


# Impact of newly diagnosed diabetes on coronavirus disease 2019 severity and hyperglycemia

Masaki Uchihara<sup>1</sup>, Ryotaro Bouchi<sup>1,2\*</sup> , Noriko Kodani<sup>1</sup>, Sho Saito<sup>3</sup>, Yusuke Miyazato<sup>3</sup>, Kotaro Umamoto<sup>1</sup>, Hirofumi Sugimoto<sup>1</sup>, Michi Kobayashi<sup>1</sup>, Sayaka Hikida<sup>3</sup>, Yutaro Akiyama<sup>3</sup>, Noriko Ihana-Sugiyama<sup>1,2</sup>, Mitsuru Ohsugi<sup>1,2</sup>, Akiyo Tanabe<sup>1</sup>, Kohjiro Ueki<sup>1,4</sup>, Jin Takasaki<sup>3,5</sup>, Masayuki Hojo<sup>5</sup>, Hiroshi Kajio<sup>1</sup>

<sup>1</sup>Department of Diabetes, Endocrinology and Metabolism, National Center for Global Health and Medicine, Tokyo, Japan, <sup>2</sup>Diabetes and Metabolism Information Center, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan, <sup>3</sup>Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan, <sup>4</sup>Department of Molecular Diabetic Medicine, Diabetes Research Center, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan, and <sup>5</sup>Department of Respiratory Medicine, National Center for Global Health and Medicine, Tokyo, Japan

## Keywords

COVID-19, Diabetes, Hyperglycemia

## \*Correspondence

Ryotaro Bouchi  
Tel.: +81-3-3202-7181  
Fax: +81-3-3202-7364  
E-mail address:  
rybouchi@hosp.ncgm.go.jp

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## ABSTRACT

**Aims/Introduction:** Diabetes is associated with poor clinical outcomes of coronavirus disease 2019 (COVID-19). However, the impact of newly diagnosed diabetes on prognosis has not been clarified. The objective of this study was to show the features and outcome of COVID-19 patients with newly diagnosed diabetes in Japan.

**Materials and Methods:** We retrospectively analyzed 62 patients with diabetes hospitalized for COVID-19 between 1 April and 18 August 2021 at the National Center for Global Health and Medicine in Tokyo, Japan. We evaluated the worst severity of COVID-19 and plasma blood glucose levels in patients with newly diagnosed diabetes or pre-existing diabetes.

**Results:** This study included 62 confirmed COVID-19 patients with diabetes, including 19 (30.6%) patients with newly diagnosed diabetes and 43 (69.4%) patients with pre-existing diabetes. Patients with newly diagnosed diabetes significantly progressed to a critical condition more frequently during hospitalization than patients with pre-existing diabetes (52.6% vs 20.9%,  $P = 0.018$ ). In addition, patients with newly diagnosed diabetes had significantly higher average plasma blood glucose levels for the first 3 days after admission than those with pre-existing diabetes.

**Conclusions:** Our study suggests that the proportion of COVID-19 patients who are newly diagnosed with diabetes is high, and they have an increased risk of developing severe disease than those with pre-existing diabetes. It might be advisable that at the point of COVID-19 diagnosis, blood glucose and glycated hemoglobin levels be assessed in all patients.

## INTRODUCTION

The coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), mainly penetrates the respiratory tract and lungs, resulting in acute respiratory distress syndrome and multiple organ failure in severe cases<sup>1</sup>. Evidence is emerging that diabetes is associated with worse clinical outcomes and higher mortality in patients with COVID-19<sup>2,3</sup>. Recently, several studies have

suggested that patients with newly diagnosed diabetes on hospital admission have a higher risk of serious conditions and mortality due to COVID-19<sup>4</sup>. However, the causes of their poor prognosis are not clearly understood. In addition, the actual situation in Japan, which has an insurance system with a well-developed public health checkup system, has not been previously reported.

Poor glycemic control during hospitalization has been associated with severe conditions and death in patients with COVID-19<sup>5</sup>, while glycemic control in COVID-19 patients with diabetes

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is extremely difficult. SARS-CoV-2 can not only potentially cause impaired insulin secretion, but can lead to severe insulin resistance<sup>6,7</sup>. In particular, after the addition of glucocorticoids to the treatment protocol for severe COVID-19, the difficulty in glycemic control was reported to be even more pronounced<sup>8</sup>. Untreated diabetes patients who were identified as having diabetes for the first time on admission are predicted to have difficulty in managing hyperglycemia after admission, but the detailed features of glucocorticoid-induced hyperglycemia in patients with newly diagnosed diabetes have not been shown to date.

Therefore, we carried out a retrospective observational study to show the features and outcomes of COVID-19 patients with newly diagnosed diabetes in Japan. In addition, we examined the characteristics of plasma blood glucose trends in patients after glucocorticoid initiation.

## MATERIALS AND METHODS

### Study design and participants

The present retrospective observational study was carried out at the National Center for Global Health and Medicine (NCGM) in Tokyo, Japan, which is one of the national designated institutions where severe COVID-19 patients were gathered during the pandemic. We retrospectively analyzed 62 patients with diabetes hospitalized for COVID-19 between 1 April and 18 August 2021 at the NCGM. The diagnosis of COVID-19 was based on the positivity of SARS-CoV-2 in real-time reverse transcription polymerase chain reaction.

The protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The study protocol was approved by the institutional review board of the National Center for Global Health and Medicine, Tokyo, Japan (approval number: NCGM-S-004328-00).

### Data collection

We collected the following information from electronic medical records: demographic data, comorbidities, vital signs and laboratory findings at admission. Laboratory findings included blood count, liver and kidney function tests, glycated hemoglobin (HbA1c) levels, coagulation profile, and inflammatory markers. We also recorded trends of biomarkers (lactate dehydrogenase [LDH] and C-reactive protein [CRP]) during the first 7 days of hospitalization. Other data included prognosis (death, discharge or hospital transfer), treatment regimens of COVID-19 (systemic corticosteroids, remdesivir, tocilizumab, baricitinib and heparin) and respiratory support (e.g., nasal or mask, high-flow nasal cannula, non-invasive positive pressure ventilation and invasive ventilation). Systemic corticosteroid regimens, including methylprednisolone therapy (intravenous, 2 mg/kg–1000 mg daily for 3–5 consecutive days with gradual tapering) and dexamethasone (oral or intravenous, 6 mg daily for 7–10 consecutive days), were chosen by the specialist in infection and respiratory care based on the severity of respiratory failure. Methylprednisolone therapy is often used in critical cases.

### Definition of COVID-19 severity

The primary outcome was that of the worst severity of COVID-19 during hospitalization. The severity of COVID-19 was categorized into four levels as critical, severe, moderate and mild. Specifically, patients were defined as in a critical condition if they required non-invasive positive pressure ventilation or invasive ventilation<sup>9</sup>, and as in a severe condition if they had clinical signs of pneumonia (fever, dyspnea, cough and tachypnea) accompanied by one of the following: respiratory rate >30 breaths/min, severe respiratory distress or oxygen saturation (SpO<sub>2</sub>) <90% on room air. A moderate condition referred to the presence of fever and respiratory symptoms with radiological findings of pneumonia. A mild condition was defined as mild clinical symptoms without any sign of pneumonia on imaging. We also evaluated the clinical outcomes, including death, alive discharge and hospital transfer.

### Definition of diabetes and glycemic control

In the present study, diabetes was categorized into two types: newly diagnosed diabetes and pre-existing diabetes. Newly diagnosed diabetes was defined as having both HbA1c  $\geq$ 6.5% (48 mmol/mol) and fasting plasma glucose  $\geq$ 126 mg/dL (7.0 mmol/L) or random blood glucose  $\geq$ 200 mg/dL (10.0 mmol/L) on admission with no prior history of diabetes. Pre-existing diabetes was defined based on self-reported history of diabetes, prior medical records before admission, reporting a diagnosis of diabetes or treatment with glucose-lowering medications.

We measured plasma glucose levels before each meal and at bedtime with a glucometer. Based on these data during the first week of hospitalization, we calculated the percentage of time, including time per day, within the target glucose range (time in range [TIR] 70–180 mg/dL; 3.9–10.0 mmol/L) and time above target glucose range (time above range [TAR] >180 mg/dL; >10.0 mmol/L). The validity of TIR and TAR using intermittent blood glucose measurements were reported previously<sup>10</sup>. We also collected data on preadmission and in-hospital glycemic management practices. In-hospital glycemic control was carried out by diabetologists through daily assessment of glycemic patterns, and adjusting basal, nutritional and correctional insulin doses accordingly. Depending on the decision of the diabetologist, continuous intravenous insulin infusion and/or glucose-lowering medications were used.

### Statistical analysis

Continuous variables were reported as the mean  $\pm$  standard deviation or median (interquartile range), and categorical variables were reported as percentages. Differences in clinical characteristics between groups were assessed by the Student's *t*-test or  $\chi^2$ -test for continuous and categorical variables, respectively. Statistical significance was set at  $P < 0.05$ . Statistical analyses were carried out using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing,

Vienna, Austria)<sup>11</sup>. Dynamic graphs of plasma glucose levels, LDH and CRP were drawn using Python (version 3.8, Python Software Foundation, Wilmington, DE, USA) programming language modules: Pandas, NumPy, Matplotlib and Seaborn.

## RESULTS

### Population characteristics

The present study included 62 confirmed COVID-19 patients with diabetes, including 19 patients with newly diagnosed diabetes and 43 patients with pre-existing diabetes. Amongst the latter, most patients with pre-existing diabetes had type 2 diabetes ( $n = 39$ ). There were two patients with type 1 diabetes, and one case each of gestational and pancreatic diabetes. The general characteristics of the study population are given in Table 1. Patients with newly diagnosed diabetes were significantly younger, and had fewer comorbidities of hypertension and dyslipidemia than those with pre-existing diabetes. There were no significant differences in sex or body mass index. From the laboratory examination at admission, patients with newly diagnosed diabetes had significantly higher mean values of HbA1c levels, aspartate aminotransferase, alanine

aminotransferase, LDH and CRP, and lower mean values of serum albumin than patients with pre-existing diabetes. The proportion of patients with newly diagnosed diabetes was higher in the younger age groups of both sexes than in the older age groups (Figure S1).

### Clinical outcomes of COVID-19

Table 2 presents the treatment and outcomes. Overall, 93.5% of the hospitalized patients at our institution were grouped as critical or with severe conditions and with the worst severity of COVID-19, just 6.5% were moderate, and no cases were mild. The mortality rate in the present study population was 9.6%. Patients with newly diagnosed diabetes progressed significantly more frequently to critical conditions during their hospitalization than patients with pre-existing diabetes (52.6% vs 20.9%,  $P = 0.018$ ). In the analysis of only patients with type 2 diabetes, as shown in Tables S1 and S2, the background of patients and clinical outcomes were similar to that of the overall population. Patients with newly diagnosed diabetes were also more frequently treated with methylprednisolone therapy and tocilizumab than patients with pre-existing diabetes.

**Table 1** | Patient characteristics

	Total ( $n = 62$ )	Newly diagnosed diabetes ( $n = 19$ )	Pre-existing diabetes ( $n = 43$ )	<i>P</i>
Age (years)	58.0 ± 14.2	51.5 ± 13.3	60.8 ± 13.8	0.015
Sex male, <i>n</i> (%)	47 (75.8)	15 (78.9)	32 (74.4)	1
BMI (kg/m <sup>2</sup> )	28.2 ± 5.7	28.2 ± 6.0	28.2 ± 5.6	0.998
Comorbidities, <i>n</i> (%)				
Hypertension	36 (58.1)	4 (21.1)	32 (74.4)	<0.001
Dyslipidemia	29 (46.8)	3 (15.8)	26 (60.5)	0.002
Coronary artery disease	5 (8.1)	0 (0.0)	5 (11.6)	0.312
Cerebrovascular disease	5 (8.1)	0 (0.0)	5 (11.6)	0.312
Past or current smoking	24 (38.7)	8 (42.1)	16 (37.2)	0.781
Laboratory at admission				
Plasma glucose, mg/dL	233.0 ± 144.6	232.2 ± 94.7	233.4 ± 162.8	0.977
HbA1c (%)	8.1 ± 1.7	8.9 ± 2.2	7.8 ± 1.3	0.018
HbA1c (mmol/mol)	65 ± 19	74 ± 24	62 ± 14	0.018
Serum albumin (g/dL)	3.3 ± 0.5	3.1 ± 0.4	3.4 ± 0.6	0.045
AST (U/L)	60.4 ± 36.8	75.2 ± 28.3	53.9 ± 38.5	0.035
ALT (U/L)	48.7 ± 32.2	61.2 ± 32.6	43.2 ± 30.8	0.041
LDH (U/L)	424.9 ± 215.7	589.3 ± 256.6	352.3 ± 147.5	<0.001
Serum creatinine (μmol/L)	97.3 ± 61.9	97.3 ± 70.7	79.6 ± 44.2	0.360
Lymphocyte count (μL)	940.5 ± 415.3	1049.6 ± 439.4	892.3 ± 400.0	0.171
Neutrophil count (μL)	4795.7 ± 2675.2	5510.6 ± 2890.6	4479.7 ± 2545.6	0.164
CRP (mg/dL)	8.3 ± 6.7	11.1 ± 7.4	7.1 ± 6.2	0.033
D-dimer (μg/mL)	8.0 ± 29.7	5.2 ± 15.9	9.2 ± 34.2	0.629
Parameters at admission				
Systolic blood pressure (mmHg)	127.2 ± 20.2	131.3 ± 18.2	125.3 ± 21.0	0.286
Body temperature (degrees)	37.7 ± 1.0	38.0 ± 1.0	37.5 ± 0.9	0.068
Oxygen saturation (%)	92.2 ± 5.8	92.5 ± 6.2	92.1 ± 5.7	0.826
Oxygen concentration (L)	3.7 ± 4.5	6.0 ± 4.8	2.7 ± 4.0	0.009

Data are expressed as number and percentage or mean ± standard deviation. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; BMI, body mass index; HbA1c, glycated hemoglobin; LDH, lactate dehydrogenase.

**Table 2** | Coronavirus disease 2019 therapies and outcomes

	Total (n = 62)	Newly diagnosed diabetes (n = 19)	Pre-existing diabetes (n = 43)	P
Worst severity classification of COVID-19, n (%)				
Critical	19 (30.6)	10 (52.6)	9 (20.9)	0.018
Severe	39 (62.9)	9 (47.4)	30 (69.8)	0.153
Moderate	4 (6.5)	0 (0)	4 (9.3)	0.303
Outcomes, n (%)				
Death	6 (9.6)	2 (10.5)	4 (9.3)	1
Discharged alive	52 (83.9)	16 (84.2)	36 (83.7)	1
Transferred	4 (6.5)	1 (5.3)	3 (7.0)	1
Worst route of oxygen delivery, n (%)				
No oxygen demand	4 (6.5)	0 (0.0)	4 (9.3)	0.303
Nasal or mask	26 (41.9)	6 (31.6)	20 (46.5)	0.403
High flow nasal cannula	13 (21.0)	3 (15.8)	10 (23.3)	0.737
Non-invasive positive pressure ventilation	14 (22.6)	9 (47.4)	5 (11.6)	0.006
Invasive ventilation	5 (8.1)	1 (5.3)	4 (9.3)	1
Glucocorticoids				
Methylprednisolone therapy	32 (51.6)	14 (73.7)	18 (41.9)	0.028
Dexamethasone	30 (48.4)	5 (26.3)	25 (58.1)	0.028
Others, n (%)				
Remdesivir	53 (85.5)	17 (89.5)	36 (83.7)	0.709
Tocilizumab	18 (29.0)	10 (52.6)	8 (18.6)	0.013
Baricitinib	14 (22.6)	4 (21.1)	10 (23.3)	1
Heparin	51 (82.3)	18 (94.7)	33 (76.7)	0.149

Data are expressed as number and percentage. COVID-19, coronavirus 2019.

As shown in Figure 1, both LDH and CRP levels at admission were higher in patients with newly diagnosed diabetes than in patients with pre-existing diabetes. Thereafter, the LDH level of patients with newly diagnosed diabetes gradually decreased, whereas the LDH level of patients with pre-existing diabetes remained high and subsequently exceeded that of the former in the latter half of the initial 2 weeks of admission. The CRP levels consistently decreased in patients in both groups.

### Glycemic control

As shown in Table 3, patients with newly diagnosed diabetes had significantly higher average plasma blood glucose for the initial 3 days after admission, higher TAR (>180 mg/dL; 10.0 mmol/L) for the first 5 days, and lower TIR (target range 70–180 mg/dL; 3.9–10.0 mmol/L) for the first 5 days than those with pre-existing diabetes. As shown in Figure 2, the dynamics of blood glucose levels showed a pattern of postprandial hyperglycemia exacerbation throughout the first week of hospitalization. During the initial 3 days after admission, the fasting blood glucose level was extremely difficult to control, especially in patients with newly diagnosed diabetes.

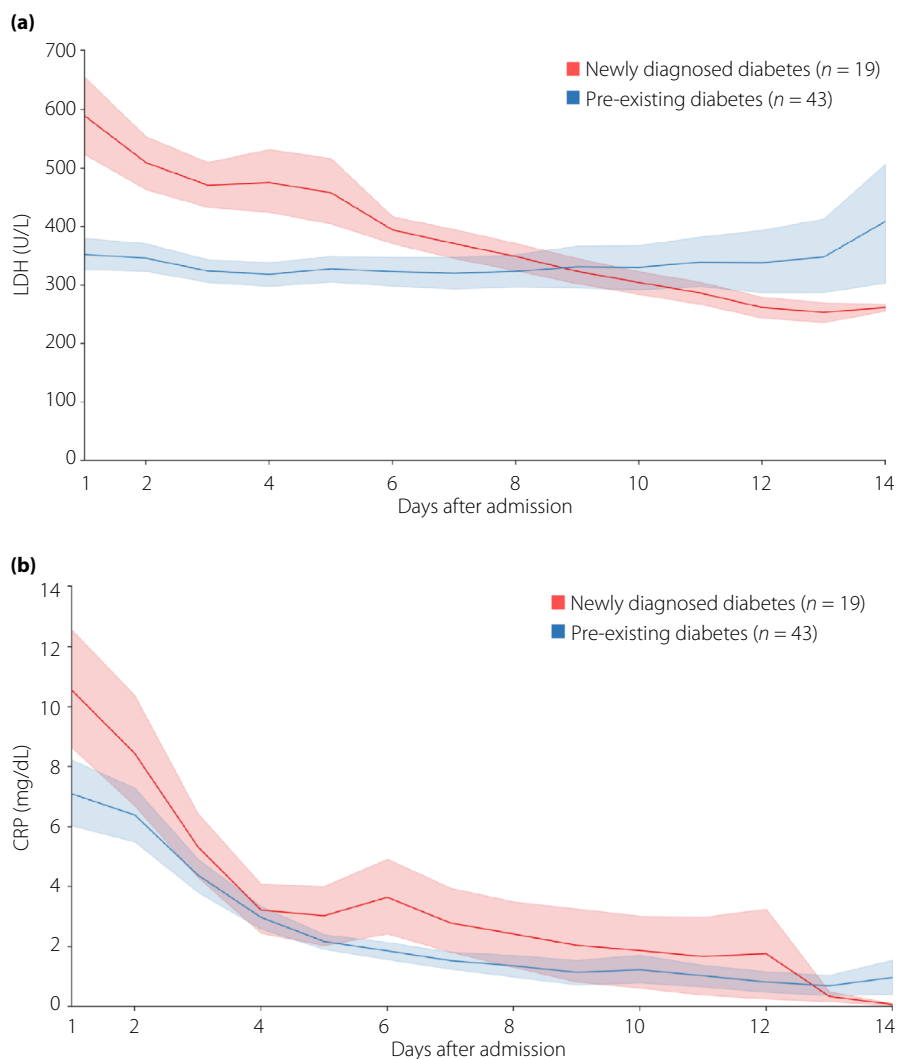
As for the treatment of diabetes, 16.7% of patients with pre-existing diabetes received insulin injections (Table S3). After admission, the total daily insulin units were not significantly different between newly-diagnosed and pre-existing diabetes, and for both groups the mean dose was >0.3 units/kg/day during the first week of hospitalization (Table S4). Continuous

intravenous insulin infusion was carried out only in patients with pre-existing diabetes and not in patients with newly diagnosed diabetes.

### DISCUSSION

The present study showed that among COVID-19 patients with diabetes who were admitted to our hospital, >30% were newly diagnosed with diabetes after admission, and they had a higher severity of COVID-19 and had difficulty in managing glycemic control during the first week of hospitalization compared with patients with pre-existing diabetes. We speculated that patients with newly diagnosed diabetes did not have an opportunity to receive treatment for diabetes before hospitalization; undiagnosed diabetes caused untreated exposure to hyperglycemia that might have contributed to the progression of organ damage and respiratory failure induced by the virus.

COVID-19 infection leads to decreased expression of angiotensin-converting enzyme 2 (ACE2), consequently leading to increased inflammation, cell damage and respiratory failure<sup>12</sup>. Chronic hyperglycemia leads to decreased ACE2 expression, which has a protective effect against inflammation, making cells more vulnerable to the inflammatory damage of the virus<sup>6</sup>. Hyperglycemia also worsens the respiratory system due to its effect on lung volume and diffusing capacity<sup>13</sup>. We found that patients with newly diagnosed diabetes had higher levels of HbA1c and inflammatory markers, including CRP and LDH, and required more oxygen on admission than patients with



**Figure 1** | Dynamic trajectories of median (a) lactate dehydrogenase (LDH) and (b) C-reactive protein (CRP) levels during the initial 2 weeks of hospitalization, with interquartile ranges by shaded regions, in patients with newly diagnosed diabetes (red) or patients with pre-existing diabetes (blue).

pre-existing diabetes. Overall, the present results were consistent with previous reports showing that newly diagnosed diabetes is associated with a higher risk of patients being critically ill with COVID-19<sup>4,13–15</sup>.

In our population, patients with pre-existing diabetes had a significantly lower HbA1c than patients with newly-diagnosed diabetes, suggesting that their relatively good glycemic control due to the previous treatment for diabetes might have influenced the relatively mild severity of COVID-19. Even though we had many patients in critical condition and although vaccination was not yet widely available during the study period, the deterioration in patient outcome was fortunately lower than that reported in previous studies, with fewer deaths<sup>16,17</sup>. Presumably, one of the reasons for fewer deaths is that our hospital is a nationally designated medical institution for infectious

diseases and has many specialists with extensive experience, including glucocorticoid therapy for severe or critical cases of COVID-19.

The association between hyperglycemia and poor prognosis of COVID-19 has been reported in several studies<sup>5</sup>. Although several reports have shown that COVID-19 patients with diabetes, especially those treated with glucocorticoids, have difficulty with glycemic control after hospitalization and require a large amount of insulin<sup>18–20</sup>, we focused on newly diagnosed diabetes and showed for the first time the detailed features of glucocorticoid-induced hyperglycemia in COVID-19 patients with newly diagnosed diabetes.

We experienced great difficulty in managing hyperglycemia during the first week of hospitalization in patients with newly diagnosed diabetes. TIR and TAR in patients with newly



**Table 3** | Glycemic control throughout the first week of hospitalization

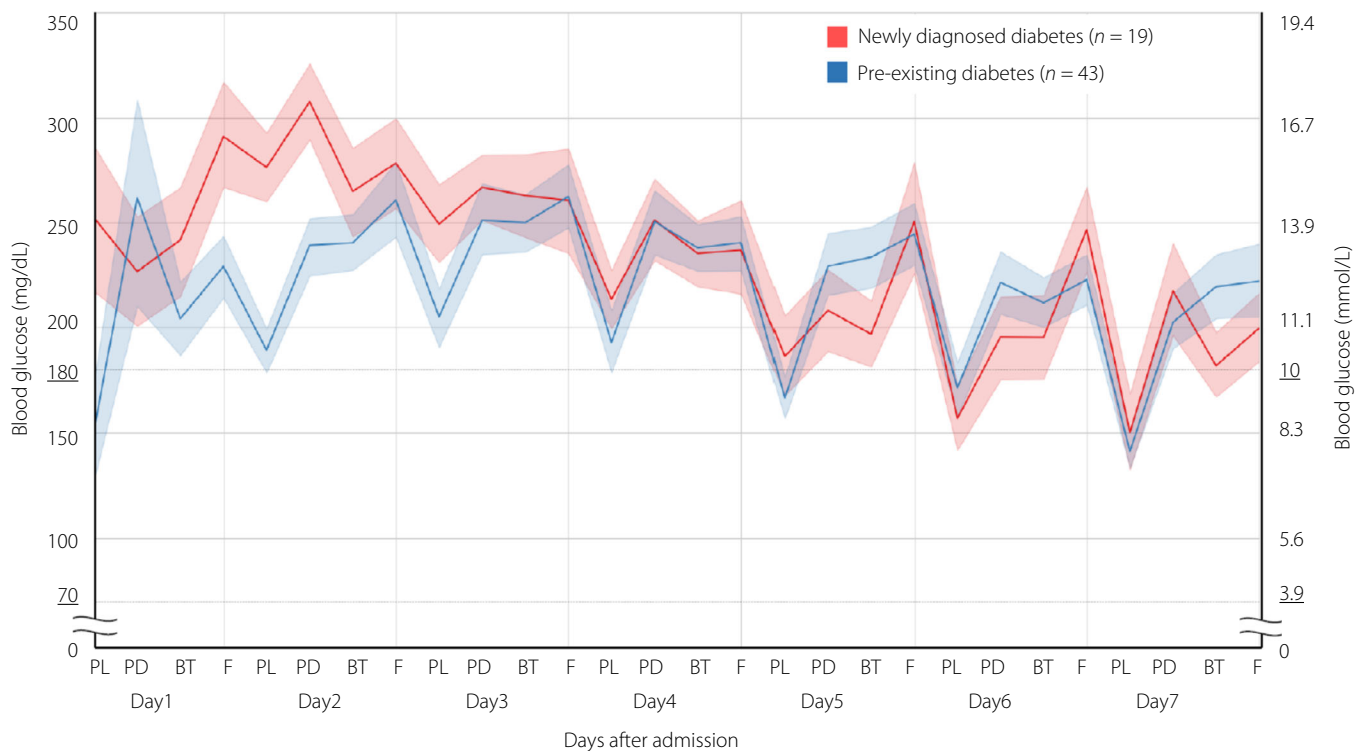
	Newly diagnosed diabetes (n = 19)	Pre-existing diabetes (n = 43)	P
Average plasma glucose (mg/dL)			
3 days	267.6 ± 48.3	233.0 ± 64.2	0.040
5 days	249.2 ± 41.2	229.0 ± 49.8	0.126
7 days	233.6 ± 39.5	220.2 ± 43.0	0.252
TAR >180 mg/dL (10.0 mmol/L), %			
3 days	88.9 ± 13.5	67.5 ± 28.3	0.003
5 days	80.3 ± 18.5	67.5 ± 24.6	0.047
7 days	72.8 ± 19.7	64.2 ± 22.9	0.162
TIR 70–180 mg/dL (3.9–10.0 mmol/L), %			
3 days	11.1 ± 13.5	33.8 ± 29.4	0.002
5 days	19.7 ± 18.5	33.2 ± 24.9	0.039
7 days	27.6 ± 20.1	35.9 ± 23.3	0.184

Data are expressed as mean ± standard deviation. PG, plasma glucose level; TAR, time above range; TIR, time in range.

diagnosed diabetes were very low and high, respectively, even though these indicators are known to be lower when assessed by the point-of-care than by continuous glucose monitoring<sup>10</sup>. There are several possible reasons for this finding. First, patients with newly diagnosed diabetes had higher HbA1c levels on admission than patients with pre-existing diabetes,

and their hyperglycemia was left untreated just before the diagnosis of diabetes, resulting in a severe state of glucotoxicity. Glucotoxicity might have caused high insulin resistance and progressive loss of pancreatic β-cell function in patients with newly diagnosed diabetes<sup>21</sup>. Second, high-dose glucocorticoid therapy administered to patients with more than moderate conditions of COVID-19 caused marked hyperglycemia. The dynamics of blood glucose levels that showed postprandial hyperglycemia were typical of glucocorticoid-induced hyperglycemia. Third, the diabetogenic influence of COVID-19 might also be considered<sup>4,22</sup>. SARS-CoV-2 might cause acute impairment of insulin secretion by binding to ACE2 receptors on β-cells, and might also damage β-cells by increasing the levels of inflammatory cytokines<sup>7</sup>. As the ACE2 receptor is expressed in the liver, adipose tissue and skeletal muscle, binding of SARS-CoV-2 to these receptors might impair the response to insulin<sup>7</sup>. In the present study, we did not collect data on insulin secretion or resistance, although we certainly required a very large amount of insulin. These findings highlight the difficulty of achieving good glycemic control at the initial stage of hospitalization; therefore, it is desirable to develop better methods of glycemic control for critical COVID-19 patients.

Under the pandemic with limited medical resources, methods of glycemic control that can reduce the direct contact with



**Figure 2** | Dynamic trajectories of median blood glucose levels throughout the first week of hospitalization, with interquartile ranges by shaded regions, in patients with newly diagnosed diabetes (red) or patients with pre-existing diabetes (blue). Point-of-care glucose levels were checked at fasting (F), prelunch (PL), predinner (PD) and bedtime (BT). The target range of blood glucose levels was between 70 and 180 mg/dL; 3.9 and 10.0 mmol/L (underlined).

COVID-19 patients are required<sup>18</sup>, so we mainly used subcutaneous injections of basal and bolus insulin. We monitored glycemic patterns to adjust the basal and bolus insulin, according to food intake and use of glucocorticoids. The degree of blood glucose elevation due to the direct effects of COVID-19 and glucocorticoids varied greatly among individuals, making it difficult to create a fixed regimen<sup>22</sup>. Several protocols for the control of dexamethasone-induced hyperglycemia and the use of remote continuous glucose monitoring have been attempted<sup>20,23</sup>.

Finally, in patients with newly diagnosed diabetes, the delay in recognizing the presence of diabetes delayed diabetologists' intervention, which might have affected their poor glycemic control, presumably leading to the severe condition of COVID-19.

In the present study, the proportion of patients with newly diagnosed diabetes was 32.8% of hospitalized COVID-19 patients with type 2 diabetes. All patients with newly diagnosed diabetes presented with HbA1c  $\geq 6.5\%$ , which means that they most likely had undiagnosed diabetes, rather than being affected by COVID-19 infection per se, acute metabolic stress or medications after admission. In a meta-analysis of eight studies, the proportion of newly diagnosed diabetes was 14.4%<sup>4</sup>, which was 31.4% in another Mexican study<sup>16</sup>.

As Japan has a well-developed health screening system and a universal health insurance system that covers all its citizens, thus achieving the longest healthy life expectancy<sup>24,25</sup>, it is surprising that many patients with newly diagnosed diabetes were found. In addition, it is worth noting that there were more patients with newly diagnosed diabetes among younger people of both sexes. In Japan, the proportion of people who failed to visit a hospital despite being diagnosed with glucose intolerance during a health checkup or interrupted a hospital visit, is high among young people, according to research by the Japan Diabetes Intervention Trial-2 (J-DOIT 2) and the Ministry of Health, Labor and Welfare<sup>26,27</sup>. Therefore, we consider it essential to encourage patients to visit a hospital promptly to prevent worsening COVID-19 prognosis.

The present study had some limitations. Because our hospital had the role of an advanced medical institution under the pandemic, many severe and critical cases were accumulated; thus, this study did not include the data of patients with mild cases. In addition, as we did not deal with data from patients without diabetes, we could not compare the data between patients with and without diabetes.

In conclusion, the present study suggests that the proportion of COVID-19 patients who are newly diagnosed with diabetes is high, and that they have a higher risk of developing severe disease than those with pre-existing diabetes. It might be plausible that at the point of COVID-19 diagnosis, blood glucose and HbA1c levels first be assessed in all patients.

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## DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: The study protocol was approved by the Institutional Review Board of the National Center for Global Health and Medicine, Tokyo, Japan (approval number: NCGM-S-004328-00, approval date: 21 October 2021). Informed consent: We applied the opt-out method to obtain consent for this study.

Approval date of registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S1** | Proportion of patients with newly diagnosed and pre-existing diabetes classified by sex and age in the 100% stacked column graph.

**Table S1** | Patient characteristics (only patients with type 2 diabetes).

**Table S2** | Coronavirus disease 2019 therapies and outcomes (only patients with type 2 diabetes).

**Table S3** | Preadmission treatments, *n* (%).

**Table S4** | In-hospital management of diabetes.