Differences in the Number of Patients with Severe Hypoglycemia by Month and Their Type 2 Diabetes Background

Jun-Ichirou Mori[1], Koh Yamashita[2]* and Toru Aizawa[2]

1) *Center for Medical Education, Faculty of Medicine, Shinshu University*
2) *Diabetes Center, Aizawa Hospital*

Severe hypoglycemia is a serious complication of diabetes that can be directly linked to life prognosis and activities of daily living. However, sufficient knowledge regarding the trend of severe hypoglycemia has not been accumulated. In this study, 330 patients with type 2 diabetes mellitus diagnosed with severe hypoglycemia were analyzed by the month of hypoglycemia onset. The patients were enrolled from those who visited the Critical Care Center of Aizawa Hospital over a 12-year period, from January 1, 2008, to December 31, 2019. The results showed that the number of patients with hypoglycemia was the lowest in February and the highest in September. Blood pressure (both systolic and diastolic) was the lowest in September and the highest in June. Blood glucose levels were the lowest in May and the highest in July. HbA1c values were the lowest in August and the highest in October. We also examined differences in the types of drugs administered. The number of drugs administered was the lowest in October and the highest in February. In addition, the proportion of DPP4 inhibitors was the highest in February for patients with hypoglycemia. The results of this study showed a month-to-month difference in the tendency of patients to visit the emergency room for severe hypoglycemia. In particular, we considered that it was necessary to pay attention to severe hypoglycemia in patients with good glycemic control in the winter months who require treatment with multiple drugs, and in patients with inadequate control in October. *Shinshu Med J 73 : 147—153, 2025*

(Received for publication September 30, 2024 ; accepted in revised form February 5, 2025)

Key words : severe hypoglycemia, type 2 diabetes, monthly change

I Introduction

Type 2 diabetes mellitus can cause damage to various organs throughout the body because of continued hyperglycemia resulting from decreased insulin secretion capacity and increased insulin resistance[1]. Regarding the treatment of type 2 diabetes, injectable preparations, such as insulin, along with various oral drugs, have been developed, and innovations in the treatment methods for type 2 diabetes are constantly advancing. However, severe hypoglycemia is known to lead to poor prognosis and dementia[2)3)]. Therefore, it is important to avoid severe hypoglycemia during treatment, and especially in older adult patients, treatment safety is required. The joint statement of the Japan Diabetes Society and Japan Geriatrics Society also indicates a lower limit of treatment goals when using drugs with a risk of hypoglycemia[4]. Nonetheless, sufficient knowledge regarding the trend of severe hypoglycemia has not been accumulated.

In this study, we investigated the factors contributing to severe hypoglycemia by analyzing the monthly trends and patient backgrounds at Aizawa Hospital Emergency and Critical Care Center.

II Patients and Methods

A Patients

Altogether, 1,185 patients with hypoglycemia were

* Corresponding author : Koh Yamashita
Diabetes Center, Aizawa Hospital, Honjo 2-5-1,
Matsumoto, Nagano 390-8510, Japan
E-mail : kohiromi221@yahoo.co.jp

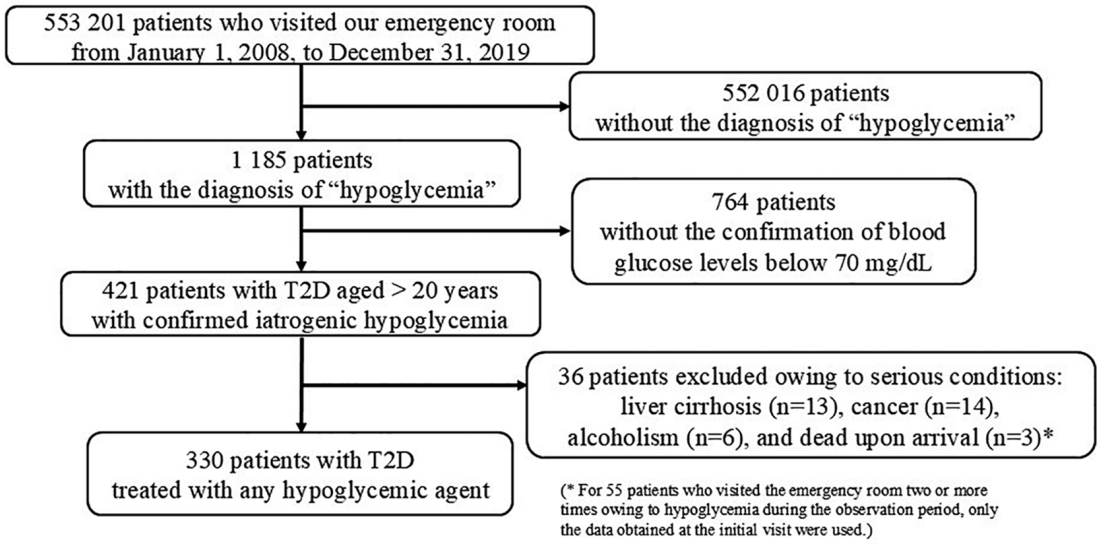

Fig. 1　Protocol for patient extraction.
T2D : type 2 diabetes mellitus.

selected from the 553,201 patients who visited Aizawa Hospital Emergency and Critical Care Center during the 12 years from January 1, 2008, to December 31, 2019. Among them, 421 patients with type 2 diabetes mellitus identified with severe hypoglycemia were 20 years of age or older at the time of consultation and had blood glucose levels confirmed to be less than 70 mg/dL at the time of hypoglycemia symptoms. Thus, 330 patients were included in this study **(Fig. 1)**.

In this study, we defined severe hypoglycemia as a plasma/blood glucose level of less than 70 mg/dL ; an event requiring the assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions ; and rapid improvement with treatment, such as glucose supplementation. In addition, the date and the time of hypoglycemia were defined by the date and the time of visit to Aizawa Hospital Emergency and Critical Care Center, respectively.

B　Anthropometry and Laboratory Data

Data on physical findings, such as state of consciousness and blood pressure, were extracted from electronic records. In addition, the results of the blood examination, such as the blood glucose levels, were extracted from electronic records.

C　Statistical analysis

Descriptive statistical analysis was performed using Wilcoxon rank sum, χ^2, or Fisher's exact test. JMP ver.17 (SAS Institute, Cary, NC, USA) was used for statistical analysis. Differences were considered statistically significant at $p<0.05$.

D　Ethical statement

This study was approved by the Ethics Review Committee of Aizawa Hospital Clinical Research (approval date : January 5, 2021 ; registry number : #2020-057). Patients could opt out of the study via the hospital's website and postings.

Ⅲ　Results

Table 1 shows the overall average value of each parameter, the month of the maximum and minimum values of each parameter, and the average value. The number of patients with severe hypoglycemia by month was the lowest in February (21 patients) and the highest in September (39 patients) **(Fig. 2)**. Their average age was 76.4 years overall, ranging from 71.1 years in June to 78.7 years in April. Overall, the proportion of males was 57.0 %, and the monthly examination showed that the highest proportion was 76.0 % in November and the lowest was 40.9 % in June. The overall average systolic blood pressure was 158.2 mmHg, with the lowest of 147.3 mmHg in September and the highest of 167.8 mmHg in June. The overall average diastolic blood pressure was 81.1 mmHg, with the

Table 1　Baseline characteristics of patients with severe hypoglycemia

	Total	Maximum	Minimum
Number of patients (month, number)	330	Sep 39	Feb 21
Age (years) [month, (mean ± SD)]	76.4 ± 10.1	Apr 78.7 ± 7.8	Jun 71.1 ± 15.0
Sex [month, (number of males, % of males)]	188, 57.0	Nov 19, 76.0	Jun 9, 40.9
Systolic BP (mmHg) [month, (mean ± SD)]	158.2 ± 30.6	Jun 167.8 ± 34.4	Sep 147.3 ± 32.3
Diastolic BP (mmHg) [month, (mean ± SD)]	81.1 ± 18.1	Jun 86.7 ± 19.6	Sep 74.9 ± 17.9
Heart rate (beats/min) [month, (mean ± SD)]	77.8 ± 15.9	Jan 83.3 ± 13.8	Oct 73.2 ± 18.7
Blood/plasma glucose (mg/dl) [month, (mean ± SD)]	35.9 ± 12.9	Jul 43.0 ± 13.9	May 31.8 ± 11.7
HbA1c (%) [month, (mean ± SD)]	6.79 ± 1.28	Oct 7.45 ± 1.60	Aug 6.20 ± 1.00
Types of medication (number) [month, (mean ± SD)]	1.8 ± 0.8	Feb 2.1 ± 1.0	Nov 1.6 ± 0.8
Types of oral hypoglycemic agents (number) [month, (mean ± SD)]	1.3 ± 1.1	Feb 1.8 ± 1.1	Oct 1.1 ± 1.0

BP – Blood Pressure ; HbA1c – Hemoglobin A1c ; SD – Standard Deviation.

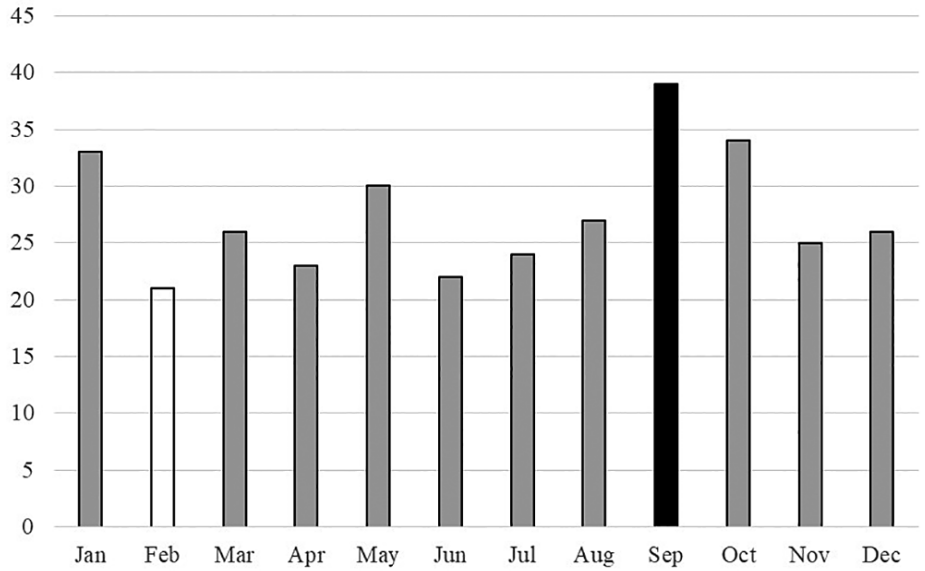

Fig. 2　Monthly distribution of patients with severe hypoglycemia. The average monthly incidence of severe hypoglycemia was 27.5 patients. The highest incidence was recorded in February (39 patients), whereas the lowest was recorded in September (21 patients).

White bar : number of patients with severe hypoglycemia in February, indicating the lowest incidence.
Black bar : number of patients with severe hypoglycemia in September, indicating the highest incidence.
Gray bar : monthly number of patients with severe hypoglycemia in the rest of months.
Jan : January, Feb : February, Mar : March, Apr : April, Jun : June, Jul : July, Aug : August, Sep : September, Oct : October, Nov : November, Dec : December

Table 2 Proportion of medications

	Total rate [% (number)]	Maximum rate [month, % (number)]	Minimum rate [month, % (number)]
BG	17.6 % (58)	Nov, 24.0 % (6)	Dec, 7.7 % (2)
SU	52.4 % (173)	Dec, 65.4 % (17)	Jun, 40.9 % (9)
TZD	13.0 % (43)	Jan, 21.2 % (7)	Jun, 0.0 % (0)
aGI	19.4 % (64)	Dec, 30.8 % (8)	Sep, 12.8 % (5)
DPP4i	24.2 % (80)	Feb, 52.4 % (11)	Oct, 8.8 % (3)
Glinide	1.8 % (6)	Aug, 7.4 % (2)	Jan/Feb/Apr～Jun/Nov/Dec, 0.0 % (0)
SGLT2i	0.3 % (1)	Mar, 3.8 % (1)	Without Mar, 0.0 % (0)
Insulin	49.7 % (164)	Jun, 59.1 % (13)	Feb, 38.1 % (8)

aGI – Alpha-Glucosidase Inhibitor ; BG – Biguanides ; DPP4i – Dipeptidyl Peptidase-4 Inhibitor ; GLP-1RA – Glucagon-Like Peptide-1 Receptor Agonist ; SGLT2i – Sodium-Glucose Cotransporter-2 Inhibitor ; SU – Sulfonylureas ; TZD – Thiazolidinediones.

lowest of 74.9 mmHg in September and the highest of 86.7 mmHg in June. The average pulse rate was 77.8 beats/min, with the lowest being 73.2 beats/min in October and the highest being 83.3 beats/min in January. Blood glucose levels during hypoglycemic attacks averaged 35.9 mg/dL overall, with the lowest of 31.8 mg/dL in May and the highest of 43.0 mg/dL in July. Overall, glycated hemoglobin (HbA1c) averaged 6.79 %, with the lowest being 6.20 % in August and December, and the highest being 7.45 % in October. The overall average number of drugs for diabetes, including insulin, was 1.8, with the lowest being 1.6 in November and the highest being 2.1 in February. The overall average number of oral hypoglycemic drugs was 1.3, the lowest was 1.1 in October, and the highest was 1.8 in February.

Table 2 shows the number of participants and their percentages according to medication type. Biguanide (BG) was administered to 17.6 % of patients (from 7.7 % in December to 24.0 % in November). Sulfonylureas (SU) were administered to 52.4 % of all patients (from 40.9 % in June to 65.4 % in December). Thiazolidinediones (TZD) were administered to 13.0 % of patients (from 0.0 % in June to 21.2 % in January). α-glucosidase inhibitors (aGIs) were administered to 19.4 % of patients (from 12.8 % in September to 30.8 % in December). Dipeptidyl peptidase-4 inhibitors (DPP4i) were administered to 24.2 % of patients (from 8.8 % in October and 52.4 % in February). Insulin preparations were administered to 49.7 % of patients (from 38.1 % in February to 59.1 % in June). Insulin secretagogue (glinide) was administered to 1.8 % of patients, but only data from three months (March, July, and October) were included (up to 7.4 % in June). Only one patient received a sodium-glucose cotransporter 2 inhibitor (3.8 % in March). A glucagon-like peptide-1 receptor agonist (GLP-1 RA) was not used in any patient (data not shown).

Next, we divided patients with hypoglycemia who visited the hospital in each month and those who visited the hospital in the other 11 months **(Table 3)**, and examined the differences in each parameter, such as age, sex, and medications for each month. There were no significant differences in age or sex at any of the time points. In terms of blood pressure, both systolic and diastolic blood pressure in September were significantly lower than those in the other 11 months (systolic blood pressure 147 mmHg vs. 159.6 mmHg, $p = 0.034$; diastolic blood pressure 74 mmHg vs. 81.9 mmHg, $p = 0.021$, respectively). Pulse rate was significantly higher in January than in the other 11 months (83.3 bpm vs. 77.2 bpm, $p = 0.042$). Blood glucose levels during hypoglycemic attacks were significantly higher in July than in the other 11 months (43.0 mg/dL vs. 35.3 mg/dL, $p = 0.009$). HbA1c values were significantly higher in October than in the other 11 months and significantly lower in December than in the other 11 months (7.45 % vs. 6.71 %, $p = 0.0042$ and 6.20 % vs.

Table 3　Comparison of parameters between each month and the other 11 months

	Age	Sex	Systolic BP	Diastolic BP	PR	Glucose concentration	HbA1c
Jan vs. other 11 month	74.7 vs. 76.6, p = 0.204	69.7 vs. 55.6, p = 0.140	162.8 vs. 157.7, p = 0.209	86.1 vs. 80.6, p = 0.082	83.3 vs. 77.2, p = 0.042*	35.2 vs. 36.0, p = 0.803	6.61 vs. 6.81, p = 0.791
Feb vs. other 11 month	77.8 vs. 76.3, p = 0.405	42.9 vs. 57.9, p = 0.254	157.0 vs. 158.3, p = 0.911	79.9 vs. 81.2, p = 0.977	74.3 vs. 78.1, p = 0.379	37.5 vs. 35.8, p = 0.580	6.49 vs. 6.81, p = 0.708
Mar vs. other 11 month	75.5 vs. 76.5, p = 0.381	53.8 vs. 57.2, p = 0.837	155.0 vs. 158.5, p = 0.527	77.7 vs. 81.4, p = 0.451	80.4 vs. 77.6, p = 0.349	35.2 vs. 35.9, p = 0.768	7.32 vs. 6.75, p = 0.181
Apr vs. other 11 month	78.7 vs. 76.2, p = 0.301	52.2 vs. 57.3, p = 0.667	166.4 vs. 157.6, p = 0.269	85.5 vs. 80.8, p = 0.188	77.8 vs. 77.9, p = 0.753	35.5 vs. 35.9, p = 0.982	6.81 vs. 6.79, p = 0.480
May vs. other 11 month	76.6 vs. 76.4, p = 0.925	63.3 vs. 56.3, p = 0.563	160.3 vs. 158.1, p = 0.842	79.7 vs. 81.2, p = 0.626	76.3 vs. 78.0, p = 0.709	31.8 vs. 36.3, p = 0.074	6.80 vs. 6.79, p = 0.713
Jun vs. other 11 month	71.1 vs. 76.8, p = 0.194	40.9 vs. 58.1, p = 0.125	167.8 vs. 157.6, p = 0.288	86.7 vs. 80.7, p = 0.209	76.5 vs. 77.9, p = 0.627	42.1 vs. 35.4, p = 0.053	7.30 vs. 6.76, p = 0.077
Jul vs. other 11 month	76.3 vs. 76.4, p = 0.878	50.0 vs. 57.5, p = 0.524	162.0 vs. 157.9, p = 0.422	80.6 vs. 81.2, p = 0.881	77.5 vs. 77.9, p = 0.693	43.0 vs. 35.3, p = 0.009*	6.49 vs. 6.81, p = 0.505
Aug vs. other 11 month	75.9 vs. 76.4, p = 0.779	59.3 vs. 56.8, p = 0.842	152.3 vs. 158.8, p = 0.131	79.7 vs. 81.2, p = 0.709	76.5 vs. 78.0, p = 0.571	32.8 vs. 36.1, p = 0.127	6.20 vs. 6.85, p = 0.058
Sep vs. other 11 month	78.0 vs. 76.2, p = 0.255	48.7 vs. 58.1, p = 0.303	147.3 vs. 159.6, p = 0.034*	74.9 vs. 81.9, p = 0.021*	78.1 vs. 77.8, p = 0.876	36.9 vs. 35.8, p = 0.379	6.83 vs. 6.79, p = 0.932
Oct vs. other 11 month	77.3 vs. 76.3, p = 0.720	70.6 vs. 55.4, p = 0.102	159.8 vs. 158.1, p = 0.776	80.2 vs. 81.2, p = 0.569	73.2 vs. 78.4, p = 0.056	32.8 vs. 36.2, p = 0.158	7.45 vs. 6.71, p = 0.042*
Nov vs. other 11 month	75.9 vs. 76.4, p = 0.803	76.0 vs. 55.4, p = 0.058	161.9 vs. 157.9, p = 0.215	80.0 vs. 81.2, p = 0.967	78.5 vs. 77.8, p = 0.851	34.4 vs. 36.0, p = 0.465	6.67 vs. 6.81, p = 0.702
Dec vs. other 11 month	78.0 vs. 76.3, p = 0.440	46.2 vs. 57.9, p = 0.303	152.2 vs. 158.8, p = 0.337	84.6 vs. 80.8, p = 0.425	80.8 vs. 77.6, p = 0.486	37.0 vs. 35.8, p = 0.626	6.20 vs. 6.84, p = 0.028*

Asterisk indicates statistically significant difference. ($P < 0.05$)

BP – Blood Pressure ; HbA1c – Hemoglobin A1c ; PR – Pulse Rate.

6.84 %, p = 0.028, respectively).

Further, we examined the drugs used to treat patients who visited each month and those who visited in the other 11 months. First, there was no significant difference in the number of drugs taken in any month, either in terms of the total number of drugs (including insulin) or the number of types of oral hypoglycemic drugs (excluding insulin). Next, we compared each drug between patients who visited our hospital in one month and those who visited during the other 11 months over a 12-month period **(Table 4)**. There were no significant differences in the use of BG, SU, aGI, glinide, SGLT2 inhibitors, or insulin in any month. The proportion of patients who received TZD in September was significantly lower than that of patients who visited in the other 11 months (2.6 % vs. 14.4 %, p = 0.041). For DPP4i, the proportion of patients who took DPP4i in February was significantly higher than that of patients who visited the other 11 months (52.4 % vs. 22.3 %, p = 0.006). In contrast, the proportion of patients who took the drug in October was significantly lower than that of patients who visited the hospital during the other 11 months (8.8 % vs. 26.0 %, p = 0.033). In this study, GLP-1 RA was not administered to any of the patients.

Ⅳ　Discussion

Considerable uncertainty persists regarding severe hypoglycemia. In this study, we analyzed monthly variations in the incidence of severe hypoglycemia, ranging from 21 (in February) to 39 (in September). Physical activity, which Kubota et al. showed to vary seasonally, may act as a potential trigger. Their findings indicated increased activity during fall and reduced levels in winter[5]. Correspondingly, the peak occurrence of hypoglycemia was in September, coinciding with increased physical activity, and the nadir was in February, the coldest winter month. Interestingly, June was the month with the youngest average age and the lowest proportion of men. However, there was no

Table 4 Comparison of medication status between each month and the other 11 months

	Number of medications	Number of OHA	BG	SU	TZD	aGI	DPP4i	Glinide	SGLT2i	Ins
Jan vs. other 11 month	1.8 vs. 1.8, p = 0.661	1.5 vs. 1.3, p = 0.393	18.2 vs. 17.5, p = 1.000	60.6 vs. 51.5, p = 0.362	21.2 vs. 12.1, p = 0.169	27.3 vs. 18.5, p = 0.247	18.2 vs. 24.9, p = 0.522	0.0 vs. 2.0, p = 1.000	0.0 vs. 0.3, p = 1.000	39.4 vs. 50.8, p = 0.271
Feb vs. other 11 month	2.1 vs. 1.8, p = 0.089	1.8 vs. 1.3, p = 0.058	19.0 vs. 17.5, p = 0.772	61.9 vs. 51.8, p = 0.499	19.0 vs. 12.6, p = 0.498	23.8 vs. 19.1, p = 0.573	52.4 vs. 22.3, p = 0.006*	0.0 vs. 1.9, p = 1.000	0.0 vs. 0.3, p = 1.000	38.1 vs. 50.5, p = 0.368
Mar vs. other 11 month	1.8 vs. 1.8, p = 0.943	1.2 vs. 1.3, p = 0.718	15.4 vs. 17.8, p = 1.000	50.0 vs. 52.6, p = 0.840	19.2 vs. 12.5, p = 0.358	15.4 vs. 19.7, p = 0.797	15.4 vs. 25.0, p = 0.345	3.8 vs. 1.6, p = 0.391	3.8 vs. 0.0, p = 0.079	53.8 vs. 49.3, p = 0.688
Apr vs. other 11 month	1.7 vs. 1.8, p = 0.737	1.2 vs. 1.3, p = 0.652	21.7 vs. 17.3, p = 0.573	47.8 vs. 52.8, p = 0.671	17.4 vs. 12.7, p = 0.520	17.4 vs. 19.5, p = 1.000	17.4 vs. 24.8, p = 0.614	0.0 vs. 2.0, p = 1.000	0.0 vs. 0.3, p = 1.000	52.2 vs. 49.5, p = 0.832
May vs. other 11 month	1.7 vs. 1.8, p = 0.394	1.1 vs. 1.3, p = 0.507	10.0 vs. 18.3, p = 0.321	56.7 vs. 52.0, p = 0.703	20.0 vs. 12.3, p = 0.253	13.3 vs. 20.0, p = 0.474	13.3 vs. 25.3, p = 0.182	0.0 vs. 2.0, p = 1.000	0.0 vs. 0.3, p = 1.000	53.3 vs. 49.3, p = 0.706
Jun vs. other 11 month	1.7 vs. 1.8, p = 0.800	1.1 vs. 1.3, p = 0.555	18.2 vs. 17.5, p = 1.000	40.9 vs. 53.2, p = 0.279	0.0 vs. 14.0, p = 0.093	13.6 vs. 19.8, p = 0.588	40.9 vs. 23.1, p = 0.072	0.0 vs. 1.9, p = 1.000	0.0 vs. 0.3, p = 1.000	59.1 vs. 49.0, p = 0.386
Jul vs. other 11 month	1.8 vs. 1.8, p = 0.735	1.2 vs. 1.3, p = 0.608	20.8 vs. 17.3, p = 0.588	45.8 vs. 52.9, p = 0.531	8.3 vs. 13.4, p = 0.753	16.7 vs. 19.6, p = 1.000	20.8 vs. 24.5, p = 0.808	4.2 vs. 1.6, p = 0.367	0.0 vs. 0.3, p = 1.000	58.3 vs. 49.0, p = 0.405
Aug vs. other 11 month	2.0 vs. 1.8, p = 0.086	1.6 vs. 1.3, p = 0.165	22.2 vs. 17.2, p = 0.596	51.9 vs. 52.5, p = 1.000	18.5 vs. 12.5, p = 0.372	22.2 vs. 19.1, p = 0.622	37.0 vs. 23.1, p = 0.157	7.4 vs. 1.3, p = 0.079	0.0 vs. 0.3, p = 1.000	44.4 vs. 50.2, p = 0.689
Sep vs. other 11 month	1.7 vs. 1.8, p = 0.463	1.2 vs. 1.3, p = 0.593	20.5 vs. 17.2, p = 0.654	51.3 vs. 52.6, p = 1.000	2.6 vs. 14.4, p = 0.041*	12.8 vs. 20.3, p = 0.388	28.2 vs. 23.7, p = 0.553	2.6 vs. 1.7, p = 0.533	0.0 vs. 0.3, p = 1.000	48.7 vs. 49.8, p = 1.000
Oct vs. other 11 month	1.6 vs. 1.8, p = 0.362	1.1 vs. 1.3, p = 0.222	14.7 vs. 17.9, p = 0.813	47.1 vs. 53.0, p = 0.588	11.8 vs. 13.2, p = 1.000	20.6 vs. 19.3, p = 0.821	8.8 vs. 26.0, p = 0.033*	2.9 vs. 1.7, p = 0.482	0.0 vs. 0.3, p = 1.000	58.8 vs. 48.6, p = 0.282
Nov vs. other 11 month	1.6 vs. 1.8, p = 0.392	1.1 vs. 1.3, p = 0.483	24.0 vs. 17.0, p = 0.411	48.0 vs. 52.8, p = 0.681	4.0 vs. 13.8, p = 0.223	20.0 vs. 19.3, p = 1.000	16.0 vs. 24.9, p = 0.466	0.0 vs. 2.0, p = 1.000	0.0 vs. 0.3, p = 1.000	52.0 vs. 49.5, p = 0.838
Dec vs. other 11 month	1.9 vs. 1.8, p = 0.405	1.5 vs. 1.3, p = 0.244	7.7 vs. 18.4, p = 0.279	65.4 vs. 51.3, p = 0.220	15.4 vs. 12.8, p = 0.760	30.8 vs. 18.4, p = 0.128	34.6 vs. 23.4, p = 0.232	0.0 vs. 2.0, p = 1.000	0.0 vs. 0.3, p = 1.000	38.5 vs. 50.7, p = 0.307

Asterisk indicates statistically significant difference. ($P < 0.05$)
BG – Biguanides ; DPP4i – Dipeptidyl Peptidase-4 Inhibitor ; Ins – Insulin ; OHA – Oral Hypoglycemic Agents ; SGLT2i – Sodium-Glucose Cotransporter-2 Inhibitor ; SU – Sulfonylureas ; TZD – Thiazolidinediones ; aGI – Alpha-Glucosidase Inhibitor.

significant difference between any month and the other 11 months with respect to age and sex distribution. Therefore, the risk of severe hypoglycemia is independent of age and sex. Regarding glycemic control, the lowest HbA1c values were noted in August, although it is acknowledged that HbA1c generally improves in summer and worsens in winter[6)-8)]. On the other hand, the HbA1c value in December was also the lowest at 6.20 %, which was significantly lower than the other 11-month value. We thought that the fact that HbA1c was significantly lower in December, when control was more likely to deteriorate[6)-8)], suggested that hypoglycemia occurred in overcontrolled patients. However, it was 7.45 % in October, which was significantly higher than that in the other 11 months. This suggests that hypoglycemia is likely to occur in October in patients with high fluctuations in blood glucose levels. The reason for this, for example, in the case of people engaged in agriculture, may be related to an increase in physical activity due to harvesting. In addition, October was also the time for department transfers, and it was thought that the timing of food intake was delayed due to the busy schedule resulting from the change in work at the new location, which might also cause hypoglycemia.

Further, each parameter was compared separately for each month and the other 11 months. We found that HbA1c values were significantly higher in patients with severe hypoglycemia in October than in those with severe hypoglycemia in other months. The fact that the rate of patients taking DPP4 inhibitors was the lowest in October may be because of medication adjustments reflecting glycemic control.

This study has several limitations. First, it was retrospective and observational, suggesting that although the phenomenon can be considered, causation cannot be established. Nonetheless, the observed differences in medication status and other variables are beneficial for devising future treatment strategies. Second, the study was conducted at a single center, raising

questions about whether the observed phenomenon is specific to our facility or more widespread. Notably, only 15.2 % of the patients in this study sought routine medical care at our hospital, whereas many others visited other hospitals. Thus, despite its single-center design, this study reflects a broader perspective, indicating that the phenomenon is not site specific. Third, the observation period was relatively long. During this time, treatment modalities evolved, influencing the incidence of severe hypoglycemia. Consequently, it is plausible that changes in treatment approaches could have introduced bias. Fourth, the sample size of this study was small. Although various factors were assessed, the scope of the analysis was limited. However, the detection of significant differences within a small cohort suggests variations over time, which may serve as valuable indicators for future therapeutic strategies.

V Conclusion

The results of this study showed a month-to-month difference in the tendency of patients to visit the emergency room for severe hypoglycemia. In particular, attention should be paid to hypoglycemia in patients with good glycemic control from summer to autumn and severe hypoglycemia in patients who require treatment with multiple drugs during the winter season. Furthermore, it should be noted that in October, even if blood glucose control is insufficient, there is a risk of severe hypoglycemia. The findings of this study might be useful for reducing the risk of severe hypoglycemia.

Acknowledgment

We would like to thank Editage (www.editage.jp) for English language editing.

References

1) Akhaury K, Wanjari A, Sinha AH, Kumar M : Hypoglycemia and Cardiovascular Disease : Exploring the Connections. Cureus 15 : e47784, 2023
2) Husain KH, Sarhan SF, AlKhalifa HKAA, Buhasan A, Moin ASM, Butler AE : Dementia in diabetes : the role of hypoglycemia. Int J Mol Sci 24 : 9846, 2023
3) Nachawi N, Rao PP, Makin V : The role of GLP-1 receptor agonists in managing type 2 diabetes. Cleve Clin J Med 89 : 457-464, 2022
4) Scheen AJ : Sodium-glucose cotransporter type 2 inhibitors for the treatment of type 2 diabetes mellitus. Nat Rev Endocrinol 16 : 556-577, 2020
5) Kubota A, Hamaguchi T : Seasonal changes in daily steps of community-dwelling older individuals with and without lifestyle-related diseases : a retrospective cohort study. J Phys Ther Sci 36 : 252-258, 2024
6) Tien KJ, Yang CY, Weng SF, Liu SY, Hsieh MC, Chou CW : The impact of ambient temperature on HbA1c in Taiwanese type 2 diabetic patients : the most vulnerable subgroup. J Formos Med Assoc 115 : 343-349, 2016
7) Higgins T, Saw S, Sikaris K, et al : Seasonal variation in hemoglobin A1c : is it the same in both hemispheres ? J Diabetes Sci Technol 3 : 668-671, 2009
8) Sakamoto M, Matsutani D, Minato S, et al : Seasonal variations in the achievement of guideline targets for HbA1c, blood pressure, and cholesterol among patients with type 2 diabetes : A nationwide population-based study (ABC study : JDDM49). Diabetes Care 42 : 816-823, 2019

(2024. 9. 30 received ; 2025. 2. 5 accepted)