Impact on Diabetes Management of the Restrictions of Social Participation to Combat the COVID-19 Pandemic at a Single Facility in Japan: A Retrospective, Observational Study

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Research article

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Abstract

Background: The aim of this study was to clarify the impact of limitations of activity due to the COVID-19 pandemic on diabetes management.

Methods: To clarify the impacts of the emergency declared on April 7 2020, 345 patients, 1109 patients, and 752 patients whose HbA1c levels were measured in both March and April, May, or June were selected. The patients to be compared were selected from the 2019 data under the same conditions. In 2019, 469 patients, 1315 patients, and 783 patients whose HbA1c levels were measured in both March and April, May, or June were selected. The impact of restricted activity on diabetes management due to the declared emergencies was assessed by comparing HbA1c levels in April, May, and June minus the HbA1c levels in March of both 2019 and 2020. Subjects with a difference in HbA1c levels greater than 0 were defined as "worsened", and subjects with a difference in HbA1c levels less than or equal to 0 were defined as "improved". The deterioration rate and the improvement rate of the HbA1c level in 2019 and 2020 were compared by the Chi-squared test. Second, the linear trends of HbA1c from April to June between 2019 and 2020 were calculated by mixed model repeated measures ANOVA.

Results: There were more patients with worsening HbA1c levels from March to April in 2020 than in 2019: 122 (26.0%) vs. 137 (39.7%), $p<0.01$. There were more patients with improved HbA1c levels from March to June in 2020 than in 2019: 478 (61.0%) vs. 512 (68.1%), $p<0.01$. Patients with improved HbA1c levels between March and May showed no significant difference between 2020 and 2019: 814 (61.9%) vs. 713 (64.3%), $p=0.23$. Slopes of HbA1c levels from April to June in 2019 and 2020 were -0.0024 (-0.0039, -0.0009) and -0.0099 (-0.0117 -0.0081), respectively. There were significant differences in the slopes -0.0075 (-0.0097, -0.0053), $p<0.01$) between the years.

Conclusions: HbA1c levels did not appear to show persistent deterioration during the observational period in 2020. Meanwhile, some diabetic patients may have shown both improved and worsened diabetes control during the COVID-19 pandemic.

Background

Coronavirus disease 2019 (COVID-19) is a disease associated with a variety of serious conditions caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Due to the COVID-19 pandemic, there were approximately 15 million people infected and more than 610,000 deaths worldwide at the time of writing [1]. Many countries around the world established urban blockades and other measures to prevent the spread of the disease. In Japan, a state of emergency was also declared, and stricter restrictions on activities were required from April 7, 2020 [2]. As a result, various activities of Japanese people were restricted until May 25, 2020, when the declaration of the state of emergency was lifted [3, 4]. People affected by activity restrictions also include patients with diabetes mellitus. As is widely known, proper exercise is required for diabetes management [5]. Many physical changes occur with proper exercise; weight loss and increased muscle mass play an important role in improving insulin sensitivity and improving diabetes management [6].

Since the declaration of the state of emergency, there was a decrease in the number of visits to medical institutions, and many patients with lifestyle-related diseases have had to change their lifestyles. However, the impact of nationwide activity restrictions on diabetes management remains unclear. The aim of this study was to clarify the impact of this set of activity restrictions on diabetes management in diabetic patients.

Methods

Study design and participants

This retrospective, observational study was based on data from patients who visited the Diabetes and Endocrine Clinics of Juntendo University Hospital from March to June 2019 and/or from March to June 2020 and were prescribed antidiabetic drugs and/or were diagnosed with diabetes mellitus. Hemoglobin A1c (HbA1c) levels measured during the observation period of the eligible patients were collected and anonymized through the Data WareHouse attached to the electronic medical record in collaboration with the Center for Promotion of Data Science. Most of the subjects of the study were living in urban areas of Japan. A total of 16,936 HbA1c tests were collected from 5,867 subjects during the period.

Experimental Design

Outcomes

The main analysis compared changes in HbA1c levels from March to June 2020 with changes in HbA1c levels over the same period in 2019 to assess the impact of limitation of activity and restriction of social participation during the COVID-19 pandemic.

Data handling and statistical analysis

In this section, the methodology is presented. Initially, 4,555 patients eligible for March-June 2020 and 5,132 patients eligible for March-June 2019 were included. The method of data handling for the analysis is shown in Figure 1. To clarify the impacts of the state of emergency declared on April 7, 2020, 345 patients whose HbA1c levels were measured in both March and April, 1,109 patients whose HbA1c levels were measured in both March and May, and 752 patients whose HbA1c levels were measured in both March and June were selected. The patients to be compared were selected from the 2019 data under the same conditions. In 2019, 469 patients whose HbA1c levels were measured in both March and April, 1,315 patients whose HbA1c levels were measured in both March and May, and 783 patients whose HbA1c levels were measured in both March and June were selected. For HbA1c levels measured multiple times in the same subject in a month, their mean values were calculated. The impact of restricted activity on diabetes management due to the declared state of emergency was assessed by comparing HbA1c levels in April, May, and June minus HbA1c levels in March in both 2019 and 2020. Obtained HbA1c level differences were compared by the Wilcoxon rank-sum test. In addition, subjects with a difference in HbA1c levels greater than 0 were defined as “worsened”, and subjects with a difference in HbA1c levels less than or equal to 0 were defined as “improved”. The deterioration rate and the improvement rate of HbA1c levels in 2019 and 2020 were compared by the Chi-squared test. Second, the linear trends of HbA1c from April to June between 2019 and 2020 were calculated by mixed model repeated measures ANOVA. In this model, a compound symmetry covariance structure was used to model a serial correlation of repeated measurements, and an unstructured covariance matrix was specified for random regression coefficients (intercept and slope). Overall slopes in each year and the difference in slopes between 2019 and 2020, and a corresponding 95% confidence interval of slopes, were calculated. This analysis was performed with the following data: 6,928 HbA1c levels of 4,813 subjects who were prescribed antidiabetic medicines or had a diagnosis of diabetes from April to June 2019, and 5,552 HbA1c levels of 4,135 subjects who were prescribed antidiabetic medicines or had a diagnosis of diabetes from April to June 2020. All statistical analyses were performed using SAS 9.4 for Windows (SAS Institute Inc., Cary, NC).

Results

Table 1 shows a comparison of the changes in HbA1c levels between 2019 and 2020. Continuous variables are presented as medians (minimum, maximum).

Table 1
Changes in HbA1c before and after the start of activity restriction

	March	April	May	June	Difference in HbA1c levels	p value*
HbA1c levels in 2019 (%)	7.6 (5.3, 15,0)	7.4 (5.2, 13.8)			-0.1 (-4.6, 3.2)	
HbA1c levels in 2020 (%)	7.5 (4.9, 16.2)	7.5 (5.1, 14.0)			0.0 (-3.7, 1.8)	< 0.01
HbA1c levels in 2019 (%)	7.2 (5.2, 15.0)		7.2 (4.5, 14.6)		0.0 (-4.9, 3.6)	
HbA1c levels in 2020 (%)	7.2 (5.1, 14.0)		7.2 (5.0, 14.6)		0.0 (-5.5, 2.3)	0.93
HbA1c levels in 2019 (%)	7.2 (5.2, 15.0)			7.1 (5.3, 14.3)	0.0 (-7.5, 3.7)	
HbA1c levels in 2020 (%)	7.1 (4.9, 14.0)			7.0 (5.0, 14.0)	-0.1 (-6.3, 3.1)	0.07

Median (min, max), Differences in HbA1c levels were calculated by subtracting the values in April, May, or June from the values in March. * Using the Wilcoxon rank-sum test.

Table 2 shows changes in diabetes management between 2019 and 2020.

Table 2
Changes in diabetes management before and after the start of activity restriction

	Worsened	Improved	p value†
March to April			
Subjects in 2019 (n)	122 (26.0)	347 (74.0)	
Subjects in 2020 (n)	137 (39.7)	208 (60.3)	< 0.01
March to May			
Subjects in 2019 (n)	501 (38.1)	814 (61.9)	
Subjects in 2020 (n)	396 (35.7)	713 (64.3)	0.23
March to June			
Subjects in 2019 (n)	305 (39.0)	478 (61.0)	
Subjects in 2020 (n)	240 (31.9)	512 (68.1)	< 0.01

Differences in HbA1c levels higher than 0 were defined as worsened; differences in HbA1c levels 0 or lower were defined as improved. †Using the Chi-squared test.

Changes in HbA1c levels from March to April were worse in 2020 than in 2019, with an HbA1c difference in 2019 of -0.1 (-4.6, 3.2) vs a difference in 2020 of 0.0 (-3.7, 1.8) ($p < 0.01$). In addition, there were more patients with worsening HbA1c levels from March to April in 2020 than in 2019, as follows: in 2019, 122 (26.0%) vs in 2020, 137 (39.7%) ($p < 0.01$). Changes in HbA1c levels from March to June were improved in 2020 compared to 2019, with an HbA1c difference in 2019 of 0.0 (-7.5, 3.7) vs a difference in 2020 of -0.1 (-6.3, 3.1) ($p = 0.07$). In addition, there were more patients with improved HbA1c levels from March to June in 2020 than in 2019, as follows: in 2019, 478 (61.0%) vs in 2020, 512 (68.1%), $p < 0.01$. Changes in HbA1c levels from March to May were not significantly different in 2020 compared to 2019, with an HbA1c difference in 2019 of 0.0 (-4.9, 3.6) vs a difference in 2020 of 0.0 (-5.5, 2.3) ($p = 0.93$). In addition, patients with improved HbA1c levels from March to May did not show a significant difference between 2020 and 2019, as follows: in 2019, 814 (61.9%) vs in 2020, 713 (64.3%) ($p = 0.23$). Second, the changes in HbA1c levels between 2019 and 2020 are shown below as a comparison of slopes. Slopes of HbA1c levels from April to June in 2019 and 2020 were − 0.0024 (-0.0039, -0.0009) and − 0.0099 (-0.0117 -0.0081), respectively, with a significant difference in the slopes − 0.0075 (-0.0097, -0.0053), $p < 0.01$) between the years.

Discussion

Short-term changes in HbA1c levels showed no persistent deterioration during the COVID-19 pandemic and the declaration of a state of emergency in Japan. On the other hand, changes in HbA1c levels appeared to show a temporary deterioration and a slight improvement trend after the declaration of a state of emergency, and some diabetic patients may have been affected by the COVID-19 pandemic and various related restrictions on social activities. To the best of our knowledge, this is the first observational study to clarify the impact of social activity restriction as a countermeasure against the COVID-19 pandemic on diabetes management in Japan.

Behavior changes may be brought about by government or social demands, or they may be due to the anxiety and stress caused by the COVID-19 pandemic [7, 8]. It has been pointed out that the use of lockdowns to combat the COVID-19 pandemic can have serious adverse effects on other health indicators, including obesity [9]. Changes in diabetes management before and after the lockdown are controversial, with reports of both worsening and improvement [10–13]. Ghosal et al. reported a simulation model that predicted worsening diabetes management with a lockdown, and Verma et al. reported worsening management of type 1 diabetes in India due to a lack of insulin/glucostrips [10, 11]. On the other hand, Fernández et al. and Bonora et al. reported improved diabetes control in patients with type 1 diabetes during lockdowns in Spain and Italy, respectively [12, 13]. They speculated that the increased time spent on self-management, generated by stopping work or reducing daily routine activity during the lockdown, may contribute to improving diabetes control. The present results suggest that overall diabetes management did not show persistent deterioration, but that some diabetic patients had worse or better diabetes control. The Japanese government requested Japanese people to restrict various social activities. Although these measures were voluntary, activity restrictions in Japan included refraining from eating out, stopping various events, starting work from home, refraining from domestic travel, etc. These restrictions of social participation caused a temporary decrease in daily workload and a decrease in the amount of alcohol intake associated with eating out. These activity changes may have provided the Japanese with different ways of using their time. Some diabetic patients who had more time to spend on diabetes management could have contributed to the increased improvement in HbA1c levels in June 2020.

It was also noted that the proportion of patients with deterioration of diabetes management in April 2020 increased compared to April 2019. Since the state of emergency was declared on April 7, 2020, this exacerbation may reflect diabetes management from February to March 2020. The anxiety and stress posed by COVID-19 prior to restrictions of social participation may have caused worsening diabetes management. Restrictions of various social activities and anxiety and stress from the COVID-19 pandemic appear to have diverse implications for short-term diabetes management.

Large-scale population behavior changes are required to reduce the transmission of COVID-19. Changes have already begun, either actively or passively, and diabetic patients can be affected both positively and negatively. The phenomena that occur in the process of these changes give us warnings and hints, which we need to be aware of, and we must seek a better approach to diabetes treatment.

Limitations

The present study has several limitations. The first limitation is that only one medical institution was involved. This facility is a university hospital in a metropolitan area in Japan, and there may have been bias in subject selection. The number of medical institutions involved should be increased to obtain more general results. Second, the activity of individual subjects was not observed directly. Changes in behaviors of subject diabetic patients after activity restriction are unclear. A direct questionnaire survey should be conducted to clarify what kind of behavioral changes have occurred in patients with diabetes. Lastly, the results presented in this study only show short-term changes in diabetes management. The declaration of a state of emergency continued from April 7, 2020 to May 25, 2020 in Japan. The amount of social activity of Japanese people seems to have recovered since June 2020. The long-term impact of changes in social activity and social structure due to the COVID-19 pandemic on patients with diabetes is still unknown. Long-term observational studies of diabetes management are needed.

Conclusions

The present results did not suggest a persistent deterioration in diabetes control during the period of social activity restriction due to the COVID-19 pandemic and the declaration of a state of emergency. On the other hand, some diabetic patients may have shown both better and worse diabetes control during the COVD-19 pandemic and the associated social changes. The COVID-19 pandemic continues to force various social changes. We need to be aware of the impact of the resulting long-term social changes on diabetes management.

List Of Abbreviations

COVID-19, Coronavirus disease 2019

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

HbA1c, hemoglobin A1c

Declarations

- # Ethics approval and consent to participate

The data used in this study were collected as part of general diabetes treatment in our hospital. Although the examinations were not designed to collect new data for our study, clinical data were retrieved of subjects from the institution's electronic medical records. The research plan was published on the facility’s website. All subjects were informed that the clinical data obtained by the medical treatment would be retrospectively analyzed and published.

In addition, it was announced that subjects could withdraw from the research study at any time. The study protocol was approved by the ethical review board of Juntendo University (No. 20-152).

- # Consent for publication

Not applicable.

- # Availability of data and materials

The datasets generated or analyzed during this study are not generally available due to severely restricted access to information by Juntendo University’s ethics committee, but they may be available on reasonable request by researchers.

- # Competing interests

The authors have the following financial relationships to disclose.

Nobuyuki Fukui and Akihiko Takahashi are employees of 4DIN Ltd.

- # Funding

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- # Authors' contributions

Toshiki Kogai: Conceptualization, Methodology, Software, Formal analysis, Writing – Original Draft. Kazutoshi Fujibayashi: Conceptualization, Methodology, Data Curation, Formal analysis, Investigation, Visualization, Writing – Original Draft, Project administration. Naotake Yanagisawa: Methodology, Formal analysis, Validation. Nobuyuki Fukui: Software, Data Curation, Validation. Akihiko Takahashi: Software, Data Curation. Toshio Naito: Writing – Review & Editing, Supervision. Ryohei Kuwatsuru: Writing – Review & Editing, Supervision. Hirotaka Watada: Writing – Review & Editing, Supervision.

- # Acknowledgements

Not applicable.

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Figures

Figure 1

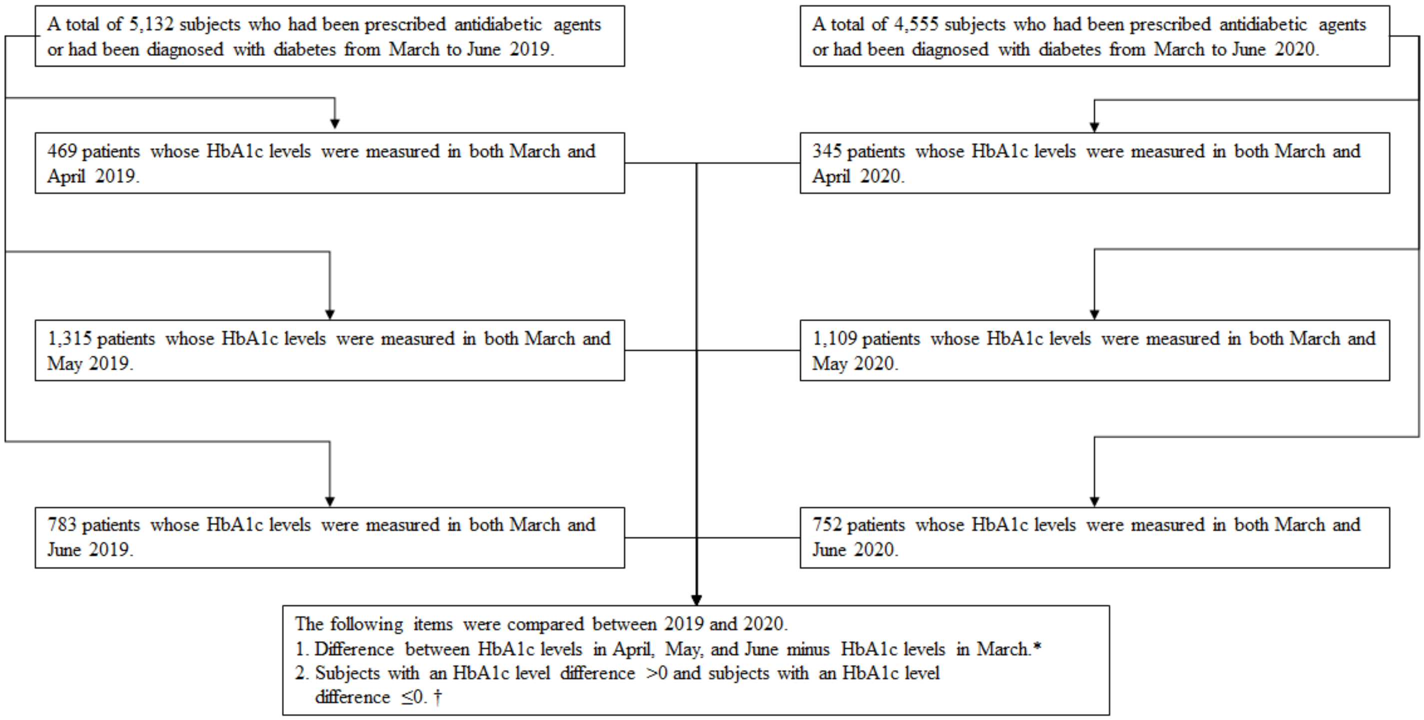

Figure 1

Methods of data handling for the analysis. *; Compared using the Wilcoxon rank-sum test. †; Compared using the Chi-squared test.