Is There a "Burnt-Out Diabetes" Phenomenon in Patients on Hemodialysis?

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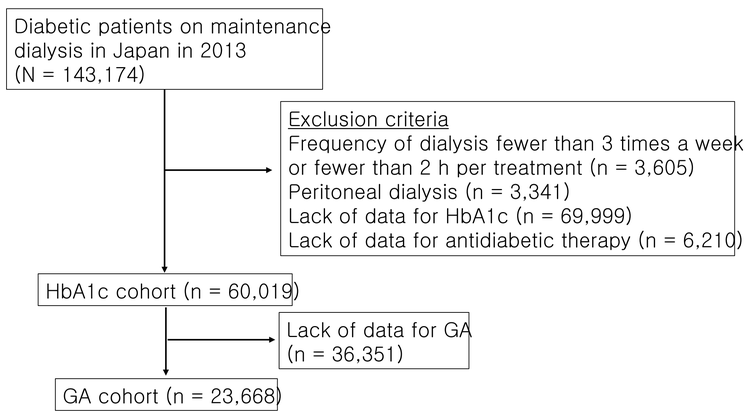
Background

In patients with diabetes on dialysis, glycemic control improves spontaneously, leading to normal glycated hemoglobin (HbA1c) levels that necessitate the cessation of antidiabetic medications; this phenomenon is known as “burnt-out diabetes.” Furthermore, the life span of red blood cells is shorter, and blood loss and hemorrhage may occur during dialysis; thus, by increasing the proportion of young erythrocytes in the blood, both anemia and erythropoiesis-stimulating agents can falsely lower the HbA1c level. In contrast, the glycated albumin (GA) level is not significantly associated with the life span of red blood cells, hemoglobin level, or erythropoiesis-stimulating agent dose in patients with diabetes undergoing hemodialysis. Therefore, GA might be a better indicator of glycemic control than HbA1c in diabetic hemodialysis patients. Therefore, to identify how many patients with diabetes undergoing dialysis experience “burnt-out diabetes,” we conducted a cohort study of a nationwide registry of the Japanese Society for Dialysis Therapy (JSDT) in 2013.

Methods

Patients with diabetes on maintenance hemodialysis therapy whose HbA1c levels were measured and whose antidiabetic therapy was recorded were included in this study. First, the “burnt-out diabetes” phenomenon was investigated in patients whose HbA1c levels were measured (HbA1c cohort). Then, the “burnt-out diabetes” phenomenon was investigated in patients who were assessed for both HbA1c and GA levels (GA cohort). To determine the risk of cardiovascular comorbidity, a multivariable logistic regression model was used, and the odds ratio and 95% confidence interval were reported.

Figure 1. Study flowchart

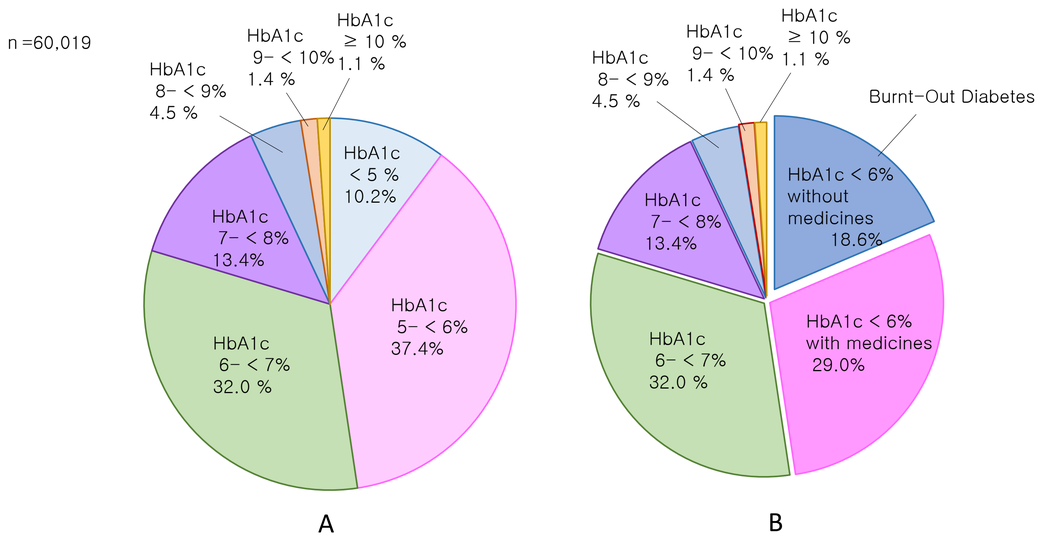


Results

Table 1. Patient characteristics in HbA1c cohort.

	HbA1c (%)							P value
	<5	5 to <6	6 to <7	7 to <8	8 to <9	9 to <10	≥10	
n	6,129	22,462	19,211	8,027	2,674	859	657	
Sex (% male)	69.9	69	69.3	69.3	69.2	69.8	66.8	0.7
Age (years)	67.3 ± 11.4	67.4 ± 11.4	67.3 ± 11.2	67.5 ± 11.3	67.3 ± 10.6	67.3 ± 10.6	67.5 ± 11.0	0.9
HD duration								
0-6 months	10.4	6	4.4	3.8	4.1	5.4	5.2	<0.001
6-24 months	27.1	21.8	17.6	17.3	18.2	17.8	14.3	<0.001
2-5 years	29.4	32.2	30	29.9	27.2	29.8	29.1	<0.001
>5 years	33.1	40	48	49	50.5	47	51.4	<0.001
BMI (kg/m^2)	22.6 ± 4.3	23.1 ± 4.7	22.4 ± 4.1	22.4 ± 4.1	22.2 ± 3.9	22.5 ± 5.5	22.4 ± 4.1	0.003
Smoking (%)	11.7	12.3	12.3	12.6	13.3	11.3	11.3	0.3
Type 2 diabetes (%)	88.1	88	87.9	87.6	88.1	88.1	87.7	0.9
HbA1c (%)	4.7 [4.5-4.9]	5.5 [5.2-5.7]	6.4 [6.2-6.6]	7.3 [7.1-7.6]	8.3 [8.1-8.6]	9.3 [9.1-9.6]	10.9 [10.4-12.1]	<0.001
Hb (g/dL)	10.5 ± 1.3	10.7 ± 1.3	11.0 ± 1.3	10.9 ± 1.2	10.8 ± 1.2	10.8 ± 1.3	10.8 ± 1.4	<0.001
Alb (g/dL)	3.6 ± 0.4	3.6 ± 0.4	3.7 ± 0.4	3.7 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	0.03
UN (mg/dL)	62 ± 16	60 ± 16	64 ± 17	62 ± 15	61 ± 16	59 ± 15	60 ± 15	0.7
Cr (mg/dL)	9.6 ± 2.7	9.5 ± 2.7	9.6 ± 2.7	9.6 ± 2.7	9.7 ± 2.7	9.5 ± 2.7	9.6 ± 2.8	<0.001
Ca (mg/dL)	8.7 ± 0.7	8.7 ± 0.7	8.9 ± 0.8	8.8 ± 0.7	8.8 ± 0.7	8.8 ± 0.7	8.8 ± 0.7	<0.001
P (mg/dL)	5.3 ± 1.4	5.3 ± 1.5	5.5 ± 1.5	5.3 ± 1.4	5.3 ± 1.4	5.2 ± 1.4	5.2 ± 1.5	0.09
Antihypertensive agents (%)	70.1	69.9	69.6	69.3	71	69	67.4	<0.001
Antidiabetic therapy (%)								
No medication	39.1	39	39.6	39.9	37.1	37.1	37.9	0.1
Insulin therapy	33.6	33.1	30.5	31.3	33.9	38.2	40.6	<0.001
Oral antidiabetic agents only	27.3	27.9	29.9	28.8	29	24.7	21.5	<0.001

Figure 2. A, Distribution of HbA1c levels in 60,019 hemodialysis patients; B, Rate of “burnt-out diabetes” phenomenon in the HbA1c cohort

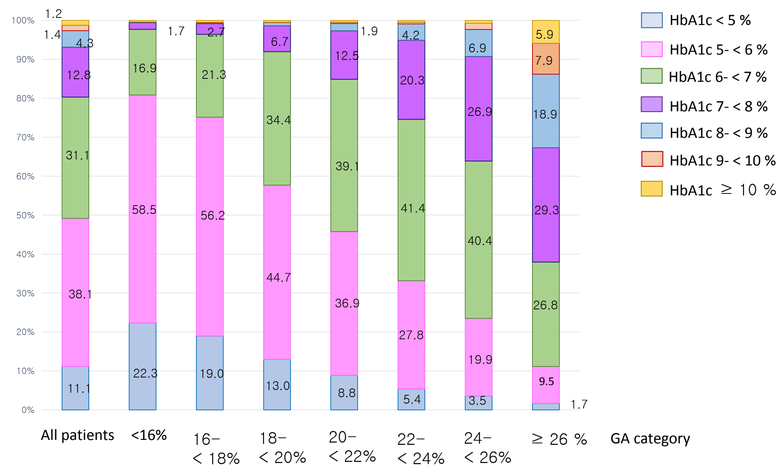


In the HbA1c cohort, 60,019 patients were included, and “burnt-out diabetes” was defined as HbA1c < 6.0% without treatment with any antidiabetic medication. The “burnt-out diabetes” phenomenon was noted in 11,159 patients (18.6%).

Table 2.

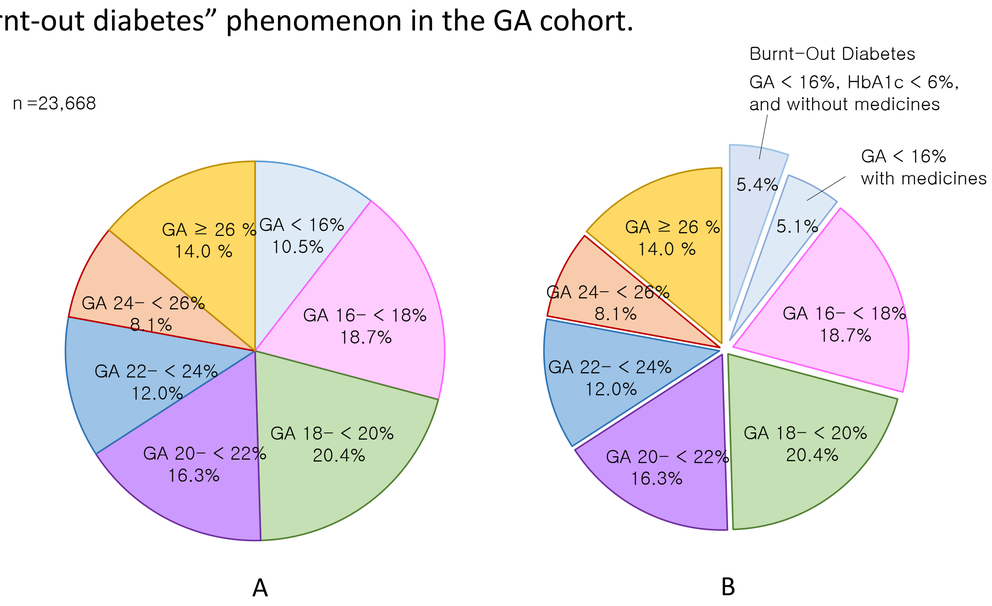
	GA (%)							P value
	< 16.0	16 to < 18	18 to < 20	20 to < 22	22 to < 24	24 to < 26	≥ 26	
n	2,479	4,416	4,828	3,863	2,847	1,922	3,313	
Sex (% male)	70.7	70.5	70.2	69.1	68.4	66.5	63	< 0.001
Age (years)	64.3 ± 11.8	68.1 ± 11.4	68.3 ± 11.3	68.5 ± 11.0	68.5 ± 10.9	68.3 ± 10.7	66.8 ± 11.6	< 0.001
HD duration (years)								
0-6 months	7.3	5.1	5.0	4.3	4.5	4.2	3.9	＜0.001
6-24 months	18.5	20.4	20.7	19.9	21.2	18.7	18.5	0.027
2-5 years	30.3	29.7	31.7	31.4	31.5	29.7	29.8	0.211
> 5years	43.8	44.8	42.6	44.4	42.8	47.4	47.8	＜0.001
BMI (kg/m^2)	23.8 ± 4.3	22.4 ± 3.9	22.4 ± 4.0	22.3 ± 3.9	22.2 ± 4.1	22.1 ± 4.1	21.8 ± 4.3	< 0.001
Smorking	15.0	12.5	12.5	11.6	11.8	11.2	11.9	< 0.001
Type 2 diabetes	92.3	93.8	92.2	90.5	89.2	87.3	82.4	< 0.001
GA (%)	14.8 [13.9-15.5]	17 [16.6-17.5]	18.9 [18.4-19.4]	20.9 [20.4-21.4]	22.9 [22.4-23.4]	24.9 [24.4-25.4]	29.3 [27.3-33]	< 0.001
HbA1c (%)	5.5 ± 0.8	5.6 ± 1.0	5.9 ± 1.0	6.1 ± 1.0	6.4 ± 1.1	6.7 ± 1.1	7.5 ± 1.5	< 0.001
Hb (g/dL)	10.8 ± 1.2	10.7 ± 1.2	10.7 ± 1.2	10.7 ± 1.2	10.7 ± 1.2	10.7 ± 1.2	10.6 ± 1.2	< 0.001
Alb (g/dL)	3.6 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	3.5 ± 0.5	< 0.001
UN (mg/dL)	60 ± 16	61 ± 15	60 ± 15	59 ± 15	59 ± 15	60 ± 16	59 ± 16	0.005
Cr (mg/dL)	10.3 ± 2.9	10.0 ± 2.7	9.6 ± 2.6	9.4 ± 2.6	9.2 ± 2.6	9.2 ± 2.6	8.9 ± 2.6	< 0.001
Ca (mg/dL)	8.7 ± 0.8	8.8 ± 0.7	8.8 ± 0.7	8.7 ± 0.7	8.7 ± 0.7	8.7 ± 0.7	8.7 ± 0.7	0.005
P (mg/dL)	5.5 ± 1.5	5.3 ± 1.4	5.2 ± 1.4	5.2 ± 1.4	5.2 ± 1.4	5.1 ± 1.4	5.2 ± 1.5	< 0.001
Antihypertesive agents	67.0	70.3	70.5	71.0	71.2	69.2	71.7	< 0.001
Antidiabetic therapy								
No medicine	57.9	61.4	43.5	33.9	25.8	21.3	14.8	＜0.001
Insulin therapy	15.9	14.7	25.1	33.7	42.7	49.4	61.3	＜0.001
Oral diabetes agents only	26.2	23.9	31.4	32.4	31.5	29.3	23.9	＜0.001

Figure 2. Distribution of HbA1c levels in each GA category



A dose-response association was noted between the GA and HbA1c categories (P < 0.001)

Figure 3. A, Distribution of GA levels in 23,668 hemodialysis patients; B, Rate of the “burnt-out diabetes” phenomenon in the GA cohort.



In the GA cohort, 23,668 patients were included, and “burnt-out diabetes” was defined in patients HbA1c < 6.0% and GA < 16.0% without treatment with any antidiabetic medication. The “burnt-out diabetes” phenomenon was found in 1,286 patients (5.4%). This rate was significantly lower in the GA cohort than in the HbA1c cohort (P < 0.0001).

Table 3. Cardiovascular comorbidity rate in 22,301 HD patients according to the GA categories

Comorbidities	All patients	GA (%)							P value
		< 16.0	16 to < 18	18 to < 20	20 to < 22	22 to < 24	24 to < 26	≥ 26	
Number of the patients	22,301	2343	4170	4550	3689	2694	1834	3121	
Myocardial infarction	13.0	14.3	12.1	12.3	13.9	13.8	14.4	13.1	0.022
Cerebral hemorrahge	5.2	5.7	4.7	5.4	5.4	5	5.7	5.8	0.443
Cerebral infarction	21.0	18.7	18.8	20	23.7	22.6	22.4	23.4	< 0.001
Limb amputation	5.8	4.7	3.7	4.6	6.5	7.1	7	8.9	< 0.001
Any cardiovascular disease	25.9	22.9	22	23.8	28.4	28	27.7	30.7	< 0.001

Cardiovascular comorbidity risk were significantly associated with GA > 18% (P<0.01).

Conclusions

The “burnt-out diabetes” phenomenon might be present in 18.6% of patients with diabetes on hemodialysis in terms of hbA1c levels. However, the rate was significantly lower at 5.4% in terms of GA levels. The risk of cardiovascular comorbidity was increased when GA was over 18%.

We declare no conflict of interest.

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