Diabetes & Metabolic Syndrome: Clinical Research & Reviews xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Glycated albumin and the risk of chronic kidney disease in subjects with Type 2 Diabetes: A study in North Indian Population

Alok Raghav[a], Jamal Ahmad[b,*], Saba Noor[b], Khursheed Alam[c], Brijesh Kumar Mishra[d]

[a] Biological Sciences and Bioengineering, Indian Institute of Technology, Kanpur, 208016, India
[b] Rajiv Gandhi Centre for Diabetes & Endocrinology, J.N Medical College, Aligarh Muslim University, Aligarh, India
[c] Department of Biochemistry, Faculty of Medicine, J.N Medical College, Aligarh Muslim University, Aligarh, India
[d] Department of Endocrinology and Metabolism, Guru Teg Bahadur Hospital, Dilshad Garden, New Delhi, Delhi, 110095, India

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Type 2 diabetes mellitus
Glycated albumin
Diabetic nephropathy

ABSTRACT

Aim: Glycated albumin (GA) suggested being alternative glycemic marker than haemoglobin A1C (HbA1c) in patients with chronic kidney diseases (CKD). We investigated the association between GA and the progression of diabetic nephropathy (DN) in T2DM subjects.
Methods: We recruited T2DM subjects with different stages of CKD who had regularly measured serum creatinine and estimated glomerular filtration rates (eGFR) according to Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, HbA1c consecutively every 3 months along with GA levels and other anthropometric and demographic measurements. We grouped age and sex matched subjects into the CKD progression, Group I healthy subjects (n = 100, M: F;50:50). Group II T2DM subjects with eGFR $\geq$90 mL/min (n = 167, M:F; 76:91). Group III of T2DM patients with eGFR 60–89 mL/min (n = 91, M:F; 44:47). Group IV T2DM subjects with eGFR 30–59 mL/min (n = 68, M:F;31:37). Group V T2DM with eGFR $\leq$ 29 mL/min (n = 21, M:F; 13:8).
Results: Pearson's correlation analysis between glycated albumin and biochemical parameters were established in all subjects. GA/HbA1c ratio increases with poor glycemic control except for nephrosis state.
Conclusion: Mean GA levels were more closely associated with DN progression than mean HbA1c in subjects with T2DM and can be implemented as an alternative diagnostic marker in nephropathy.

1. Introduction

Diabetes nephropathy progressively affecting up to a third of patients with diabetes mellitus leading to a severe cause of end-stage renal disease (ESRD) worldwide. According to a recent study by Vohra et al., 40% of patients needs renal replacement therapy having diabetes mellitus (DM) (Vora et al., [1]). In the year 2001, 11, 000 diabetes mellitus patients with DM in the UK were on long-term renal replacement [1]. Consistently increased urinary albumin excretion in patients with T2DM has been shown to be the marker of early development of nephropathy complications [2]. DM patients with microalbuminuria showed a significant decrease in renal function with average annual fall of 5.3 mL/min in eGFR compared to healthy (0.2 mL/min) subjects [3]. Reporting of abnormal eGFR in DM complications showed increased risk of mortality in such subjects [4]. GA/HbA1c ratio variation in DM complications provides an alternate marker for renal dysfunction though abnormal eGFR is a reliable marker for clinical conclusions in renal disorder in 40% DM patients with CKD [5,6]. There are several possible hypothesis and explanation accounting for these abnormalities in eGFR and glycated albumin with increased albumin excretion rate. Primarily the progression of various CKD stages in DM subjects is heterogeneous and also the abnormal renal function is associated with increased albumin excretion rate and GA/HbA1c ratio [5,7]. Vascular and tubulointerstitial morphology can be affected in DM patients leading to abnormal eGFR values.

The American Diabetes Association (ADA) recommends the routine screening to DM subjects with progressive diabetic nephropathy and CKD [2]. The most widely accepted guidelines of National Kidney Foundation were implicating in measuring eGFR and stages of CKD using serum creatinine values in DM

* Corresponding author.
E-mail address: jamalahmad11@rediffmail.com (J. Ahmad).

https://doi.org/10.1016/j.dsx.2018.01.005
1871-4021/

patients [8]. The hypothesis of estimating GA in assessing short-term glycemic control in DM subjects with CKD complications and abnormal eGFR provides essential information for renal dysfunction. Previous literature on the efficacy of HbA1c in assessing renal dysfunction in CKD complications showed a reliable statement in clinical diagnosis with limitations worldwide [9–11]. Glycation is a continuously occurring process in DM targeting haemoglobin and serum proteins. Glycated albumin provides a short-term glycemic control due its turnover period of 15–20 days than haemoglobin (120 days) [12–14]. Glycation of proteins mainly albumin impairs the renal permeabilities of glomerular capillary walls in-turn affecting the glomerular filtration barrier into the mesangial spaces thereby making renal dysfunction in DM patients with CKD [15,16].

Referring to the data from the UKPDS published by Adler et al. in 2003 reported that there is 2.0% yearly progression of micro-albuminuria from the initial diagnosis of DM, from micro-albuminuria to macroalbuminuria 2.8%, and from macroalbuminuria to increased serum creatinine values or renal replacement therapy 2.3% [17]. Progression prevalence of micro-albuminuria and macroalbuminuria in T2DM during 10 years was found to be 24.9% and 5.3% respectively [17]. Strict glycemic control has been shown to outcomes from diabetic nephropathy. Studies have demonstrated the correlation of HbA1c with fructosamine and GA as an alternative medium for measuring the glycemic index, particularly in adverse conditions when the HbA1c diagnosis is unreliable [18]. The main reason for limiting the use of fructosamine and GA as the alternate glycemic marker is the lack of clinical trials and studies establishing their role apart from HbA1c. Plenty of the clinical studies and research have focused on establishing HbA1c as a reliable glycemic marker and scanty of data for GA as an alternate marker in assessing glycemic control in DM remains to be ascertained. Although self-monitoring of blood glucose (SMBG) coupled with glycated haemoglobin (HbA1c) to assess the progression of CKD in DM plays an important role but there are evidence increasing for the implication of GA for prediction of diabetic complications at early stages of CKD in T2DM. This study was planned to establish GA cut off value and GA/HbA1c ratio in DM subjects at different stages of CKD in North Indian Population.

2. Subjects and research design

In this study, we recruited 355 subjects with T2DM who were registered at tertiary care centre of North India, Rajiv Gandhi Centre for Diabetes & Endocrinology, J.N Medical College, Aligarh Muslim University, Aligarh, India. Age and sex-matched non-diabetic healthy subjects (N = 100) were served as control subjects who were the attendants of DM patients recruited in this study. Written informed consent from each recruited subjects was obtained post explanation of the study objectives and procedures. The study was approved by Institutional Human Ethics committee of J. N Medical College, Faculty of Medicine, Aligarh Muslim University, Aligarh, India. We implicated following inclusion criteria:1) patients who were regularly visiting the diabetic centre and have kidney function eGFR recorded using serum creatinine; and 2) patients who tested for HbA1c and GA values consecutively every 3 or 6 months. The exclusion criteria for this study were patients with end-stage renal disease (ESRD) on dialysis, T1DM, gestational diabetes (GDM), liver disorders, acute infectious disease.

2.1. Ethics statement

The study protocol was approved by the Institutional Ethics Committee, Faculty of Medicine, J.N Medical College, Aligarh Muslim University, India (Certificate approval No. 1894/FM) (Govt. of India). The experimental procedure performed on human subjects in accordance with guidelines and regulation of Institutional Ethics Committee, Faculty of Medicine, J.N Medical College, Aligarh Muslim University, India. Each subject was informed about

Table 1
Clinical characteristics of the study subjects stage wise as per KDOQI guidelines.

Variable	Healthy subjects Group I	eGFR ≥90 mL/min Group II	eGFR 60–89 mL/min Group III	eGFR 30–59 mL/min Group IV	eGFR ≤29 mL/min Group V	P value[a] ANOVA between groups
N	100	167	91	68	21	–
M:F	50:50	76:91	44:47	31:37	13:8	–
Age (Years)	49 + 14.65	47.37 + 9.57 (0.2727)	49.79 + 1.89 (0.6103)	53.25 + 9.60 (0.0369)	58.00 + 7.8 (0.073)	.0539
DM Duration (years)	–	7.12 ± 4.16	7.70 ± 4.68#	8.15 ± 5.20$	8.91 + 2.28@	.9588
BMI (kg/m^2)	21.8 ± 2.94	25.22 + 7.65*	27.80 + 9.46#	27.1 + 4.12$	29.73 + 3.63@	<.001
SBP mm of Hg	118.5 ± 5.30	136.9 ± 8.22*	158.7 + 6.35#	161.3 ± 9.52$	171.8 + 8.63@	<.001
DBP mm of Hg	81.1 ± 1.9	87.37 ± 4.66*	94.1 ± 3.90#	96.2 ± 5.10$	99.4 + 6.12@	<.001
Fasting Glucose(mg/dL)	99.2 ± 19.52	115.3 + 28.05*	125.65 + 5.27#	137.21 + 42.14$	142.35 + 50.27@	<.001
PP Glucose(mg/dL)	102.43 + 33.14	188.57 + 71.29*	201.2 ± 28.3#	211.74 + 81.73$	241.00 + 78.90@	<.001
Serum Creatinine (mg/dL)	0.811 ± 0.05	1.02 ± 0.08*	1.32 ± 0.05#	3.57 ± 0.92$	4.83 ± 0.85@	<.001
HDL (mg/dL)	42.42 ± 4.87	45.84 ± 4.65*	47.20 ± 2.10#	51.74 ± 4.35$	55.15 ± 5.44@	<.001
LDL (mg/dL)	71.30 ± 3.33	86.56 ± 9.32*	91.54 ± 6.23#	95.33 ± 4.11$	98.71 ± 6.36@	<.001
VLDL (mg/dL)	28.06 ± 1.63	31.23 ± 2.99*	33.70 ± 3.65#	35.66 ± 2.74$	38.11 ± 6.32@	<.001
HbA1c (%)	4.95 ± 0.78	6.26 ± 2.02*	8.02 ± 1.90#	8.73 ± 2.21$	9.71 ± 2.95@	<.001
GA%	14.2 ± 2.25	24.53 ± 9.00*	28.23 ± 8.51#	29.66 ± 7.23$	21.65 ± 6.52@	<.001
GA/HbA1c ratio	2.86 ± 0.46	3.91 ± 0.66*	3.51 ± 0.26#	3.39 ± 0.45$	2.22 ± 0.53@	<.001
Fructosamine (nmol/mg)	256 ± 12.36	294 ± 8.45*	323 ± 7.65#	358 ± 9.54$	405 ± 21.36@	<.001
Diabetic complications Values are n (%)						
Retinopathy	–	88 (52.6)	50 (54.94)	40 (58.8)	17 (80.9)	–
Neuropathy	–	27 (16.6)	19 (20.8)	18 (26.4)	08 (38.0)	–
PVD	–	68 (40.7)	41 (45.0)	36 (54.0)	14 (66.6)	–
HTN	–	121 (72.4)	71 (78.0)	59 (86.0)	21 (100)	–

Variables are presented as mean ± SD. The * represents significant p < .0001 in Group II v/s Group I The # represents significant p < .0001 in Group III v/s Group I The $ represents significant p < .0001 in Group IV v/s Group I The @ represents significant p < .0001 in Group V v/s Group I.

Please cite this article in press as: A. Raghav, et al., Glycated albumin and the risk of chronic kidney disease in subjects with Type 2 Diabetes: A study in North Indian Population, Diab Met Syndr: Clin Res Rev (2018), https://doi.org/10.1016/j.dsx.2018.01.005