi Sivakumar<sup>5</sup>**

<sup>1</sup>Head, Department of Biochemistry Mahatma Gandhi Medical College and Research Institute (SBVU) Pilliyarkuppam Puducherry – 607402 India.

<sup>2</sup>Assistant Professor Department of Biochemistry Mahatma Gandhi Medical College and Research Institute Puducherry – 607402.

<sup>3</sup>Research Scholar Department of Biochemistry Mahatma Gandhi Medical College and Research Institute Puducherry – 607402.

<sup>4</sup>Assistant Professor Department of Biochemistry Mahatma Gandhi Medical College and Research Institute Puducherry – 607402.

<sup>5</sup>Final Year MBBS Student Mahatma Gandhi Medical College and Research Institute Puducherry – 607402.

**\*Author for Correspondence: Prof. R. Ramesh**

Head, Department of Biochemistry Mahatma Gandhi Medical College and Research Institute (SBVU) Pilliyarkuppam Puducherry – 607402 India.

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**ABSTRACT**

**Introduction:** Diabetes Mellitus (DM) is a worldwide public health problem that affects millions of people from all racial and ethnic groups and also the leading cause for Chronic Kidney Disease (CKD).<sup>[1]</sup> The rapidly increasing prevalence of Type 2 Diabetes Mellitus (T2DM) worldwide and especially in India assures that the proportion of CKD attributable to T2DM will continue to rise. **Materials And Methods:** The study was conducted in the Department of Biochemistry at Mahatma Gandhi Medical College and Research Institute, Puducherry, in collaboration with the Department of Nephrology. 100 patients between 35 – 65 years diagnosed as T2DM and CKD were included. Non-diabetic CKD, ESRD patients, hepatobiliary, endocrine and cardiovascular disorders were excluded. Blood glucose, serum creatinine, total protein, Glycated albumin and Cystatin C were analyzed. eGFR using Cockcroft – Gault, MDRD, CKD-EPI and Cystatin C formula was calculated. **Results:** The creatinine concentration had an average of 4.89mg%, cystatin C levels varied from 3.98 to 5.80mg/L with an average of 4.89 mg/dl. The calculated GFR shows that the mean eGFR as estimated by MDRD formula is 37.2ml/min, cystatin C based formula is 38.29ml/min, CKD-Epi formula 34.92ml/min and CCF formula 41.8ml/min. The mean values of eGFR calculated by MDRD and cystatin C based formula were almost equal while eGFR CCF calculated and CKD Epi formula gave higher and lower values respectively. **Conclusion:** Glycated albumin has been directly implicated as a causal factor in the development of nephropathy due to its direct interaction with the receptors on mesangial cells so following T2DM patients with CKD by estimating glycated albumin which is a simple test can provide insight about both their GFR and glycemic status.

**KEYWORDS:** T2DM, CKD, glycated albumin, eGFR, Cystatin C, MDRD, Creatinine.

**INTRODUCTION**

Diabetes Mellitus (DM) is a worldwide public health problem that affects millions of people from all racial and ethnic groups and also the leading cause for Chronic Kidney Disease (CKD).<sup>[1]</sup> The rapidly increasing prevalence of Type 2 Diabetes Mellitus (T2DM) worldwide and especially in India assures that the proportion of CKD attributable to T2DM will continue to rise. The National Kidney Foundation defines CKD as kidney damage with Glomerular Filtration Rate (GFR) less than 60ml/min/1.73m<sup>2</sup> for three months or more and also stages according to the levels of GFR thus making eGFR estimation essential for both evaluation

and management of T2DM patient with CKD.<sup>[2,3]</sup> GFR also predicts the time of onset for the need of renal replacement therapy such as dialysis.

The accepted gold standard for measuring GFR are based on determining the clearance of exogenous substance such as inulin or chromium tagged EDTA, but these tests are expensive, time consuming so the concept of eGFR using prediction equation is now recommended by the National Kidney Foundation for the diagnosis and risk stratification of CKD.<sup>[4]</sup> Most of the eGFR formulas are based on creatinine related equation which may become unpredictable as creatinine concentration is influenced

by dietary intake, creatinine supplements disease of the skeletal muscle and rapidly changing kidney functions.<sup>[5]</sup>

Cystatin C a low molecular weight protease inhibitor is found to be a better substitute than creatinine based equation for predicting GFR but its estimation is costlier and not routinely estimated in all labs.<sup>[6,7]</sup> Glycated albumin (GA) marker formed by non-enzymatic glycosylation of albumin is considered as one of the short term indicator of glycemic status and it has been revealed that increased levels of GA are linked to both the presence and severity of impaired kidney function.<sup>[8,9]</sup>

At present there are very few studies regarding the role of glycated albumin in the diagnosis and management of T2DM patient with CKD. So the present study was undertaken to explore the role of glycated albumin as a predictor of GFR in T2DM patients with CKD.

### MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry at Mahatma Gandhi Medical College and Research Institute, Puducherry, in collaboration with the Department of Nephrology after obtaining institute ethics committee's approval.

A total of 100 patients in the age group between 35 – 65 years clinically diagnosed as T2DM with CKD where included in the study. Cases of non-diabetic CKD, End Stage Renal Disease patients on dialysis, patients with co-existing hepatobiliary disorders, endocrine disorders and cardiovascular disorders were excluded from the study.

3ml of blood was collected from the patients and the samples were analysed for blood glucose, serum creatinine, total protein, Glycated albumin and Cystatin C using fully automated chemistry analyzer and by international federation of clinical chemistry approved methods. eGFR using Cockcroft – Gault, Modification of Diet in Renal Disease, CKD-EPI and Cystatin C based formula was calculated using online calculations.

### STATISTICAL ANALYSIS

The data are presented as mean and standard deviation. For comparison, ANOVA was used. Correlation and regression analysis was performed to find out the association between glycated albumin and eGFR.

### RESULTS

The Study included 100 patients diagnosed with T2DM and CKD who attended the Nephrology OPD of Mahatma Gandhi Medical College. The anthropometric and biochemical parameters of the patients are presented in Table 1. The average age of the patient included in the study was 54 with a standard deviation of 12 and the mean BMI was 26.62 Kg/m<sup>2</sup>. The creatinine concentration had an average of 4.89mg% while cystatin C levels varied from 3.98 to 5.80mg/L with an average of 4.89mg/dl. The calculated eGFR is presented in Type

2 and it shows that the mean eGFR as estimated by MDRD formula is 37.2ml/min, cystatin C based formula is 38.29ml/min, CKD-EPI formula is 34.92 ml/min and CCF formula is 41.8 ml/min. The mean values of eGFR calculated by MDRD and cystatin C based formula were almost equal while eGFR calculated by CCF and CKD EPI formula gave higher and lower values respectively.

Correlation analysis as depicted in Table 3 and Fig: 1 revealed negative correlation between Glycated albumin and eGFR calculated by MDRD and cystatin C based formulas with a 'r' value of -0.768 and -0.778 respectively while eGFR calculated based on CKDEPI and CCF formula did not show good correlation (r value = -3.83 and -0.540 respectively). Table 4 shows that the correlation eGFR calculated by MDRD formula and CCF, CKDEPI and cyst C formula r values are 0.413, 0.512 and 0.751 respectively. The correlation between MDRD and cystatin c based formula was found to be higher compared with other methods used to estimate eGFR.

**Table 1: Anthropometric and Biochemical parameters in T2DM with CKD.**

Parameter	Mean±SD(n=100)
Age	54.47±12.48
Weight (kg)	65.50±3.69
Height (cm)	157.34±0.03
BMI (kg/m <sup>2</sup> )	26.62±1.75
FPG (mg/dl)	158.93±40.29
Creatinine (mg/dl)	4.58±0.85
Cystatin c (mg/l)	4.89±0.91

**Table 2: Mean and SD for different eGFR formulas.**

Parameter	Mean±SD(n=100)
CCF (ml/min)	41.80±4.73
CKD-EPI (ml/min)	34.92±4.50
MDRD (ml/min)	37.20±4.47
CYS C (ml/min)	38.29±4.58
GLYCATED Albumin (%)	21.24±3.81

**Table 3: Correlation and Regression analysis of Glycated albumin vse GFR.**

	Pearson Correlation	R Square Value
CCF	-0.768**	0.591
	0.000	0.000
MDRD	-0.778**	0.606
	0.000	0.000
CKDEPI	-0.383**	0.147
	0.003	0.003
CYSCF	-0.540**	0.292
	0.000	0.000

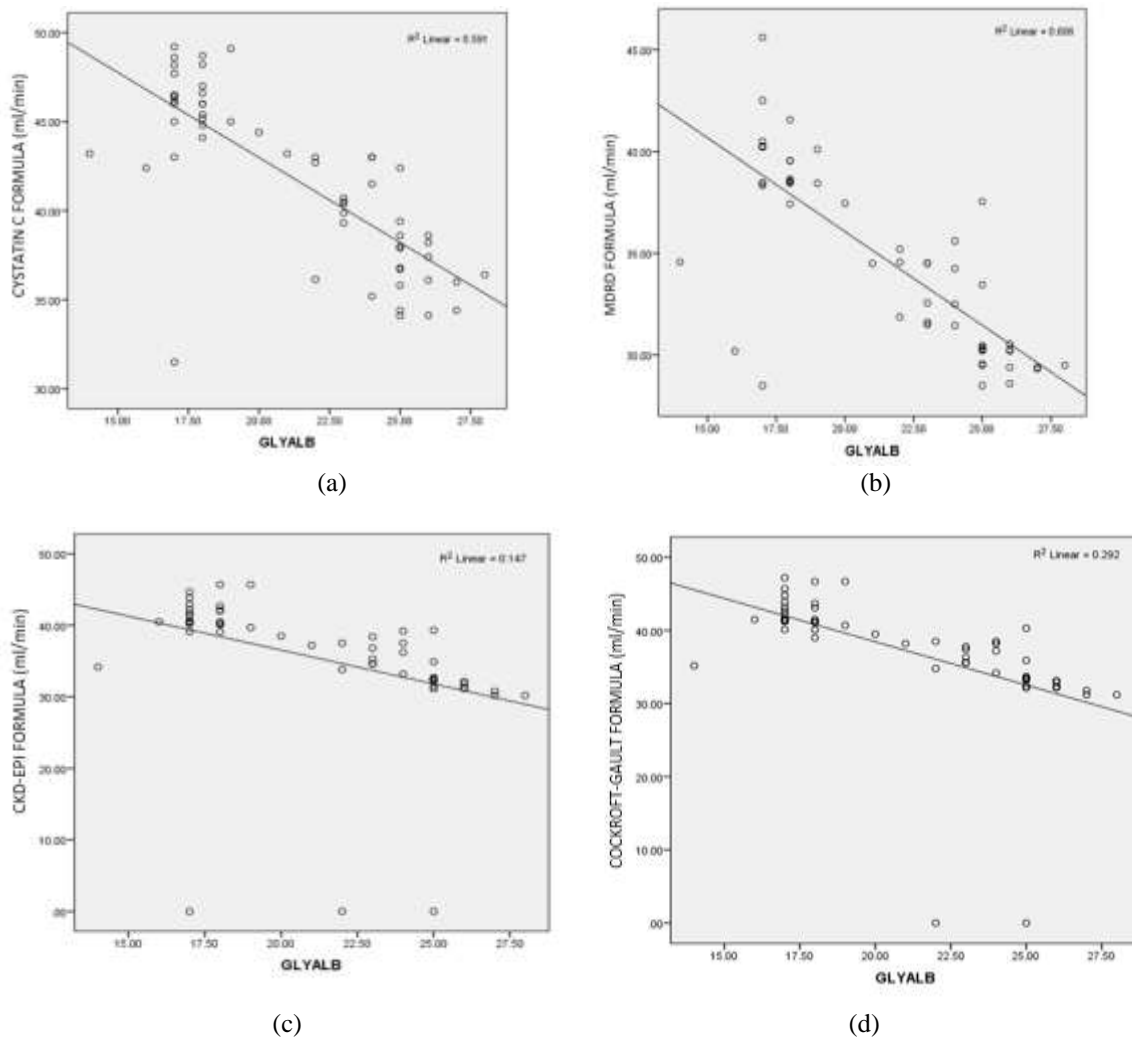
**TABLE 4: Correlation between MDRD method and other methods of eGFR estimation.**

Tests	Correlation	Sig.
MDRD & CCF	.734	0.0005
MDRD & CKDEPI	0.413	0.0005
MDRD & CYSCF	0.751	0.001

**TABLE 5: Comparison of difference between estimation of eGFR by MDRD with other methods.**

Tests	Mean	SD	95% Confidence Interval (Lower – Upper)	p Value
MDRD & CCF	-2.71	3.13	- 3.53 to 1.89	0.000
MDRD & CKDEPI	-1.53	2.80	- 0.26 to - 0.45	0.006
MDRD & CYSCF	0.52	4.12	-0.22 to 1.26	0.156

Table 5 compares the difference between estimated of eGFR by MDRD and other methods. A higher mean difference of eGFR was found between MDRD and CCF formula (95% CI – 3.53 to 1.89) followed by CKDEPI (95% CI - 0.26 to – 0.45) and Cystatin C based formulas (95% CI -0.22 to 1.26).



**Fig. 1. Correlation analysis of Glycated albumin with different eGFR Formulas [(a) Cystatin C (b) MDRD formula (c) CKD – EPI formula and (d) Cockcroft-gault formula].**

## DISCUSSION

The eGFR calculated by CCF formulae was higher when compared to that of others by 10% which was in accordance with previous literature and can be explained by presence of weight in CCF formula and widely dispersed BMI among T2DM patients.<sup>[5,10]</sup> As GFR calculated by CCF formula is proportional to body weight it over estimated GFR. MDRD and Cystatin C based formula does not require body weight in their calculation and can be more accurate than CCF in predicting GFR and renal function.<sup>[6]</sup> Our study showed no statistical difference in eGFR calculated by MDRD and Cystatin C based formula so they can be interchanged without effecting interpretation.<sup>[11]</sup> The difference among eGFR estimated by MDRD, CCF and CKD EPI formula were found to be statistically significant and hence can be concluded interchanging three methods will affect the interpretation and also management of T2DM patient with CKD.<sup>[12]</sup>

Our study showed statistically significant correlation between glycosylated albumin and eGFR calculated by MDRD and Cystatin c based formula. Pervious study shows that glycosylated albumin levels correlated with AGE related fluorescence and number of glycation sites so can be a good marker for monitoring glycemic control of T2DM and also for predicting the functional changes of albumin.<sup>[13]</sup> In our study regression analysis showed a linear relationship between glycosylated albumin and eGFR calculated by MDRD and Cystatin C based formulas suggesting glycosylated albumin can be used as a predictor to assess GFR in T2DM patients with CKD. Glycosylated albumin has been directly implicated as a casual factor in the development of nephropathy due to its direct interaction with the receptors on mesangial cells so follow up of T2DM patients with CKD by estimating glycosylated albumin which is a simple test can provide insight about both their GFR and glycemic status.<sup>[14,15]</sup>

### Limitations of the study

- Our study compared only eGFR's and not GFR calculated by gold standard methods was used for comparison.
- Sample size was also limited to 100 and limited to our geographical location a multi centric study could be more appropriate and useful in this regard.

## CONCLUSION

In the present study there was no statistical difference in eGFR calculated by MDRD and Cystatin C based formula so they can be interchanged without affecting interpretation. The difference among eGFR estimated by MDRD, CCF and CKD EPI formula were found to be statistically significant and hence can be concluded interchanging three methods will affect the interpretation and also management of T2DM patient with CKD. Glycosylated albumin which is a simple test can provide insight about eGFR in patients with T2DM with CKD and their glycemic status.

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