# Original

# The Changes in Blood HbA1c Levels of the Patients with Diabetes Mellitus, Who Used Teleconsultation in the COVID-19 Pandemic -A Single Center Study-

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#### Summary

We provided teleconsultation to outpatients for the purpose of infection control in the COVID-19 pandemic between March 1<sup>st</sup> and October 31<sup>st</sup>, 2020. The patients eligible for teleconsultation were only those who were taking oral anti-hypoglycemic agents. Doctors obtained information about patients' condition through telephone, and the patients received their regular prescriptions via fax at the nearest pharmacy. The present study examined the changes of HbA1c levels after teleconsultation on patients with diabetes mellitus (DM). We enrolled 218 outpatients with DM, who used teleconsultation and analyzed changes in HbA1c levels after teleconsultation. HbA1c levels in all patients significantly decreased after teleconsultation. Patients with HbA1c levels that increased by more than 0.5% after teleconsultation, suggesting that in the younger generation, lifestyle changes due to the COVID-19 pandemic such as teleworking, might have reduced daily exercises. Despite a single-center study, our teleconsultation did not deteriorate HbA1c levels of patients with diabetes, who were taking oral anti-hypoglycemic agents. However, physicians should pay attention to younger, especially female, patients whether their glycemic control would be worsened at the first visit after teleconsultation use.

Key Words: teleconsultation, remote medicine, Diabetes mellitus, COVID-19, pandemic

Received March 1, 2023; accepted July 9, 2023; advance publication by J-STAGE May 21, 2024

https://doi.org/10.51040/dkmj.2023-008

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#### Introduction

The SARS-CoV-2 coronavirus disease 2019 (COVID-19) pandemic<sup>1)</sup> still poses a significant threat worldwide. The first cases of COVID-19 were detected in Japan in early March 2020<sup>2,3)</sup>. Since then, outpatients, including patients with diabetes mellitus (DM), have refrained from seeing an attending doctor for regular visits<sup>4,5)</sup>. To minimize the COVID-19 pandemic, the Japanese government declared the first state of emergency on 7 April that lasted until May 25<sup>th</sup>, 2020. Prior to and during the first state of emergency, we provided teleconsultation to outpatients between March 1<sup>st</sup> and October 31<sup>st</sup>, 2020. The present study examined the changes of HbA1c levels after teleconsultation on outpatients with DM.

# Materials and Methods

# Teleconsultation

Teleconsultation was provided by telephone to outpatients of our center for the purpose of infection control in the COVID-19 pandemic between March 1st and October 31st, 2020. Regarding patients with DM, those who were receiving insulin and/or GLP-1 receptor agonist injection therapy were not permitted to use teleconsultation. Only the patients with DM under administration of oral anti-hypoglycemic agents were eligible for teleconsultation use. Under the criteria above, the patients were allowed to use teleconsultation if they desired irrespective of the glycemic control status and the content of prescription. When a physician determined that a patient was not eligible for teleconsultation, the patient visited our center for in-person consultation. Briefly, at teleconsultation, doctors obtained information on a patient's status by phone, and patients received regular prescriptions at their nearest pharmacy by fax. Basically, doctors did not change the regular prescriptions at the teleconsultation use.

## Study design

This was a retrospective cohort study conducted at the Dokkyo Medical University Saitama Medical Center, Koshigaya, Saitama Japan. We enrolled 218 outpatients with DM who used teleconsultation (males 99, females 119, age 69.0 (median) (21-92: min-max) years). The present study was approved by the Ethical Committee on human research at the Dokkyo Medical University Saitama Medical Center (approval number: #21047), and procedures were performed according to the Declaration of Helsinki. Informed consent was obtained by opt-out online.

#### HbA1c measurements

We employed (RE) Nordia N<sup>®</sup> (Sekisui Medical, Tokyo, Japan) for HbA1c measurements.

#### Statistical analysis

Data are presented as mean  $\pm$  standard deviations. Data not normally distributed are presented as median (min-max) and p < 0.05 was considered to be significant. The Mann-Whitney test was used to assess differences in continuous variables between two groups. The Wilcoxon signed-rank test was performed to examine differences between two paired groups before and after telemedicine. Statistical analyses were performed using SPSS 28.0 for Macintosh (SPSS Inc., Chicago, IL, USA) and GraphPad Prism Version 9.2.0 for macOS (GraphPad Software, San Diego, CA, USA).

# Results

Analyses of all 218 patients revealed that the duration until the first visit after teleconsultation was 6.0 (3-10) months and the frequency of telemedicine use was 1.0 (1-3) time. The numbers of patients with HbA1c levels that increased by 0.5% and decreased by 0.5% in the first visit after teleconsultation were 24 and 43, respectively. The HbA1c levels of all patients significantly decreased after teleconsultation (before 7.1 (5.4-11.0) vs after 6.9 (5.2-12.0) %, p = 0.0014) (Table 1, Fig. 1A). The body weight and BMI of all patients remained unchanged after teleconsultation (Table 1).

Analyses of 99 male patients revealed that the duration until the first visit after teleconsultation was 5.0 (3-10) months and the frequency of teleconsultation use was 1.0 (1-3). The numbers of patients with HbA1c levels that increased by 0.5%, and decreased by 0.5% in the first visit after telemedicine were 14 and 21, respectively. The HbA1c levels of male patients didn't change after teleconsultation (before 7.2 (5.4-11.0) vs after 7.0 (5.2-11.4) %, p = 0.1131) (Fig. 1B).

Analyses of 119 female patients revealed that the duration until the first visit after teleconsultation was

before	after	p value
69 (21-92)		N.A.
99/	119	N.A.
65 (33-130)	66 (33-130)	N.S.
25.2 (15.1-40.1)	25.0 (15.1-43.1)	N.S.
7.1 (5.4-11.0)	6.9 (5.2-12.0)	0.0014**
20 (10-67)	20 (9- 77)	N.S.
18 (5-98)	18 (6-120)	N.S.
117 (38-963)	118 (37-705)	N.S.
55 (26-105)	51 (30-102)	N.S.
$107.9 \pm 27.0$	$108.4 \pm 25.4$	N.S.
66.6 (18.1-157.9)	65.7 (16.2-169.1)	N.S.
	$69 (2)$ $99/$ $65 (33-130)$ $25.2 (15.1-40.1)$ $7.1 (5.4-11.0)$ $20 (10-67)$ $18 (5-98)$ $117 (38-963)$ $55 (26-105)$ $107.9 \pm 27.0$	$\begin{array}{c} 69 \ (21-92) \\ 99/119 \\ \hline \\ 65 \ (33-130) \\ 25.2 \ (15.1-40.1) \\ 25.0 \ (15.1-43.1) \\ 7.1 \ (5.4-11.0) \\ 20 \ (9-77) \\ 18 \ (5-98) \\ 18 \ (6-120) \\ 117 \ (38-963) \\ 118 \ (37-705) \\ 55 \ (26-105) \\ 51 \ (30-102) \\ 107.9 \ \pm \ 27.0 \\ \end{array}$

Table 1Anthropometric and laboratory data of all patients before and<br/>after telemedicine use (n = 218).

Data are expressed as means  $\pm$  SD or medians (min, max), where appropriate. BW: body weight, BMI: body mass index, AST: aspartate amino-transferase, ALT: alanine aminotransferase, TG: triglyceride, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, eGFR: estimated glomerular filtration rate. Asterisks indicates a significant difference (P < 0.01) by the Wilcoxon signed-rank test. N.A.: not applicable, N.S.: not significant.

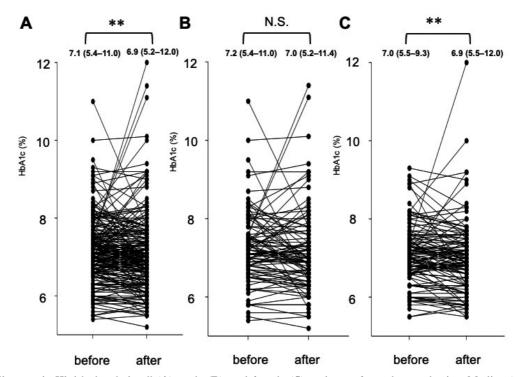


Figure 1 Changes in HbA1c levels in all (A), male (B), and female (C) patients after teleconsultation. Median (min-max) is indicated on top of the graph. N.S.: not significant. An asterisk indicates that the difference between the denoted pairs is significant at a confidence level of p < 0.01 (\*\*) by Wilcoxon signed-rank test. n = 218 (A). 99 (B), 119 (C).</p>

6.0 (3-10) months and the frequency of teleconsultation use was 1.0 (1-3). The numbers of patients with HbA1c levels that increased by 0.5%, and decreased by 0.5%

in the first visit after teleconsultation were 10 and 22, respectively. The HbA1c levels of female patients significantly decreased after teleconsultation (before 7.0

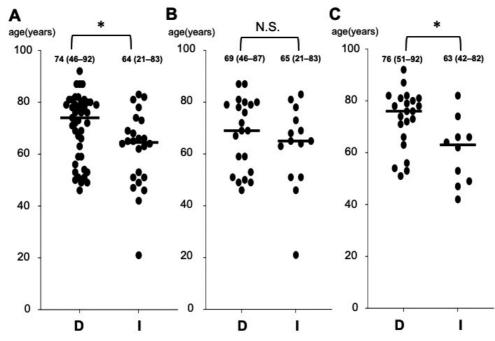


Figure 2 Differences in age between patients (all (A), male (B), and female (C)) with HbA1c levels that increased (I) or decreased (D) by more than 0.5% after teleconsultation. Median (min-max) is indicated on top of the graph. N.S.: not significant. An asterisk indicates that the difference between the denoted pairs is significant at a confidence level of p < 0.05 (\*) by Mann-Whitney test.

n = 43 (D), 24 (I) in A, 21 (D), 14 (I) in B and 22 (D), 10 (I) in C.

(5.5-9.3) vs after 6.9 (5.5-12.0) %, p = 0.0030) (Fig. 1C).

Patients with HbA1c levels that increased by more than 0.5% after teleconsultation were significantly younger than those with HbA1c levels that decreased by more than 0.5% (64 (21-83) vs 74 (46-92) years old, p = 0.0179) (Fig. 2A). Similar results were obtained for female patients (63(42-82) vs 76(51-92) years old, p = 0.0132) (Fig. 2C), but not male patients (65(21-83) vs 69 (46-87) years old, N.S.) (Fig. 2B). The duration until the first visit after teleconsultation did not significantly differ between the two groups (Fig. 3).

#### Discussion

Even before the COVID-19 pandemic, remote medicine including teleconsultation was reported to control blood glucose levels effectively<sup>6</sup>, and performed well for health economics<sup>7</sup>. During the pandemic, many studies were published on the effectiveness of remote medicine for the care of patients with DM<sup>8-10</sup>. Also in the current study, HbA1c levels of the patients with DM were significantly decreased after teleconsultation use and the duration until the first visit after teleconsultation was not associated with glycemic control.

Patients with elevated HbA1c levels were significantly younger than those with decreased HbA1c levels after teleconsultation and were mainly female, suggesting that lifestyle changes due to the COVID-19 pandemic, such as teleworking, could have reduced daily activity more in the younger generation than in the older generation. A previous study indicated that a reduction in physical activity, particularly due to transitioning to remote during the COVID-19 pandemic, led to increase HbA1c levels in patients with type 2 DM, who were under 65 years old<sup>12)</sup>. Although the current study didn't employ a questionnaire about their lifestyle, the similar lifestyle changes would have affected those patients. In addition, it has been known that younger females were more vulnerable to reduced daily activity than males<sup>13)</sup>.

In the present study, outpatients receiving insulin and/or GLP-1 receptor agonist injection therapy were excluded, because we determined that those who received insulin and/or GLP-1 receptor agonist injection therapy were required in-person recuperation guidance such as dose adjustment.

There are some limitations in the current study.

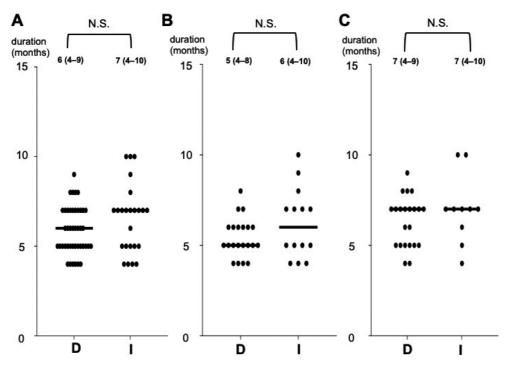


Figure 3 Differences in the duration (months) until the first visit after teleconsultation between patients (all (A), male (B), and female (C)) with HbA1c levels that increased (I) or decreased (D) by more than 0.5% after teleconsultation. Median (min-max) is indicated on top of the graph. N.S.: not significant.
n = 43 (D), 24 (I) in A, 21 (D), 14 (I) in B and 22 (D), 10 (I) in C.

First, as glycemic control in patients receiving therapy only with oral anti-hypoglycemic agents is generally good, the current study may be biased. Second, as it is said there would be seasonal variation in HbA1c levels<sup>14</sup>, as the current study could overestimate or underestimate of glycemic control. Third, this was a singlesite retrospective study. A large-scale multicenter study on the effectiveness of teleconsultation for glycemic control is warranted.

In conclusion, despite a single-center study, our teleconsultation did not deteriorate HbA1c levels of patients with diabetes, who were taking oral antihypoglycemic agents. However, physicians should pay attention to younger, especially female, patients whether their glycemic control would be worsened at the first visit after teleconsultation use.

#### Data availability

Data that support the present results are available from the corresponding author upon reasonable request.

#### Author contributions

K.H. conceived the project, evaluated data, wrote the manuscript, and supervised the entire project; S.F. collected and analyzed data; S.K. analyzed data, wrote the manuscript, and prepared figures and tables; M.Y., H.S., A.U., T.O., M.K., S.S., K.A., H.T., Ka.H., K.M., Ke. H., T.T., and K.T. performed telemedicine and collected data. All authors discussed the results, commented on the manuscript, and gave final approval of the version to be submitted.

#### Author disclosure statement

The authors have nothing to disclose.

## **Competing interests**

The authors declare no competing interests.

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