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【 ORIGINAL ARTICLE 】

The Effects of Stress on Glycemic Control Brought on by Changes in Social Conditions Due to COVID-19

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Abstract:

Objective The stress brought on by changes in social conditions due to COVID-19 is diverse. However, there have been no studies examining the relationship between the type of stress felt by an individual due to such changes in social conditions and the degree of change in HbA1c, prompting us to conduct this study.

Methods We conducted a collaborative study at two diabetes clinics. A total of 1,000 subjects responded to the questionnaire. Data on HbA1c and body weight before and after the declaration of the state of emergency were collected.

Results We conducted a questionnaire on some stressors, but when comparing the two groups with respect to whether or not they felt stress from each item, only "school closures for children," seemed to be associated with a significant difference in the amount of change in HbA1c. In the stressed group, i.e. the group of parents who experienced stress due to their children's schools being closed, the HbA1c value changed from 7.30 ±0.78 to 7.30±1.13 (p=0.985). By contrast, in the unstressed group, the HbA1c value significantly decreased from 7.28±0.98 to 7.06±0.85 (p<0.001). In addition, as a result of comparing the amount of change between the 2 groups, a significant decrease was observed in the unstressed group compared with the stressed group (p=0.032). There was no significant difference in body weight change between the two groups.

Conclusion Stress that cannot be avoided by one's own will, such as school closures for children, may affect glycemic control.

Key words: COVID-19, diabetes, lockdown, state of emergency, stress

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Introduction

The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections has caused anxiety, depression, and a high degree of stress in people (1-6). These effects are caused by not only the virus itself and coronavirus disease 2019 (COVID-19) but also social and economic changes implemented to prevent the spread of infection. Various regulations have been put in place globally to prevent the spread of the SARS-CoV-2. In Japan, the Prime Minister declared an emergency in seven prefectures - Tokyo, Kanagawa, Saitama, Chiba, Osaka, Hyogo, and Fukuoka - on April 7, 2020, and expanded the scope nationwide on April 16, continuing to May 25. The strictest policy is a complete lockdown, and some countries have adopted that measure. In Japan, the government chose not to lock down the country, instead instating a wide range of regulations that are almost as disruptive.

The government urged people to refrain from going out except for what is necessary to maintain their livelihood and health. Many restaurants are only open for a short duration. Public facilities, such as parks, museums and libraries, have been closed. Telework has been recommended for companies, with the goal of reducing office attendance by 70%. Educational institutions were closed from May 2, before the declaration, and gradually reopened after the initial declaration period had ended. Gatherings fitting the "three Cs" were avoided, and large-scale gatherings nationwide were canceled or postponed.

These regulations can affect one's work and cause stress, but the simple inability to go outdoors due to regulations

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can also be stressful. Many things can be stressors, such as getting less exercise, not going out to eat, spending more time together as a family than usual, and frustrations suffered by individual family members.

Relationship problems and major life events, such as marriages and career changes (7, 8), can stress the mind and body and may lead to depression. The timing and details of such stress vary from person to person. A person relying on his or her ingenuity can manage conventional stress, but the regulations that have been implemented to prevent the spread of the SARS-CoV-2 infection affect everyone at the same time, and individuals cannot simply aboid them. The inability to go outside may be a stressor that the average person has rarely experienced.

The deterioration of glycemic control due to conventional mental stress has been reported in several studies. Depression has been reported to increase the risk of developing type 2 diabetes mellitus (T2DM) by about 60% (9, 10). Depression rates in diabetics are also higher than in the general population (11-14). There is a two-way link between diabetes and depression, and that understanding may provide better treatment and improve treatment (15, 16).

Still, there are few reports on the relationship between diabetes and stress from the new coronavirus-instigated lockdown measures. It has been reported that the higher the stress level, the more difficult it is to control blood glucose (17), and loss or interruption of work due to lockdown may be a significant factor in reducing the time in range (TIR) (18). However, the stress brought on by changes in social conditions due to COVID-19 is diverse. No study has yet examined the relationship between the type of stress felt by an individual due to these changes in social conditions and the amount of change in HbA1c.

In a survey of 1,000 people before and after the state of emergency, we reported that, in the absence of serious economic stagnation or completely disrupted distribution, patients were allowed time to do what they liked and could probably improve their glycemic control status if they saw this time as an opportunity (19). In the present study, we examined the effects of lockdown-induced stress on the glycemic control brought on by changes in social conditions due to COVID-19.

COVID-19 has yet to show signs of abating throughout the world, and it is possible that imposing a state of emergency will include prohibitions on going outdoors. In addition, it is expected that new infectious diseases will also bring with them restrictions on people going outdoors. Our report is expected to be useful for the management of diabetes in such situations.

Materials and Methods

Study design

This study was a two-center observational study in Japan (Tokyo and Chiba). Subjects were enrolled between July 10 and September 23, 2020. Since the amount of change in HbA1c could not be estimated, a strict sample size calculation was not performed. We set the target number of cases at 1,000 cases (500 cases at each facility). If too much time has passed, memory of events before and after the declaration becomes less reliable, so we estimated and set the number of subjects in this study to be able to gather during the study periods. There was no intentional selection of subjects by the researchers. We uniformly requested cooperation from those who could provide their consent within the period.

Patients who met all of the following inclusion criteria were included in this study (the rationales for the criteria are provided in parentheses). We showed them in the next chapter. No exclusion criteria were used in the study. Subjects were provided with written information on the study, gave their written consent, and responded to the patient questionnaire using the recollection method (Supplementary material 1). Data on HbA1c and body weight before and after the declaration in daily clinical practice were collected. Data after the declaration were represented by data obtained at the date closest to three months after the declaration selected from among the data obtained at least two but less than six months after the declaration.

Inclusion criteria

(1) Patients who saw a doctor regularly (to examine data before and after the declaration).

(2) Patients at any age and of either sex (to understand actual conditions, regardless of age or sex).

(3) Patients with diabetes (to assess the status of glycemic control in patients with diabetes).

(4) Patients who provided their informed consent for study participation (to conduct the study in accordance with ethical guidelines).

Ethic approval and consent to participate

This study was registered with the Clinical Trials Registry (https://www.umin.ac.jp/; UMIN000041065) and undertaken in accordance with the study protocol, the Declaration of Helsinki and the Ethical Guidelines for Clinical Studies of the Japanese Ministry of Health, Labor, and Welfare. This study was approved by the ethics committee at the Diabetes and Lifestyle Center, Tomonaga Clinic. All participants provided their written informed consent before participation.

Survey items

The survey items included age, sex, occupation, changes before and after the declaration (HbA1c, body weight, employment status, dietary life, status of frequency of eating out, food intake, reason for change in food consumption, status of drunkenness, alcohol consumption, frequency of drinking, reason for change in alcohol consumption, amount of exercise and physical activity, body weight measurement, mental status, status of outpatient visits, medication adherence and presence or absence of perceived effects of self-

Table 1. Types of Stress and Changes in HbA1c (%) before and after the Declaration of the State of Emergency.

Types of stress	Applicable/ not applicable	n	before	after	delta
Economic aspects	Stressed	162	7.42±1.13	7.25±1.16	-0.17±0.90
	Unstressed	835	7.25±0.93	7.03±0.79	-0.22±0.58
	p		0.045*	0.003*	0.342
Work	Stressed	282	7.33±1.04	7.12±0.96	-0.21±0.73
	Unstressed	715	7.26±0.94	7.05±0.82	-0.21±0.60
	p		0.259	0.221	0.954
Family	Stressed	116	7.29±0.86	7.09±0.92	-0.20±0.70
	Unstressed	881	7.28±0.98	7.06±0.86	-0.21±0.63
	p		0.877	0.798	0.912
School closure for their own children	Stressed	40	7.30±0.78	7.30±1.13	0.00±0.82
	Unstressed	957	7.28±0.98	7.06±0.85	-0.22±0.63
	p		0.881	0.078	0.032*
Change in employment status	Stressed	172	7.37±1.09	7.22±0.99	-0.15±0.76
	Unstressed	825	7.26±0.94	7.04±0.83	-0.22±0.61
	p		0.172	0.012*	0.182
Lack of objects	Stressed	42	7.62±0.91	7.55±1.03	-0.07±0.61
	Unstressed	955	7.26±0.97	7.05±0.85	-0.22±0.64
	p		0.019*	<0.001*	0.158
Others	Stressed	75	7.44±1.09	7.24±1.00	-0.20±0.68
	Unstressed	922	7.26±0.96	7.05±0.85	-0.21±0.64
	p		0.140	0.073	0.853

*p<0.05 Student's t-test between applicable and not (delta). Data are mean±SD or p value.

quarantining associated with the declaration on the management of lifestyle-related diseases) and current methods of glycemic control.

Endpoints

In this analysis, we analyzed the effect of each stress on HbA1c at first, and considering the results, we performed an exploratory analysis.

Statistical analyses

Data analyses were performed using R version 3.5.2 [R Foundation for Statistical Computing, Vienna, Austria (https://www.R-project.org)]. When comparing data between groups, Fisher's exact test was used for nominal variables, and the Tukey-Kramer test or Student's t-test was used for continuous variables and Mann-Whitney U test was used for ordinal variables. To compare the value of HbA1c and body weight before and after the declaration, a paired t-test was used. Cases with no responses to the questionnaire were defined as "unknown" and excluded from testing. In addition, in the comparison of HbA1c changes between groups, we performed an analysis of covariance (ANCOVA) of items that significantly differed in the patient background comparison between the two groups as covariates. A 2-sided significance level of 5% was applied. The analytical results included in the text are expressed as the mean±standard deviation.

Results

The types of stress and changes in HbA1c are shown in Table 1, and changes in work style and changes in HbA1c are shown in Supplementary material 2. Whether having a stress caused by school closures for respondents' own children or not was the only item to show a significant difference for changes in HbA1c. No significant difference was found in the amount of change due to differences in work styles (Supplementary material 2).

The amount of change in HbA1c was evaluated by identifying two groups: the stressed (parents who experienced stress due to the closing of their children's schools) and the unstressed (parents who experienced no such stress). Within each group, we evaluated the change in HbA1c before and after the declaration of emergency, and between the groups, we evaluated the amount of change in HbA1c. We also compared the patient backgrounds between the two groups. The main patient background details are shown in Table 2. The stressed group tended to be younger and had a higher proportion of women than the unstressed group. There were no significant differences between the two groups in terms of complications, medical history or medication information. Changes in HbA1c values in both groups are shown in Fig. 1a, and changes in body weight are shown in Fig. 1b. In the unstressed group, the HbA1c value changed from 7.28±0.98 to 7.06±0.85, showing a significant decrease ($p<0.001$), whereas in the stressed group, the HbA1c value

Table 2. Patient Characteristics.

Item (unit)	Stressed (n=41)	Unstressed (n=959)	p value
Age (years)	52.3±10.8	58.2±11.6	0.001*
Male/female	24 (58.5%)/17 (41.5%)	722 (75.3%)/237 (24.7%)	0.026†
HbA1c (%)	7.30±0.78	7.28±0.98	0.881
Body weight (kg)	69.3±12.7	69.5±13.4	0.929
Type			
Type 1 diabetes mellitus	2 (4.9%)	51 (5.3%)	1.000
Type 2 diabetes mellitus	39 (95.1%)	907 (94.6%)	
MODY	0 (0%)	1 (0.1%)	
Complication			
Diabetic nephropathy	4 (9.8%)	189 (19.7%)	0.155
Diabetic retinopathy	7 (17.1%)	240 (25%)	0.354
Diabetic neuropathy	5 (12.2%)	231 (24.1%)	0.091
Hypertension	22 (53.7%)	624 (65.1%)	0.137
Dyslipidemia	33 (80.5%)	800 (83.4%)	0.668
Hyperuricemia	4 (9.8%)	205 (21.4%)	0.079
Arteriosclerosis	0 (0%)	16 (1.7%)	1.000
Obliterans			
Cardiovascular disease	0 (0%)	30 (3.1%)	0.630
Ischemic heart disease	1 (2.4%)	59 (6.2%)	0.507
Cardiac failure	0 (0%)	5 (0.5%)	1.000
Cerebral stroke	1 (2.4%)	29 (3%)	1.000
Pharmacotherapy			
Dipeptidyl peptidase-4	18 (43.9%)	541 (56.4%)	0.148
Inhibitors			
Biguanide	30 (73.2%)	687 (71.6%)	1.000
Sulfonylurea	1 (2.4%)	86 (9%)	0.250
Thiazolidine	0 (0%)	6 (0.6%)	1.000
α-glucosidase inhibitors	5 (12.2%)	112 (11.7%)	0.807
Sodium-glucose	16 (39%)	314 (32.7%)	0.401
Cotransporter-2 inhibitors			
Glinides	5 (12.2%)	76 (7.9%)	0.372
Insulin	8 (19.5%)	195 (20.3%)	1.000
Glucagon-like peptide-1	4 (9.8%)	51 (5.3%)	0.277
Receptor agonist			
Dietary and exercise			
Therapy alone	4 (9.8%)	47 (4.9%)	0.151
Change of pharmacotherapy			
Same	33 (80.5%)	835 (87.1%)	0.206
Addition/increase of dose	1 (2.4%)	9 (0.9%)	
Stop/decrease of dose	7 (17.1%)	115 (12%)	

*p<0.05, Student's t-test. †p<0.05, Fisher's exact test Data are mean±SD or n (%).

changed from 7.30±0.78 to 7.30±1.13, with no significant change observed (p=0.985). In addition, a significant decrease was observed in the unstressed group when comparing the amount of change between the two groups (p= 0.032). Furthermore, the body weight decreased significantly from 69.51±13.44 to 69.17±13.61 kg in the unstressed group (p<0.001), whereas in the stressed group, the body weight changed from 69.32±12.68 to 68.81±12.30 kg; although there was a tendency for the body weight to decrease in the stressed group, no significant change was observed (p=0.062). In addition, no significant difference was observed in the amount of change between the two groups (p=0.547).

On comparing the two groups with regard to the patient questionnaire, some responses showed a significant difference (Fig. 2a-c), while others showed no significant difference between the two groups (Supplementary material 3). Furthermore, in the ANCOVA, we used the HbA1c value before the declaration and the items with significant differences as covariates: gender; age; stress level before the declaration; anxiety level before the declaration; stress due to family; frequency of going out due to self-quarantine; and

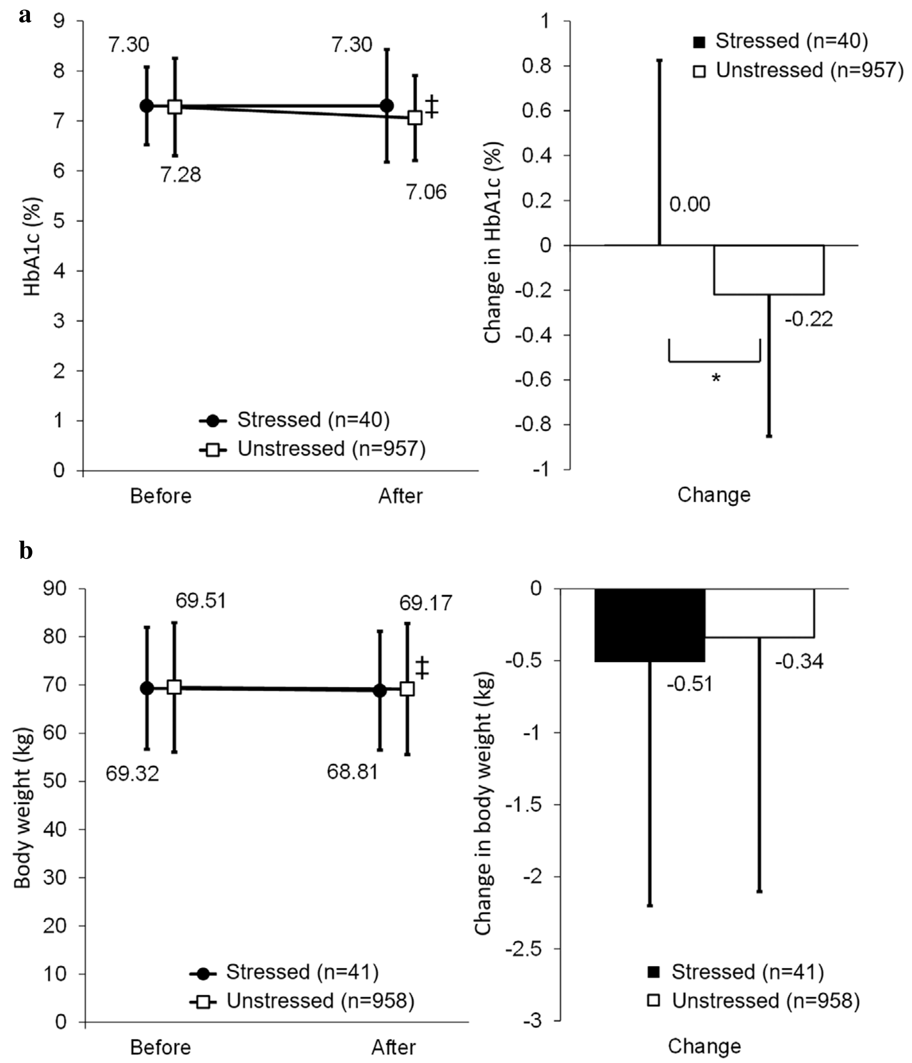

Figure 1. **a: Changes in HbA1c. Data are presented as the mean±standard deviation. *p<0.05 Student's t-test. ‡p<0.05 versus before paired t-test. There were three cases with no HbA1c data before the declaration. b: Changes in body weight. Data are presented as the mean±standard deviation. N.S. Student's t-test. ‡p<0.05 versus before paired t-test. There was one case with no weight data before the declaration.**

change in frequency of eating out. A significant difference in the amount of change in the HbA1c value was also observed between the two groups according to an ANCOVA (Fig. 3) (p=0.014). A correlation analysis of the stress level and HbA1c change in all cases revealed no significant correlation between the stress level before and after the declaration and the amount of change in HbA1c. However, a significant positive correlation was found between the amount of change in stress level and the amount of change in HbA1 c (Supplementary material 4). Regarding stress and anxiety, we also compared the values before and after the declaration within each group (Supplementary material 5). In the stressed group, the stress level tended to increase but showed no significant change, whereas the level of anxiety increased significantly.

Discussion

This result shows that if a school closure for children becomes a stressor for parents, it may affect glycemic control. The presence or absence of other stress was not a significant factor in glycemic control. The stress caused by a school closure for respondents' own children can be broadly divided into two components. One is the stress of losing educational opportunities. This stress is caused by the family being subject to force majeure, an unwillingly imposed condition. The other is the stress caused by the children being at home, associated with an increased burden of housework for parents and decreased time for parents to spend on their own. Cases involving both types of stress can result in the compounding of stress. While we do not intend to criticize the virus mitigation policies in place, it is important to pay

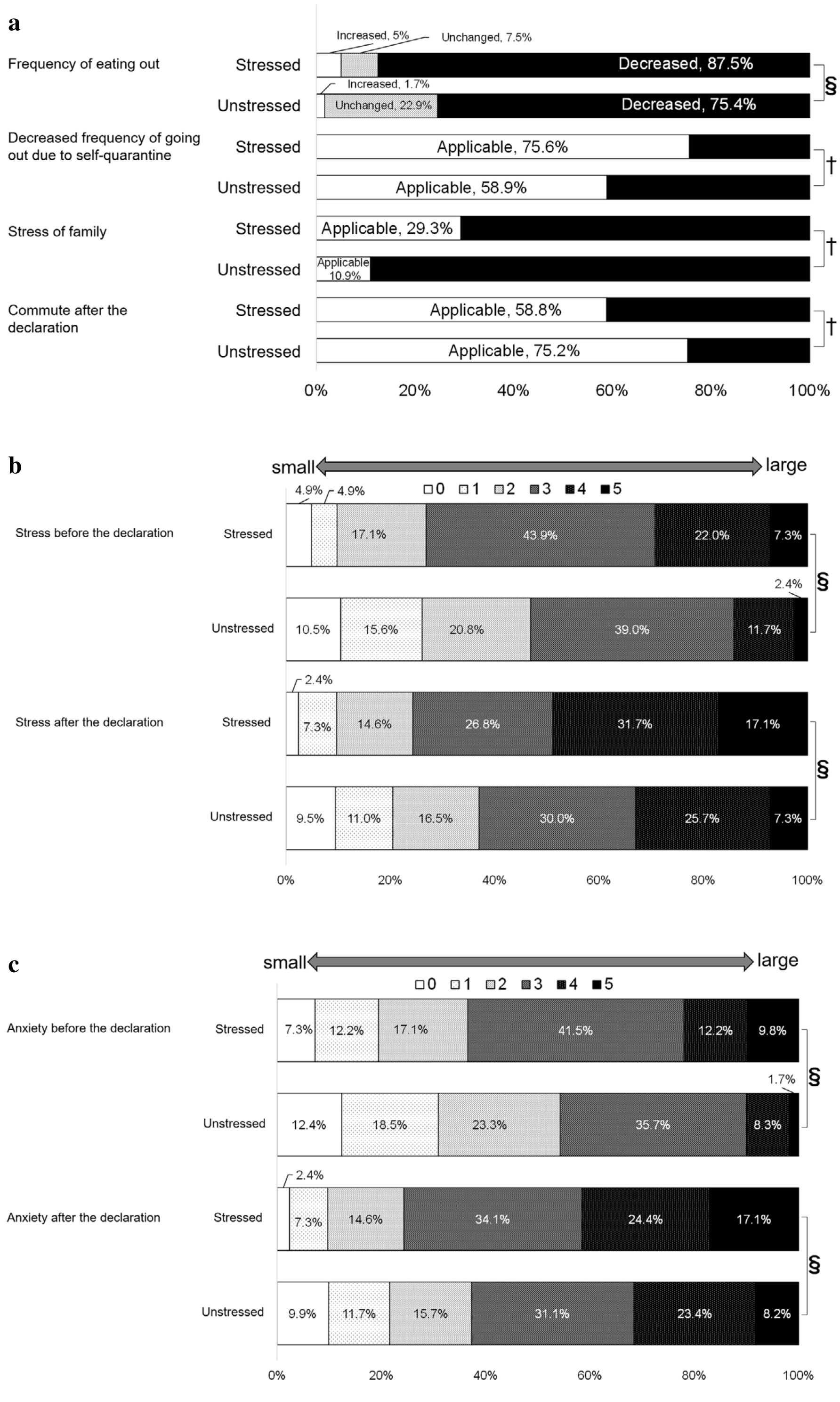

Figure 2. **a: Responses to the questionnaire. †p<0.05 Fisher's exact test. §p<0.05 Mann-Whitney U test. ("Frequency of eating out" was analyzed as "Increase: 1, Unchanged: 0, Decreased: -1"). b: Responses to the questionnaire (stress). The stress level was described in 5 grades from 0 to 5. The graph shows the percentage of each response. §p<0.05 Mann-Whitney U test. c: Responses to the questionnaire (anxiety). The anxiety level was described in 5 grades from 0 to 5. The graph shows the percentage of each response. §p<0.05 Mann-Whitney U test.**

attention to the stress levels experienced by patients at the start of their diabetes management regimen and perform glycemic control and stress management in parallel.

Stress caused by school closure for children is an independent risk factor

Stress reportedly poses a risk of initiating the onset diabetes. Mooy et al. reported that people who have experienced

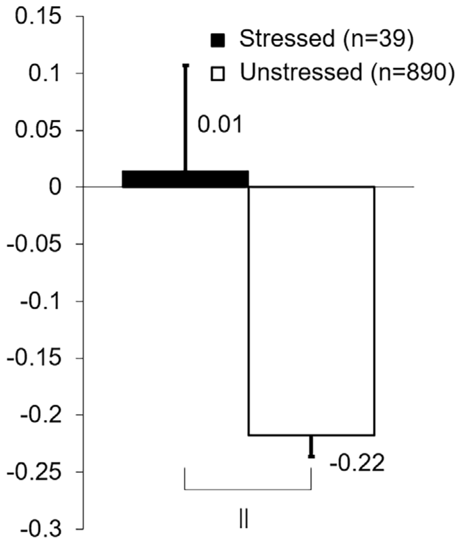

Figure 3. Change in HbA1c (ANCOVA). Data presented as the least square mean±standard error. ||p<0.05 ANCOVA. Covariates: Pre-declaration HbA1c, gender, age, stress level (before), anxiety level (before), family stress, changes in frequency of eating out, changes in frequency of going out. "Commuting" was not included in the covariates due to the small number of responses. Regarding stress and anxiety data, there were significant differences in these values between the two groups both before and after the declaration, but the value before the declaration was adopted as the covariate.

significant life events in the last 5 years were at a 1.6-times greater risk of developing T2DM than those without such experience (7). Kumari et al. also reported that people who have experienced two or more significant life events were at an increased risk of diabetes (8). Individuals who have experienced neglect and psychological abuse in childhood have also been reported to be at an increased risk of diabetes in adulthood (20). Reports of worsening glycemic control due to chronic stress have also described a disordered lifestyle in some cases (21, 22). Rod et al. found that people with high levels of stress were less likely to quit smoking [odds ratio (OR)=0.58; 95% confidence interval (CI): 0.41-0.83], more likely to be physically inactive (OR=1.90; 95% CI=1.41-2.55) and less likely to stop their excessive consumption of alcohol (OR=0.43; 95% CI=0.24-0.79) than those with lower levels of stress (21). These negative spirals make glycemic control difficult.

We previously reported that individuals who saw this situational change as an opportunity to change their diet and exercise habits improved their glycemic control (19). There was, however, no significant difference in eating habits or exercise between the groups, and parental stress caused by school closure for children was an independent risk factor. Regarding body weight, there was a tendency for body weight to decrease during the declaration, even in the stressed group. These results suggest that the stress itself, not the disordered lifestyle resulting from it, may have affected blood glucose.

We conducted a questionnaire on some stressors, but when comparing the two groups with respect to whether or not they had stress due to each item, only "school closures" showed a significant difference in the amount of change in HbA1c. It is distressing for parents when school closures cause their children to lose educational opportunities. In Japan, the closure of educational institutions continued for about a month. Parents can neither make up for that loss nor manage it willfully. There was no significant difference in stress due to changes in working conditions or finances, so the fact that there was a significant difference in this stressor is due to its peculiarity.

Furthermore, as mentioned at the beginning of the discussion, not only the stress of losing educational opportunities but also other stress caused by the children remaining at home must be considered. Tani et al. reported a survey of parents' problems, anxieties and worries due to school closures (23). This report consisted of parents of all ages from nursery school to high school, and more than 80% considered both the opportunity loss for children and increased household burden to be issues contributing to stress. The lack of time to oneself is reportedly stressful for mothers who are employed (24). Losing educational opportunities combined with the stress caused by their children being at home may have induced complex stress. In the stressed group, no significant increase in stress level was observed, but a significant increase in anxiety level was observed (Supplementary material 5). This result suggests that anxiety about their children's educational environment may have had a greater psychological effect on parents than the stressful feeling of losing their own free time due to their children staying at home.

UNICEF reported an overview of school closures from March 11, 2020, to February 2, 2021, in more than 200 countries and territories (25). In this report, the Japanese school closure period was the fifth shortest. Our results indicated a significant difference in HbA1c values between the stressed and unstressed groups. However, the HbA1c value in the stressed group did not show a significant increase over the study period. If the period had been longer, we might have seen a greater impact. We hope that further data from other countries will be reported in the future.

Allostatic load may have been involved

In this comparison of the two groups, the stressed group had significantly higher levels of anxiety and stress both before and after the declaration of emergency. An ANCOVA showed a significant difference between the stressed and unstressed groups, even after correction. However, this may have been because the additional new stress functioned as an allostatic load affecting glycemic control.

Allostasis is the process of adapting to acute stress, resulting in the maintenance of bodily stability over the course of a change. To respond to with stressors, active biological activation occurs throughout the body, which then quickly recovers to baseline values. Allostatic loads are excessive loads that dysregulate this dynamic process. This load can reduce the body's ability to return to prestress levels for various parameters, including an inadequate biological response to stress, an inability to initiate an appropriate stress response and inadequate stress recovery (26, 27). In a rat study using foot shock stress, a single period of stress at 2 weeks old had no marked effect on glucose or insulin parameters, but a second instance of stress at 8-10 weeks old increased the glucose and insulin levels, resulting in decreased insulin sensitivity and glucose tolerance (28). A study of 1,000 people reported that high allostatic loading was associated with an increased risk of T2DM (29). However, allostatic loading and diabetes may be related to each other. When Steptoe et al. conducted the same acute stress test on 140 individuals with T2DM and 280 healthy controls of matching age, gender and income, they found that T2DM participants showed cardiovascular and neurological stress in response to acute stress; reduced endocrine, inflammatory and metabolic responses; and an impaired recovery after stress (30). While whether diabetes or allostatic loading is the first to appear is unclear, our results show that allostatic load may have affected glycemic control, given that stress was an independent factor, and the original stress level was high. In our study, a significant positive correlation was found between the amount of change in stress level and the amount of change in the HbA1c value (Supplementary material 4). Generalization is difficult, as the questionnaire is our own original, but for diabetes management in patients with high stress levels, special care targeting stress may be necessary (15, 16).

Mechanism underlying the deterioration of glycemic control due to stress

Several mechanisms have been reported concerning how stress adversely affects glycemic control. Chronic stress reactions and depression are often characterized by long-term activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, which were found to be associated with the development of abdominal obesity, and this may explain why depression and chronic stress increase the risk of diabetes. Chronic stress activates the hypothalamus-pituitary-adrenal axis and the sympathetic nervous system, thereby increasing the production of cortisol in the adrenal cortex and that of adrenaline and noradrenaline in the adrenal medulla (31). Chronic hypercortisolemia and prolonged sympathetic nervous system activation not only promote insulin resistance and visceral obesity but also lead to metabolic syndrome and diabetes mellitus (32). Another mechanism by which stress might influence the risk of developing diabetes mellitus is through activation of the immune system. T2DM has been characterized as a chronic low-grade inflammatory state involving multiple inflammatory mechanisms and metabolic pathways (33).

Importance of glycemic control after understanding patients' background characteristics

Changes in work style are not necessarily bad for diabetes management. We analyzed changes in the presence or absence of telecommuting and commuting before and after the declaration of the state of emergency and the amount of change in HbA1c, but no significant difference was found in the amount of change in HbAlc due to differences in work style (Supplementary material 2).

When people are prohibited from going outside, some take this as an opportunity, while others see it as a loss of opportunity; such patients should not be treated in the same way. Although many reports have found that negative psychological factors indicate an increased risk of T2DM, few have investigated the relationship between positive psychology (e.g. an optimistic outlook) and the risk of T2DM. Evidence concerning positive psychological factors comes from a meta-analysis of depression and work stress (20, 34-38). We await further reports on the relationship between positive psychology and diabetes.

In addition, in the present analysis, glycemic control was poorer in the stressed group than in the unstressed group. However, spending more time with one's family can have a positive effect on glycemic control. In diabetic patients, there are many reports stating that having a family and enjoying the understanding and support of family members improve the prognosis (39-43). Therefore, even if patients experience the same event, diabetes must be managed with an understanding of differences in background characteristics among patients.

In addition, previous reports have shown more significant effects in men concerning stress and diabetes than in women (21, 44). In our report, the proportion of women in the stressed group was higher than that in the unstressed group, but an ANCOVA demonstrated the effects of stress even when gender was a covariate. While there was no marked effect of gender on these results, sensations of stress may differ by gender, and we await further data on the relationship between gender and diabetes.

Limitations

Several limitations associated with the present study warrant mention. First, the study was conducted in Tokyo and its commuter town of Ichikawa in Chiba Prefecture. Therefore, its subject population was limited to patients in urban areas, and the results cannot be reliably generalized throughout Japan. Second, the lockdown was not complete, and the self-quarantine period requested by the government also differed from that in other countries. Third, the questionnaire used was created independently and was not a universally standardized form that used the recollection method. Fourth, as not all patients at the sites were included in the study, the actual conditions of patients who were unable to provide their informed consent, including those who did not visit hospitals or who were transferred to other hospitals, could not be determined. Fifth, the school closure for children started about a month before the state of emergency. Therefore, it is possible that the value before the declaration reflected the effect in no small measure. Sixth, stress due to respondents' children's schools being closed was limited to 41 cases. For items that showed no marked difference between groups, this effect may have been the cause. Even after correction by an ANCOVA, the possibility of confounding with other patient background factors cannot be ruled out. Finally, we did not confirm whether or not the respondents actually had children. We hope that more accurate studies will be conducted with rigorously randomized research in the future.

Conclusion

Stress that cannot be avoided by one's own will, such as school closures for children, may affect glycemic control. Some people can tolerate issues that affect them personally but may struggle dealing with issues affecting their own children. This may have affected the glycemic control of the subjects in the present study. In addition, not only this stress but also the increased burden of housework and lack of personal time alone may have become combined stressors. It is therefore important to pay attention to the stress levels experienced by patients at the start of their diabetes management regimen and perform glycemic control and stress management in parallel.

The authors state that they have no Conflict of Interest (COI).

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