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Comparison of glycated albumin and hemoglobin A_{1c} levels in diabetic subjects on hemodialysis

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Glycated albumin is thought to more accurately reflect glycemic control in diabetic hemodialysis patients than hemoglobin A_{1c} because of shortened red cell survival. To test this, glycated hemoglobin and albumin levels were measured in blood samples collected from 307 diabetic subjects of whom 258 were on hemodialysis and 49 were without overt renal disease. In diabetic subjects with renal disease, relative to those without, the mean serum glucose and glycated albumin concentrations were significantly higher while hemoglobin A_{1c} tended to be lower. The glycated albumin to hemoglobin A_{1c} ratio was significantly increased in dialysis patients compared with the controls. Hemoglobin A_{1c} was positively associated with hemoglobin and negatively associated with the erythropoietin dose in hemodialysis patients, whereas these factors and serum albumin did not significantly impact glycated albumin levels. Using best-fit multivariate models, dialysis status significantly impacted hemoglobin A_{1c} levels without a significant effect on glycated albumin. Our results show that in diabetic hemodialysis patients, hemoglobin A_{1c} levels significantly underestimate glycemic control while those of glycated albumin more accurately reflect this control.

Kidney International (2008) **73,** 1062–1068; doi:10.1038/ki.2008.25; published online 20 February 2008

KEYWORDS: diabetes mellitus; end-stage renal disease; glycated albumin; glycemic control; hemodialysis; hemoglobin A_{1c}

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Received 11 September 2007; revised 29 October 2007; accepted 4 December 2007; published online 20 February 2008

The vascular complications of diabetes mellitus, including kidney disease, heart attack, and stroke are increasing rapidly throughout the world.[1] Diabetic nephropathy now accounts for nearly 50% of incident dialysis patients in the United States, and cardiovascular disease is the leading cause of death.[2] It is important to control conventional atherosclerotic risk factors in diabetic dialysis patients, including blood glucose, hypertension, hyperlipidemia, and smoking to reduce cardiovascular disease events.

Several clinical tests are useful for measuring long-term glycemic control in the general diabetic population. These same tests are routinely performed in diabetic subjects with chronic kidney disease and end-stage renal disease (ESRD); however, their accuracy in these patients has not been rigorously tested.[3] Hemoglobin A_{1c} (HbA_{1c}), the most widely used assay, measures the percentage of circulating hemoglobin that has chemically reacted with glucose and reflects ambient blood glucose control over the prior 120 days, with the most profound effect in the preceding 30 days.[3,4] Factors that shorten red blood cell (RBC) survival, including severe nephropathy, may reduce HbA_{1c} since the time necessary for glucose to chemically bond with RBCs decreases.[5] If this significantly impacts HbA_{1c}, dialysis patients and clinicians would be falsely comforted by relatively low HbA_{1c} values despite high risk for subsequent cardiovascular disease and infectious complications. Previous studies attempting to address this concern were underpowered.[6,7]

Inaba *et al.*[8] determined that HbA_{1c} underestimated long-term glycemic control in dialysis patients with diabetes, after comparing the mean of random blood glucose concentrations, HbA_{1c}, and percentage of glycated albumin (% GA). They found that the % GA assay provided a more accurate assessment of glycemic control among Japanese hemodialysis patients. The current study attempted to validate this clinically important result and extend its application to other ethnic groups.

RESULTS

Simultaneous blood samples were collected from 307 diabetic patients, 258 were receiving chronic hemodialysis treatments

Table 1 | Demographic and clinical characteristics of study population

Variable	Diabetic ESRD (*N*=258)	Diabetes, no nephropathy (*N*=49)	*P*-value
Age, years	63.2 (12.0)	59.1 (13.8)	0.060
DM duration, years	19.1 (10.8)	11.8 (8.4)	<0.0001
% male	53.1	40.8	0.115
% African American	63.6	32.7	<0.001
Height, inch	67.3 (4.0)	67.3 (3.8)	0.93
Weight, lb	189.7 (48.8)	237.3 (63.7)	0.007
% DM type 2	93.8	93.9	0.983
% ACEi/ARB	50.0	81.4	0.001
% current/former smokers	43.2	47.9	0.545
% transfused prior 90 days	7.0	0	0.089
Serum creatinine, mg per 100 ml	NA	1.0 (0.3)	—
Serum glucose, mg per 100 ml	172 (62)	146 (66)	0.024
Glycated albumin, g per 100 ml	0.69 (0.28)	0.62 (0.24)	0.071
Serum albumin, g per 100 ml	3.7 (0.4)	4.0 (0.6)	0.012
% glycated albumin	18.7 (7.3)	15.3 (5.5)	0.002
Hemoglobin, g per 100 ml	11.8 (1.1)	12.7 (1.8)	0.058
HbA_{1c}, %	6.8 (1.6)	7.3 (1.4)	0.058
% GA/HbA_{1c}	2.72 (0.6)	2.07 (0.5)	0.0001
Erythropoietin dose, U week^{-1}	22 876 (20 579)	NA	—

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DM, diabetes mellitus; ESRD, end-stage renal disease; HbA_{1c}, hemoglobin A_{1c}; NA, not applicable; % GA, percentage of glycated albumin.

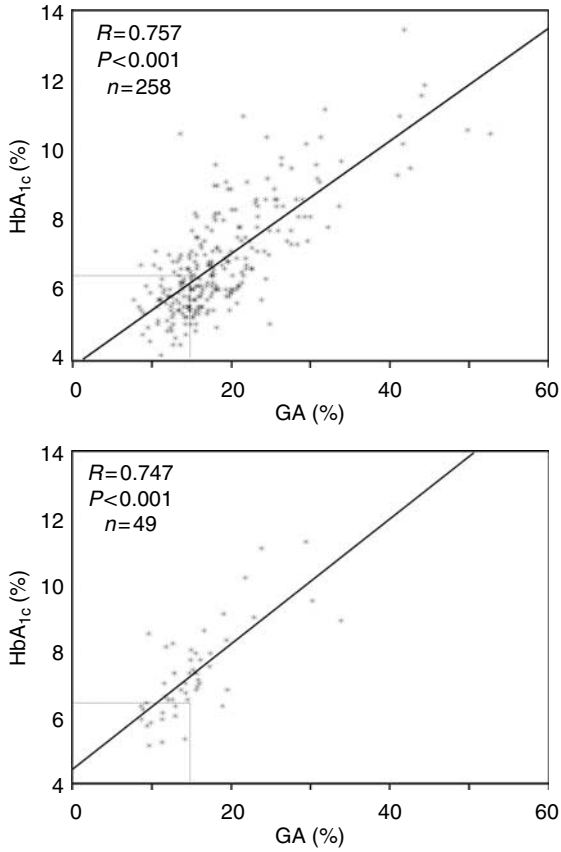

Figure 1 | Correlation between HbA_{1c} and glycated albumin, by ESRD status. Relationship between % HbA_{1c} and % GA in diabetic subjects with ESRD (upper panel) and without nephropathy (lower panel). Slopes of the lines differ between groups (0.163 for diabetes mellitus (DM)-ESRD, 0.190 for DM nonnephropathy patients, $P=0.0001$). Reference lines represent normal values.

and erythropoietin for advanced chronic kidney disease (ESRD), and 49 were without kidney failure. Table 1 contains demographic characteristics of the study population. All patients with ESRD received erythropoietin, with mean average (s.d.) weekly dose 22 876 (20 579) units. In all, 7% (18/258) of dialysis patients and 0% of those without kidney failure received a blood transfusion within the 90 days preceding the study. Subjects without kidney failure had mean serum creatinine concentration 1.0 (0.3) mg per 100 ml and ESRD patients had mean urea reduction ratio 70.9 (8.8)%, K_t/V 1.5 (0.4), hemoglobin 11.8 (1.1) g per 100 ml, transferrin saturation 25.4 (10.8)%, and ferritin 567 (424) ng ml^{-1}. Overall, the mean (s.d.) serum glucose concentration in all participants was 168 (63) mg per 100 ml. The nonnephropathy group had a mean (s.d.) serum glucose concentration of 146 (66) mg per 100 ml and in ESRD subjects 172 (62) mg per 100 ml. The coefficient of variation was 100*(63/168) or 37.5%.

In ESRD patients, relative to those without kidney disease, mean (s.d.) serum glucose concentrations were higher (172 (62) vs 146 mg per 100 ml (66); $P=0.024$), % GA was higher (18.7% (7.3), range: 7.7–52.7 vs 15.3% (5.5), range: 8.6–33.8%; $P<0.0001$), and HBA_{1c} was lower (mean (s.d.), range: 6.8% (1.6), 4.1–13.5 vs 7.3% (1.4), 5.1–11.3%; $P=0.058$) (Table 1). The % GA/HbA_{1c} ratio was significantly higher in ESRD patients relative to those without nephropathy (2.72 (0.6) vs 2.07 (0.5); $P=0.0001$). The % GA/HbA_{1c} ratio in diabetic subjects with ESRD compared with those without kidney disease should approximate 1, if these assays performed equally in both groups. Instead, the % GA/HbA_{1c} ratio in dialysis patients compared with subjects without nephropathy was 1.31 (2.72/2.07).

Figure 1 displays the correlation between HbA_{1c} and % GA in hemodialysis patients and subjects without kidney disease. A significant difference in the slope of the line expressing this relationship among hemodialysis patients (slope = 0.163) and subjects without nephropathy (slope = 0.190) was observed ($P=0.0001$). Figure 2 displays HbA_{1c} and % GA correlations with recent random blood glucose measures. No significant differences in the relationship between % GA and glucose concentrations were observed between participants on hemodialysis and those without kidney disease ($P=0.19$), whereas marked differences were observed with HbA_{1c} and glucose concentrations ($P<0.0001$).

Table 2 contains the results of subgroup analyses. In analyses restricted to African Americans, % GA/HbA_{1c} ratios were 2.77 in subjects with ESRD and 1.98 in those with normal kidney function ($P=0.0001$). Among non-African Americans (predominantly Caucasians), the ratios were 2.62 in those with ESRD and 2.12 in those without kidney disease