ONLINE LETTERS

## **OBSERVATIONS**

## The Ratio of Glycosylated Albumin to Glycosylated Hemoglobin Differs Between Type 2 Diabetic Patients With Low Normoalbuminuria and Those With High Normoalbuminuria or Microalbuminuria

lycosylated albumin (GA) stands as an alternative glycemic marker when glycosylated hemoglobin measurements exhibit abnormal values owing to the various complications affecting the life span of erythrocytes (1). However, GA is affected in patients with albumin metabolism disorders such as nephrotic syndrome, liver cirrhosis, and

thyroid disorders (2). Moreover, there are several reports on the renal handling of GA in diabetic nephropathy (3–5). The stage of diabetic nephropathy may affect the GA/A1C ratio. In this study, we examined the effect of the urinary albumin-to-creatinine ratio (UACR) on GA/A1C in type 2 diabetic patients with normoalbuminuria or microalbuminuria.

This was a cross-sectional study. A total group of 835 patients with type 2 diabetes was divided into four groups according to their UACR, as follows: the low-normoalbuminuria group consisted of 261 patients with <15 mg/g creatinine; the high-normoalbuminuria group consisted of 143 patients with 15–29 mg/g creatinine; the low-microalbuminuria group consisted of 343 patients with 30–149 mg/g creatinine; and the high-microalbuminuria group consisted of 88 patients with 150–299 mg/g creatinine. The GA/A1C ratio and the correlation between GA and A1C were compared among the four groups.

Table 1 shows the clinical characteristics of those patients categorized into the four groups according to the UACR. The GA/A1C ratio of low-normoalbuminuria patients  $(2.8 \pm 0.4)$  was significantly lower than those of other groups (highnormoalbuminuria group  $2.9 \pm 0.4$ ;

low-microalbuminuria group  $2.9 \pm 0.4$ ; high-microalbuminuria group  $3.0 \pm 0.3$ ). A positive association between GA and A1C was found in each UACR group (lownormoalbuminuria group r = 0.696, P < 0.001; high-normoalbuminuria group r = 0.658, P < 0.001; low-microalbuminuria group r = 0.794, P < 0.001; highmicroalbuminuria group r = 0.916, P <0.001). The correlation coefficient between GA and A1C was significantly higher in highmicroalbuminuria group than in the other groups (low-normoalbuminuria group P < 0.001; high-normoalbuminuria group P < 0.001; low-microalbuminuria group P < 0.001).

Ghiggeri et al. (3) classified type 1 diabetic patients on the basis of the urinary albumin excretion rates of 15 and 150 mg/day, whereas Cha et al. (4) classified type 2 diabetic patients with normoalbuminuria into two subgroups of high and low albumin excretion. They demonstrated that the renal selectivity for GA, which was calculated from the ratio of the urinary to serum levels of GA, was inversely correlated with albumin clearance (3) or UACR (4). On the basis of these findings, we divided patients with normoalbuminuria or microalbuminuria into four groups of UACR: <15, 15–29,

Table 1—Clinical parameters in each UACR group

Characteristics	Low-normoalbuminuria group ( $n = 261$ )	High-normoalbuminuria group ( $n = 143$ )	Low-microalbuminuria group ( $n = 343$ )	High-microalbuminuria group ( $n = 88$ )	P value
Sex, n (male/female)	168/93	78/65	197/146	64/24*	0.014
Age (years)	$62.9 \pm 11.4$	$65.8 \pm 10.3 \dagger$	$68.2 \pm 10.5 \dagger$	$65.9 \pm 11.8$	< 0.001
Duration of diabetes (years)	$9.9 \pm 6.3$	$11.3 \pm 8.5$	$12.6 \pm 8.1 $	$14.8 \pm 8.7 $ ‡,§	< 0.001
BMI (kg/m <sup>2</sup> )	$25.2 \pm 4.1$	$24.0 \pm 4.0 \dagger$	$24.6 \pm 3.7$	$24.4 \pm 3.1$	0.042
Systolic BP (mmHg)	$129 \pm 18$	$130 \pm 18$	$132 \pm 18$	$135 \pm 19 \dagger$	0.017
Diastolic BP (mmHg)	$75 \pm 12$	$72 \pm 12$	$73 \pm 11$	$73 \pm 11$	0.138
UACR (mg/g creatinine)	$8.5 \pm 3.4$	$21.5 \pm 4.3 $ ‡	$73.8 \pm 32.9 $ †,	$213.2 \pm 43.1 $ ‡,  ,¶	< 0.001
Serum creatinine (mg/dL)	$0.76 \pm 0.17$	$0.76 \pm 0.20$	$0.82 \pm 0.20 \#$	$0.87 \pm 0.22 $	< 0.001
$eGFR (mL/min/1.73 m^2)$	$75.5 \pm 17.0$	$74.2 \pm 20.9$	$68.2 \pm 18.7$ ‡,§	$68.4 \pm 20.9 \dagger$	< 0.001
A1C (%)	$7.2 \pm 0.9$	$7.1 \pm 0.8$	$7.6 \pm 1.1 $ ,	7.8 ± 1.6#,**	< 0.001
Hb (g/dL)	$14.0 \pm 1.3$	$13.7 \pm 1.5$	$13.5 \pm 1.4 \ddagger$	$13.8 \pm 1.5$	< 0.001
GA (%)	$20.1 \pm 3.6$	$20.9 \pm 3.9$	$22.2 \pm 4.7 $ ‡,§	$23.5 \pm 6.5 \stackrel{*}{,} **$	< 0.001
Serum albumin (g/dL)	$4.2 \pm 0.3$	$4.3 \pm 0.3$	$4.2 \pm 0.3$	$4.1 \pm 0.3 \dagger, 8$	0.015
GA/A1C ratio	$2.8 \pm 0.4$	$2.9 \pm 0.4$ #	$2.9 \pm 0.4 \#$	$3.0 \pm 0.3 $ ‡	< 0.001
Treatment of diabetes					0.005
Diet	32* (12.3)	10 (7.0)	19* (5.5)	5 (5.7)	
OHA and/or GLP-1RA	172 (65.9)	96 (67.1)	217 (63.3)	50 (56.8)	
Insulin	57* (21.8)	37 (25.9)	107 (31.2)	33* (37.5)	

Data are expressed as n (%) or mean  $\pm$  SD unless otherwise stated. Low-normoalbuminuria group, UACR <15 mg/g creatinine; high-normoalbuminuria group, UACR 15–29 mg/g creatinine; low-microalbuminuria group, UACR 30–149 mg/g creatinine; high-microalbuminuria group, UACR 150–299 mg/g creatinine; BP, blood pressure; Hb, hemoglobin; OHA, oral hypoglycemic agent; GLP-1RA, glucagon-like peptide-1 receptor agonist; eGFR, estimated glomerular filtration rate. \*Absolute value of adjusted residual >1.96. †P < 0.05 vs. low-normoalbuminuria group. †P < 0.001 vs. low-normoalbuminuria group. P < 0.001 vs. low-normoalbuminuria group. P < 0.01 vs. low-normoalbuminuria group. P < 0.01 vs. low-normoalbuminuria group. P < 0.01 vs. high-normoalbuminuria group.

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30-149, and 150-299 mg/g creatinine. We found that the coefficient correlation between GA and A1C as well as the GA/A1C ratio were higher in high-microalbuminuria patients than in low-normoalbuminuria patients. In those patients with a UACR <15 mg/g creatinine, the urinary excretion rate of GA appears to be high and the GA/A1C ratio may be low. In those patients with an UACR > 150 mg/g creatinine, the urinary excretion rate of GA appears to be low and the GA/A1C ratio may be high. The GA/A1C ratio and the correlation coefficient between GA and A1C appear to vary according to the UACR. To make accurate conversions between GA and A1C values, the UACR should be taken into account.

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