Original Article

Comparative Study between Available Laboratory Techniques for Monitoring Blood Sugar Control in Diabetic Patients with Proteinuric Diabetic Nephropathy

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Abstract

Background: Strict glycemic control in patients with diabetes decreases the incidence of diabetic complications, which can determine the quality of life and prognosis of such patients, so we attempted to compare the available laboratory techniques: glycated albumin and glycated hemoglobin with SMBG as a gold standard in monitoring the control of diabetic state in proteinuric diabetic kidney disease patients. **Patients & Methods**: This study included 60 type 2 diabetic patients classified to two groups (group I: 30 patients with different grades of albuminuria A2/A3 and group II: 30 patients without albuminuria A1) All participants were subjected to history taking, full clinical examination and routine investigations. 7-point SMBG regimen, testing blood glucose before and after each of the three meals and at bedtime over the course of 3 days was taken every month for 4 months. HbA1c was done by HPLC technique after 2 months from the beginning of the study and at the end of the study. Glycated albumin was done by turbidimetric immunoassay every 5 weeks.**Results**: There was a positive significant correlation between **glycated albumin** and **ACR** among the proteinuric group. There was a positive correlation between **SMBG** and **HbA1c** among the two groups of the study. There was a positive correlation between **HbA1c** and **eGFR. Conclusion:** HbA1c is affected by eGFR and renal function while glycated albumin is affected by the levels of ACR and proteinuria, so combined assessment of HbA1c and glycated albumin may be useful for glycemic evaluation in DKD patients.

Introduction

Diabetes mellitus (DM) is characterized by occurrence of microvascular (nephropathy, retinopathy and neuropathy) and macrovascular (atherosclerotic cardiovascular) complications.(1) Diabetic kidney disease (DKD) is considered as one of the major micro-vascular problems of diabetes mellitus and has become the most general single cause of end-stage kidney disease. One of the earliest changes of renal function in diabetes is an increase in GFR, or hyperfiltration, which is observed in patients with type 1 as well as in many patients with type 2diabetes and is accompanied by an increase in renal size. The next observable change is the development of albuminuria. (2)

Strict glycemic control in patients with DM decreases the incidence of diabetic complications, which can determine the quality of life and prognosis of such patients. (3) There are many markers to be used to assess glycemic states in diabetic patients. (4)The International Diabetes Federation (IDF) recommends SMBG for achieving glycemic goals. (5) HbA1c is affected by a number of factors including uremia, anemia of multifactorial etiology, decreased levels of erythropoietin, and decrease in RBCs survival. CKD patients frequently receive erythropoietin, with the expectation of an increase in the production of RBCs and which may lead to an erroneous low HbA1C value. (6)

Glycated albumin, because of its shorter half-life (21 days) compared with glycated hemoglobin, could be used as a shorter-term glycemic control for diabetes. Glycated albumin could be influenced by many conditions, such as thyroid dysfunction, nephrotic syndrome and liver cirrhosis. Therefore a combined detection of HbA1C and glycated albumin may improve the efficacy of diagnosis and improvement of a novel therapeutic potential. Therefore we attempted to compare the available laboratory techniques: glycated albumin and glycated hemoglobin with SMBG as a gold standard in monitoring the control of diabetic state in proteinuric diabetic kidney disease patients. [7]

Patients & Methods

This study was composed of 60 type2 diabetic patients classified into two groups: Group I: 30 patients with different grades of albuminuria A2/A3 and Group II: 30 patients without albuminuria A1. All patients provided written informed consent before participation in this study.

Exclusion criteria:

Patients with known thyroid diseases, liver diseases, malignancy, alcoholic patients, patients on corticosteroid therapy, patients with other causes of anemia rather than diabetic kidney diseases including history of blood loss and history of blood transfusion four months before the study and patients with active inflammatory state were all excluded from the study.

Methods

All patients in the study were subjected to: a full history taking stressing on: duration of DM, management of DM, complication of DM (hypoglycemia, hyperglycemia, microvascular and macrovascular complications), history of any renal diseases (urinary tract infection, stones, and hematuria), history of thyroid diseases, history of recent excessive alcohol intake, history of recent steroid therapy and history of hepatic symptoms. Full clinical examination stressing on, Puffiness of eyelids, ascites and lower limb edema. laboratory investigations were done including; complete urine analysis, urinary albumin /creatinine ratio, serum urea and serum creatinine, estimated GFR (eGFR)byMDRDequation,serum.cholesterol,.triglycerides,.HDL.cholesterol.and LDL cholesterol, complete blood picture, serum uric acid, liver function tests (serum albumin, alanine transaminase, aspartate transaminase.), lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum TSH.

7-point SMBG regimen, testing blood glucose before and after each of the three meals and at bedtime over the course of 3 days was done every month for 4 months.

HbA1c was done by HPLC technique after 2 months from the beginning of the study and at the end of the study.

Glycated albumin was done by turbidimetric immunoassay every 5 weeks.

Results

The study included 60 patients with type 2 diabetes mellitus. The patients were divided into 30 patients with albuminuria and 30 patients without albumniuria. Demographic, anthropometric, and laboratory parameteters among studied groups are summarized in table I

As illustrated in table II , there was no statistically significant difference in SMBG levels and HbA1c levels between the two groups

Table III and IV showed correlations between different parameters among the two groups of the study.

Table (I): Comparisons between the two studied groups regarding to demographic, anthropometric and laboratory parameters.

	Group I (n = 30)	**Group II (n = 30)**	**p**
Sex Male Female	14(46.7%) 16(53.3%)	13(43.3%) 17(56.7%)	0.795
Age	60.83 ± 8.99	54.57 ± 12.75	0.032*
CKD	8(26.7%)	0(0.0%)	FEp=0.005*
DR	25(83.3%)	4(13.3%)	<0.001*
Neuropathy	17(56.7%)	13(43.3%)	0.302
Hypertension	24(80.0%)	16(53.3%)	0.028*
Cardiac complication	11(36.7%)	7(23.3%)	0.260
History of DFI	1(3.3%)	0(0.0%)	FEp=1.000
PVD	0(0.0%)	1(3.3%)	FEp=1.000
ACR	1037.50 ± 1053.42	20.04 ± 8.58	<0.001*
Cholesterol	215.13 ± 58.78	207.17 ± 43.29	0.553
TG	146.27 ± 49.08	133.57 ± 42.40	0.288
HDL	37.10 ± 6.55	44.43 ± 10.35	0.002*
LDL	98.97 ± 13.82	88.27 ± 13.11	0.003*
S. albumin	3.93 ± 0.40	4.08 ± 0.23	0.076

Table (II):Comparisons between the two studied groups regarding to mean of SMBG, mean of HbA1c

	Group I (n = 30)	**Group II (n = 30)**	**p**
SMBG	176.3 ± 53.08	207.5 ± 64.94	0.058
HbA1c	7.76 ± 1.60	8.34 ± 1.83	0.198

Table (III): Correlations between different parameters in group I

Group I	R	p
SMBG & diastolic BP	0.396*	0.030*
HbA1c& eGFR	0.378*	0.040*
GA & ACR	0.497	0.005*
GA & albumin	–0.574	<0.001*
GA & weight	–0.485*	0.007*
Cr& TG	0.362*	0.050*
eGFR & LDL	–0.408*	0.025*
TG & pulse	0.373*	0.043*
HDL & diastolic BP	0.425*	0.019*
Cholesterol & systolic BP	–0.424*	0.020*
Diastolic BP & albumin	0.384*	0.036*
Weight & CRP	0.419*	0.021*

Table (IV): Correlations between different parameters in group II

Group II	R	p
SMBG & cholesterol	0.659*	<0.001*
HbA1c & cholesterol	0.648*	<0.001*
HbA1c & Urea	–0.384*	0.036*
HbA1c &S.cr	–0.434*	0.017*
HbA1c &TG	0.454*	0.012*
eGFR & systolic BP	–0.447*	0.013*
Cholesterol & albumin	–0.525*	0.003*

Discussion

Diabetes Mellitus (DM) is not a single disease, but a syndrome characterized by hyperglycemia that result from defects in insulin secretion or insulin sensitivity in target tissues or both.Diabetic kidney disease (DKD) is one of the most serious microvascular complications, which significantly impacts morbidity, mortality and quality of life

Today, SMBG is considered an important aspect of the management of glycemic Control. SMBG is widely and routinely applied in large clinical trials, where it is used to understand the glycemic state HbA1c is the most widely used and accepted test for monitoring glycemic control in individuals with diabetes. HbA1c is affected by a number of genetic, hematologic, and illness-related factors.

Serum glycated albumin (GA) was hypothesized to be an alternative marker for glycemic control in patients with diabetes, as it not affected by changes in the survival time of erythrocytes in case of type 2 diabetes with hemoglobinopathies

Thus, this prospective study aimed to compare the available laboratory techniques: glycated

albumin and glycated hemoglobin with SMBG as a gold standard in monitoring the control of diabetic state in proteinuric diabetic kidney disease patients.

In the present study, there was a positive significant correlation between glycated albumin and ACR and a negative significant correlation between glycated albumin and S. albumin among the proteinuric group. The results of the present study also showed no significant correlation between glycated albumin and ACR among the non proteinuric group which coincides with results of Viswanathan V et al. [8] Okada et al [9] disagree with our results, as they found negative correlation between glycated albumin and ACR in the nephrotic range of proteinuria only, with no relation between GA and ACR among non-nephrotic range of proteinuria. Also Inaba et al [10] found negative significant correlation between glycated albumin and serum albumin.

Also In the present study, there was no significant association between GA and eGFR in both the two groups of the study, which can be interpreted by the fact that GA may not be influenced by renal function and so glycated albumin might be a better marker of glycemic assessment in advanced CKD. This result coincides with results of Okada et al. [9]

In the present study, it has been found a positive correlation between eGFR and HbA1c among proteinuric group and a negative correlation between HbA1c and B. urea and S. creatinine among non proteinuric group which coincides with the results of Paisey R et al. [11]

There was significant difference between the two studied groups as regards the age (p=0.032). Proteinuric patients were older than non proteinuric one. This result was supported by Thakkar et al. [12] In the present study, there was a significantly increased prevalence of hypertension in the proteinuric group compared to the non proteinuric group. Also we found a positive correlation between diastolic blood pressure and level of HDL, albumin and mean of SMBG. Finally there was negative correlation between systolic blood pressure and both of cholesterol and eGFR. These findings were supported by many studies including Bonaa KH et al, Ahbap E et al. [13, 14]

In the present study and during evaluation of lipids profile, we found numerous findings. Firstly, we found a statistically significant differences between the two studied groups regarding HDL-C and LDL-C. LDL-C was higher in the proteinuric group than in non the proteinuric group but HDL-C was higher in non the proteinuric group than in the proteinuric group.

Secondly, in the proteinuric group we found a positive correlation between S. creatinine and TG, a positive correlation between heart rate and TG, a negative correlation between LDL and eGFR among the proteinuric group.

Finally, in the non proteinuric group, we found a positive correlation between cholesterol and both of SMBG and HbA1c, a positive correlation between hemoglobin and TG and a negative correlation between cholesterol and S.albumin. These results agree with a lot of studies such as Palazhy S et al and Al Jameil N et al. [15, 16]

In the present study, we found a positive correlation between weight and CRP and a negative correlation between weight and glycated albumin among the proteinuric group. These results coincide with the result of Okada et al, Miyashita et al. [17]

Conclusion

HbA1c is affected by eGFR and renal function while glycated albumin is affected by the levels of ACR and proteinuria, so combined assessment of HbA1c and glycated albumin may be useful for glycemic evaluation in DKD patients.

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