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Glycated Albumin - Biomarker for Glycaemic Control and Prognostic Factor in Chronic Kidney Disease Patients

Ranjithkanna M[1], Rajesh N[2], Velvizhi M[3], Thirunavukarasu MR[4*]

[1,2,3]Assistant Professor, Department of General Medicine, Karur Medical College, Karur, India.
[4]Department of Community Medicine, Government Medical College and ESIC Hospital, Coimbatore, India.

Corresponding Author: Dr. Thirunavukarasu MR

ABSTRACT

Background: Chronic kidney disease is a public health problem of global concern. In HD patients, GA seems more reliable because it is not influenced by the erythrocyte lifespan or erythropoietin and iron therapy, so it could serve as an alternative marker for glycemic control in these patients. Efficacy for glycemic control in HD patients has not yet been firmly established because most studies have examined the correlation between GA and the mean of random serum glucose concentrations instead of continuous glucose monitoring. **Aims and objectives:** To assess the role of glycated albumin as a biochemical marker in glycemic control in chronic kidney disease patients (G5D) on hemodialysis.

Methods: The present study was a hospital based analytical cross sectional study, carried out in the inpatient department of General Medicine in collaboration with the departments of Biochemistry and Nephrology, Govt. Rajaji Medical College Hospital, Madurai. The study included 50 type 2 diabetic patients with chronic kidney disease (G5D) admitted under department of general medicine. **Statistical analysis:** All the data was entered and analyzed using SPSS version 20.0.

Results: Serum glycated albumin levels equal to or greater than 2 8.15 % was considered as a predictor factor for T2DM –CKD- G5 on Hemodialysis with sensitivity of 84% and specificity of 64%, and area under the ROC curve (AUC) of 0.803 with (P<0.001**).Serum HbA1c levels equal to or greater than 6.45 was considered as a cut off value with sensitivity of 56 and specificity of 44, and area under the ROC curve (AUC) of 0.501 which was insignificant (p=0.992).

Conclusion: Glycated Albumin can be a useful predictor of glycemic control in diabetic with chronic kidney disease on hemodialysis.

Keywords: Chronic kidney disease, Glycated albumin, Glycemic control Hemodialysis, G5D

INTRODUCTION

Chronic kidney disease (CKD) is a Public health problem of global concern. Apart from CVD risk, CKD can lead to a wide array of multi system and metabolic derangements, which complicate the management of these patients.[1] This culminates in reduced quality of life, increased health care costs and premature death. After HIV/AIDS and diabetes mellitus, CKD is the third largest condition responsible for premature death. It is also the eighteenth in the list of causes of deaths worldwide. Global Burden of Disease (GBD) study 2015 has ranked CKD as the eighth leading cause of death in India.[2,3]

Chronic kidney disease (CKD) is a pathophysiologic process with decline in glomerular filtration rate and abnormal kidney function. The term end-stage renal disease represents a stage of CKD

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due to accumulation of toxins, fluid, and electrolytes excreted by kidney physiologically, otherwise it leads to death. These toxins can be mechanically removed by renal replacement therapy, which includes haemodialysis, peritoneal dialysis and kidney transplantation In DM, CKD-G5D good glycaemic control remains important to prevent or delay the progression of the vascular complications, to reduce cardiovascular disease (CVD) morbidity and mortality and to avoid hypoglycaemia-related mortality.

HbA1c has been widely used in CKD-G5D patients for glycaemic control to assess the risk of complications and survival. However, as we noted, it suffers some limitations.[4-6] In HD patients, GA seems more reliable because it is not influenced by the erythrocyte lifespan or erythropoietin and iron therapy, so it could serve as an alternative marker for glycaemic control in these patients. Since GA has a mean life of 20 days, it could also be useful for assessing the effects of some medications in a shorter time than HbA1c.[7] However, its efficacy for glycaemic control in HD patients has not yet been firmly established because most studies have examined the correlation between GA and the mean of random serum glucose concentrations instead of continuous glucose monitoring.

MATERIALS AND METHODS

Study Setting

The present study was undertaken in the inpatient department of General Medicine in collaboration with the departments of Biochemistry and Nephrology, Govt. Rajaji Medical College Hospital, Madurai.

Study Design: Hospital based analytical cross sectional study.

Sample Size: 50 patients admitted to Government Rajaji Hospital, Madurai Medical College, during the study period.

Inclusion Criteria

Chronic kidney disease (G5D), e GFR <15ml/min/1.73m2, Patients with Type 2 diabetes.

Exclusion Criteria

Patients without Type 2 diabetes, Patients on peritoneal dialysis, and Patients with e GFR >15ml/min/1.73m2

Data collection Tool

Socio-demographic characteristics of the patient were recorded in addition to physical examination. The biochemical parameters like complete blood count, renal function test, liver function test, fasting blood glucose level glycated albumin HbA1c and serum albumin were done.

Statistical Analysis

The data was entered and analyzed by using Statistical Package for Social Sciences (SPSS) (version 21.0) software package. Descriptive statistics was used to define the study population. Categorical and ordinal variables were expressed as frequency/percentages. Continuous variables were expressed as mean and standard deviation. A p value of less than 0.05 was considered to be statistically significant. Receiver Operating Characteristic Curve was used to assess predicting markers in T2DM / CKD-G-V on HD. The optimal cut off for serum GA was derived from the ROC curve with the sensitivity and 1–specificity. The Youden index (Y = sensitivity + specificity– 1) was calculated to assess the discriminative power of the diagnostic test which ranges from (0 to 1) and value 1 signifies perfect diagnostic test.

RESULT

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In the present study, the study participants were grouped into 2 groups (25 in each group) namely the study group (T2DM / CKD-G5D on HD) and control group (T2DM / CKD-G5 not on HD).

Socio-demographic characteristics

Our results showed that among the study participants in the study group the mean age was 52.16± 11.07 years. While the mean age of those in the control group was 48.48 ±8.95 years. The gender distribution of the study participants showed that the study participants were predominantly male. Though females were more in the control group, no statistical significance was observed.

Biochemical parameters

The concentration of FPG was decreased in study group (147.44 ± 44.87) compared to controls (153.48 ± 33.92), but it was not statistically significant (p= 0.594).We also observed that there was significant decrease (p=0.03) in the haemoglobin levels of participants in the study group (s-7.3 ± 1.28; c-8.22 ± 1.47).There was no significant difference in HbA1c levels (p=0.985) and Sr.Albumin levels (p=0.423) between both groups.

Serum glycated albumin was significantly elevated in CKD cases on Haemodialysis (29.7 ± 1.57) as compared to controls with CKD not on Haemodialysis (26.93 ± 2.83). This increase was found to be statistically significant (p=<0.001)

Receiver operating curve for HbA1c and Serum glycated albumin in the diagnosis of T2DM –CKD- G5 on Haemodialysis

Serum glycated albumin levels equal to or greater than 2 8.15 %was considered as a predictor factor for T2DM –CKD- G5 on Haemodialysis with sensitivity of 84% and specificity of 64%, and area under the ROC curve (AUC) of 0.803 with (P<0.001**). Serum HbA1c levels equal to or greater than 6.45 was considered as a cut off value with sensitivity of 56 and specificity of 44, and area under the ROC curve (AUC) of 0.501 which was insignificant (p=0.992). According to youden's index which determines the discriminative power of the test serum glycated albumin values (0.48) was better predictor marker than HbA1c values among Haemodialysis group. However, HbA1c does not accurately reflect glycaemic status in certain conditions. Among patients with chronic kidney disease (CKD), erythrocyte lifespan is decreased by recent transfusions, and other alterations which lead to reduction in HbA1c levels. Hence sensitivity and specificity were very low for HbA1C. Hence HbA1C was not served as better predictor marker for T2DM – CKD- G5 on Haemodialysis. Serum Glycated Albumin is better marker for Type 2 CKD Grade5 on haemodialysis.

Table 1: Socio-demographic characteristics of the study participants (n=50)

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	Study group n (%)	Control group n (%)	p value
Age (mean ± SD) in years	52.16 ± 11.07	48.48 ±8.95	0.203
Gender			
Male	15 (60%)	12 (46%)	0.571
Female	10 (40%)	13 (54%)	

**** p value <0.05 was considered to be statistically significant***

Table 2: Biochemical parameters of the study participants (n=50)

**** p value <0.05 was considered to be statistically significant***

Biochemical parameters (mean ± SD)	Study group n (%)	Control group n (%)	p value
FPG (mg/dl)	147.44 ± 44.87	153.48 ± 33.92	0.594
Urea (mg/dl)	143.64 ± 43.28	109.24 ± 36.3	**0.001***
Creatinine (mg/dl)	9.52 ± 3.20	6.46 ± 1.45	**0.001***
Sr.Albumin (g/dl)	3.92 ± 0.74	3.70 ± 1.08	0.423
Hemoglobin (g/dl)	7.3 ± 1.28	8.22 ± 1.47	**0.031***
HbA1c (%)	6.7 ± 0.72	6.71 ± 0.79	0.985
Sr. Glycated Albumin (%)	29.7 ± 1.57	26.93 ± 1.57	**0.001***

Table 3: AUC for prediction of markers for T2DM –CKD- G5 on Hemodialysis

Test Result Variable(s)	Area	Std. Error	p value	95% Confidence Interval
HbA1c (%)	.501	.083	0.992	0.337 – 0.664
Serum glycated albumin (%)	.803	.066	0.001*	0.673 – 0.933

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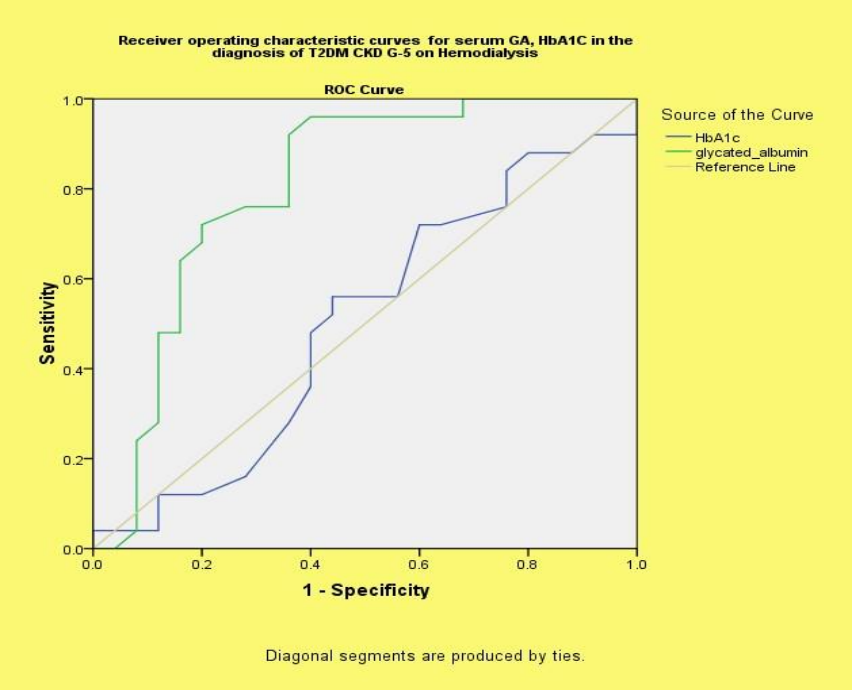

Figure 1: Receiver operating curve for HbA1c and Serum glycated albumin in the diagnosis of T2DM –CKD- G5 on Hemodialysis

DISCUSSION

Chronic kidney disease is associated with insulin resistance.Insulin degradation is seen in advanced stages of Chronic kidney disease.It is important to monitor the glycemic homeostasis in patients with Chronic kidney disease.But it was still found that HbA1C was the gold standard to monitor the glycemic index in the CKD .Many authors stated that HbA1c does not reflect the actural glycemic state in Diabetic patients in HD.Many studies have been done to evaluate the glycated albumin in CKD patients.

According to many studies the HbA1c level tends to decrease in CKD patients on HD which is due to significantly reduced lifespan of RBC which is 20-50% and hemoglobin turnover which is increased which leads to decreased exposure time to ambient glucose.Thus HbA1c is found to be decreased or lower in HD diabetes which suggest that HbA1c formation reduction in the Diabetes HD inspite of the elevated blood glucose level (16,17,18).

The study participants in the study group the mean age was 52.16 ± 11.07 years in cases and 48.48 ±8.95 years in controls.In Ahmed et al study the mean age of study participants in cases was 62.5 ± 5.1 wherea in control group it was 27.9 ± 5.4 which is lower than our study results. The gender distribution of the study participants showed that the study participants were predominantly male.In Ahmed et al study the female preponderance were more in both cases and control group.

The sensitivity and specificity of the Glycated albumin was found to be 84% and 64% with area under the curve was 0.8 which is statistically significant.Whereas in HbA1c the sensitivity was 56%,Specificity was 44% and area under the curve was 0.5.The discriminative power of the serum glycated albumin was found to be better than the Serum glycated Hemoglobin .In Ahmed et al study the sensitivity of GA was found to be 90.91%,Specificity 50% ,AUC 0.730 and

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optimal cutoff point was found to be >=2.0.Similarly the sensitivity of HbA1c was found to be 86.36%,Specificity 61.11% ,AUC was 0.768 and optimal cut off point was found to be>=4.6(19) Gan et at (20) in his study done in 2018 stated that hyperglycemia was underestimated in Advance CKD patients with Diabetes as HbA1c does not reflect the glycemic index accurately.Inba et al also stated that Low HbA1c was noted in CKD patients on HD who treated with Erythropoiten. Thus we know that increase in GS levels is found to be associated with increased oxidative stress, pro inflammatory responses and endothelial dysfunction. This clearly indicates that the GA plays a major role in the pathogenesis of the vascular complication in the Diabetes patients with End stage renal disease.

CONCLUSION & RECOMMENDATIONS

The glycated albumin (GA) is a test that reflects short-term glycemia and is not influenced by situations that falsely alter A1C levels. GA is the higher glycated portion of fructosamine. It is measured by a standardized enzymatic methodology, easy and fast to perform.GA can be used as a marker to assess the glycemic state in Type 2 Diabetes Mellitus patients with normal albumin excretion in urine or in microalbuminuria. Thus it can predict the microalbuminuria development in Type 2 Diabetes Mellitus in Diabetic HD patients .

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Conflict of interest: None declared

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