Determination of serum glycated albumin and high sensitivity C-reactive protein in the insight of cardiovascular complications in diabetic chronic kidney disease patients

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Abstract

Background: Left ventricular hypertrophy (LVH) has been proved as one among the cardiovascular complications and predominant in patients with CKD. In CKD patients, Glycated albumin (GA) express a superior marker of glycemic control than HbA1c. Nevertheless, the precision of GA for the prediction of cardiovascular diseases among the CKD population has been ineffectively reported. The present study looks at the part of GA, HbA1c in CKD to envisage vascular complications.

Materials and methods: One hundred and ninety-four patients were selected in the present study. The study has a control group (Group I, N: 52) and participants were divided into two groups based on vein diseases (Group II, N: 42; two vessels and group III, N: 100; triple vessel disease). Serum glycated albumin, hsCRP and other routine parameters were estimated in all the three groups. 2-dimensional echocardiography (2D Echo) has been done by a cardiologist to all the study patients for assessing ejection fraction and distinguish the sort of vessel diseases.

Results: Group I compared with group II and III shown there was a significant association among blood glucose, serum creatinine, HbA1c, mean blood glucose, GA, ejection fraction and hsCRP. Additionally, observed that increased levels of HbA1c, GA and creatinine inversely related to the left ventricle ejection fraction. Notwithstanding, GA and hsCRP predict precisely the left ventricle ejection fraction than different parameters.

Conclusion: GA alongside hsCRP might be appropriate markers for anticipating cardiovascular diseases particularly left ventricle hypertrophy in diabetic CKD population.

Keywords: CKD, glycemic control, Left Ventricular Hypertrophy, GA, HbA1c.

DOI: https://dx.doi.org/10.4314/ahs.v20i1.36

Cite as: Vijayaraghavan B, Padmanabhan G, Ramanathan K. Determination of serum glycated albumin and high sensitivity C-reactive protein in the insight of cardiovascular complications in diabetic chronic kidney disease patients. Afri Health Sci. 2020;20(1):308-13. https://dx.doi.org/10.4314/ahs.v20i1.36

Introduction

Cardiovascular disease (CVD) is the main life-threatening factor in chronic kidney disease (CKD).¹ LVH is the most proved indicator of cardiovascular mortality in CKD patients.² LVH has a frequency of almost 40% in patients with CKD, and it continuously raises with CKD until 75% in ESRD patients.³⁵ Numerous factors impact on the left ventricular structure in CKD patients. Unusual blood vessel stiffness and systolic hypertension contradicting left ventricular ejection cause a pressure afterload, with the development of concentric LVH.⁶

Population-based studies in Western and Asian nations have demonstrated that the risk of CVD increases as renal function declines. Based on this finding, the National Kidney foundation framed a team to elevate the perception of CVD in CKD, and characterized by CKD utilizing parameters, for example, diminished eGFR 60 ml/min/1.73 m².⁷ An accomplice of CKD patients treated by nephrologists is required to precisely investigate renal and CV events. Nevertheless, few studies have been di-
rected on the prevalence of left ventricular hypertrophy (LVH) in a predialysis population.8-11 However, there are restricted biomarkers accessible to assess the cardiovascular cause in CKD. Glycated albumin is the overwhelming circulatory Amadori-type glycated protein in vivo and plays a remarkable part in the advancement of diabetic vascular complications. Henceforth, this study was directed to study the association between the serum level of glycated albumin and the presence and seriousness of CVD in patients with diabetic CKD.

Materials and methods

Study Population
A total of 194 consecutive patients with diabetic CKD from a private nephrology outpatient clinic, Tiruchirappalli, India were included. Renal insufficiency was defined by serum creatinine concentration has been less than 1.5 mg/dl and if more than the cut-off considered as renal failure. DM was diagnosed using the American Diabetes Association criteria. Those with type 1 DM, acute coronary syndrome, previous myocardial infarction and other inflammation-related diseases were excepted from the study. The hospital's Ethics Committee has approved the procedure and all patients were given written informed consent prior to the study. 2-dimensional echocardiography was done by the same cardiologist to all the study patients.

Biochemical investigations
Blood samples were collected and serum concentrations of hemoglobin A1c (HbA1c), high sensitive C reactive protein (hsCRP), blood urea, creatinine, total protein, albumin, and globulin were assessed using standard methods. The serum glycated albumin level was measured with the improved bromocresol purple method using the Lucia TM glycated albumin-L assay kit (Asahi Kasei Pharma, Japan).

Statistical analysis
Statistical analysis was performed using Medcalc statistical software (Belgium). Data are presented as mean ± SD. Means ‘t’ test was used to test the relationship between the serum levels of glycated albumin and HbA1c and severity of vessel diseases and also with other parameters. A value of p<0.05 was considered statistically significant. Relative risk, odds ratio, and diagnostic sensitivity analyses were also performed.

Results
The study participants were divided into three groups (Group I: Control; Group II: Two vessel Disease; Group III: Triple vessel disease). 52 patients (Group I) considered as control; 42 patients (Group II) had two vessel disease and 100 patients (Group III) had triple vessel disease. The laboratory parameters of diabetic CKD patients with vessel diseases were compared with the control (Table 1). The control group compared with group II and III respect with age, blood urea, total protein, albumin, and globulin showed statistically not significant. Serum creatinine had shown a statistical significance when compared with controls in both groups (P<0.0001). Similarly, the blood glucose levels were also significant in both groups when compared with control (P<0.0001). The three months glycemic control marker HbA1c were compared control with group II (P=0.0041) and group III (P=0.0010) had shown statistically significant. Interestingly, the newly emerging glycemic marker glycated albumin showed a highly significant difference in both the groups (Group II: P= 0.0001, Group III: P< 0.0001) when compared with control. Also, GA had shown that it was more significant than the HbA1c. Similarly, ejection fraction was also significant in both the groups when compared with control (P< 0.0001). The one among available independent marker for inflammation high sensitive C reactive protein (hsCRP) has also shown significance with control in both the groups (P< 0.0001).
**Table 1. Basic laboratory parameters among groups**

|                          | Control N:52 | Group II N:42 | Group III N:100 |
|--------------------------|--------------|---------------|-----------------|
| **Age in years**         | 59.42±12.38  | 54.52±12.13   | 55.05±9.28      |
|                          | *P*=0.0573   | *P*=0.8074    | *P*=0.0555      |
| **Blood Urea mg/dl**     | 61.53±36.6   | 59.47±45.10   | 65.82±45.35     |
|                          | *P*=0.8074   | *P*=0.5565    |                 |
| **Serum Creatinine mg/dl** | 1.17±0.35 | 2.24±1.14     | 3.40±1.05       |
|                          | *P*<0.0001   | *P*<0.0001    |                 |
| **Blood glucose mg/dl**  | 113.96±28.36 | 234.70±62.73  | 359.45±104.83   |
|                          | *P*<0.0001   | *P*<0.0001    |                 |
| **Total Protein mg/dl**  | 6.91±0.78    | 6.94±1.09     | 6.86±0.83       |
|                          | 0.8769       | 0.7197        |                 |
| **Albumin mg/dl**        | 3.32±0.67    | 3.22±0.88     | 3.31±0.66       |
|                          | 0.5332       | 0.9299        |                 |
| **Globulin mg/dl**       | 3.62±0.44    | 3.71±0.47     | 3.53±0.52       |
|                          | 0.1431       | 0.2886        |                 |
| **HbA1c %**              | 7.08±0.17    | 9.24±3.20     | 10.37±2.48      |
|                          | *P*=0.0041   | *P*=0.0010    |                 |
| **MBG mg/dl**            | 167.78±51.13 | 219.64±134.92 | 356.49±89.35    |
|                          | *P*<0.0001   | *P*<0.0001    |                 |
| **Glycated Albumin (GA) %** | 23.59±7.48 | 26.64±6.04    | 34.08±10.61     |
|                          | *P*=0.0001   | *P*=0.0001    |                 |
| **Left ventricle ejection** | 73.96±6.44 | 51.29±19.02   | 45±12.63        |
| fraction %               | *P*<0.0001   | *P*<0.0001    |                 |
| **hsCRP μg/dl**          | 0.85±0.28    | 1.66±0.04     | 2.35±0.73       |
|                          | *P*<0.0001   | *P*<0.0001    |                 |

The development of triple vessel disease has 8.1 and two vessel diseases have 6.75 times higher than control (Table 2). The odds ratio showed that 4.51 times CVD risk as frequent in GA abnormal groups than the control group. Table 3 showed the sensitivity (95.59 %), specificity (82.76 %) and positive likelihood ratio, negative likelihood ratio and accuracy of GA.

The outcomes of the current study evidently showed that the creatinine, blood glucose, HbA1c, MBG, GA and hsCRP levels were significant and proportional to the vessel diseases. The ejection fraction has been significant and inversely proportional to the vessel disease. However, the overall results clearly demonstrated that GA and hsCRP have been highly significant with vessel disease when compared with other parameters.
Table 2. Relative risk analysis

|                  | Relative risk | 95 % CI       | Z statistic | Significance level |
|------------------|---------------|---------------|-------------|--------------------|
| Triple Vessel Disease | 8.1000        | 3.7986 to 17.2721 | 5.415       | P < 0.0001          |
| Two Vessel Disease  | 6.7500        | 3.1087 to 14.6564 | 4.827       | P < 0.0001          |

Table 3. GA-Diagnostic Test Evaluation

| Statistics            | Value     | 95% CI        |
|-----------------------|-----------|---------------|
| Sensitivity           | 95.59%    | 90.64% to 98.36% |
| Specificity           | 82.76 %   | 70.57% to 91.41%   |
| Positive Likelihood Ratio | 5.54    | 3.15 to 9.75     |
| Negative Likelihood Ratio | 0.05    | 0.02 to 0.12     |
| Accuracy              | 91.75%    | 86.95% to 95.21%   |

Discussion

Diabetes mellitus (DM) is one among the main foundation of CKD and is highly connected with cardiovascular morbidity and mortality. Levels of hemoglobin A1C (HbA1C) have been utilized rather than blood glucose levels to screen for DM in the general population since it is an effectively measured, long-term glycemic focus marker that is connected with clinical outcome. In the CKD population, HbA1C is a less unsurprising marker in light of the shorter red blood cell lifespan, utilization of erythropoietin infusions and vitamins C and E, and the existence of hypertriglyceridemia. Earlier studies uncovered that HbA1C levels have a tendency to be lower in patients with CKD; hence, glycated albumin (GA) levels might be a more reliable marker in patients with advanced renal dysfunction.

We assessed the association between GA and hsCRP levels and cardiovascular problems in CKD patients. As far as anyone is concerned, this might be the first kind of study to observe the association between GA and hsCRP in diabetic CKD patients. Cardiovascular Disease (CVD), the main source of death, is generally accelerated via cardio metabolic risk and CKD. CVD and kidney disease are firmly interrelated and dysfunction of one organ cause failure of the other, eventually prompting the failure of both organs. Patients with end-stage renal disease (ESRD) are at much higher risk of mortality because of CVD. There is restricted markers of accessible appreciation with CV diseases. However, a suitable marker could predict the two noteworthy diseases has not been accounted for. Consequently, it is imperative to recognize reasonable markers for CVD, in patients with diabetic CKD.

GA represents the biggest part of circulating glycated proteins (≈80% of aggregate) in-vivo. Late studies have shown that glycated albumin activates nuclear component κB and the extracellular signal-regulated kinases/c-Fos/initiating protein-1 pathway, prompting enlistment of monocyte chemoattractant protein-1 and interleukin-6 gene expression and incitement of cell multiplication and relocation. That recommends glycated albumin assumes an essential part of the event and acceleration of CVD in DM.

The present study observed that the GA levels increased when the ejection fraction decreases and also it increases based on the number of vessels having a block. This
may be due to the increased GA levels are connected with increased oxidative stress, impaired endothelial function, and pro-inflammatory responses suggesting that GA may contribute a role in the pathogenesis of vascular complications. This study emphasizes that GA may be a valuable CVD marker in patients with Diabetic CKD. The advancement of cardiovascular disease is connected with poor glycemic control as reflected by the high GA level. Our study also demonstrated that patients having poor glycemic control leads to the risk of developing CVD.

Previous studies have demonstrated that hsCRP elevation is connected with CVD in the healthy general population. As of late, CKD and high hsCRP were observed to be additively connected with a higher risk of CVD and observed to be independent indicators of cardiovascular events after acute coronary syndrome. The present study comes about likewise affirmed that HSCRP levels exceptionally connected with CVD in diabetic CKD. These findings proposed that high hs-CRP levels gave prognostic data about CVD in patients with diabetic CKD. HbA1c levels were connected with a higher prevalence of CKD and CVD cross-sectionally, paying little mind to diabetes status. The present study additionally affirms the same results. However, the significance level of its predictive power has been poor when compared with GA.

Conclusion
GA is accurate, sensitive and a good marker for predicting CVD risk in patients with diabetic CKD, in addition to serving as a glucose control index. Along with GA, hsCRP could also assist as a concomitant marker for diagnosis of CVD. High GA levels were associated with poor ejection fraction which helps us to identify the LVH status in diabetic CKD patients.

Data availability statement
The patient’s data used to support the findings of this study are available from the corresponding author upon request.

Funding Source
Nil (Self-funded).

Conflict of interest
The authors declare that there is no conflict of interest regarding the publication of this paper.

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