


Glycemic control in children and teenagers with type 1 diabetes around lockdown for COVID-19: A continuous glucose monitoring-based observational study

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Keywords

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ABSTRACT

Aims/Introduction: The coronavirus disease 2019 (COVID-19) pandemic urged authorities to impose rigorous quarantines and brought considerable changes to people's lifestyles. The impact of these changes on glycemic control has remained unclear, especially the long-term effect. We aimed to investigate the impact of COVID-19 lockdown on glycemic control in children and adolescents with type 1 diabetes.

Materials and Methods: This observational study enrolled children with type 1 diabetes using continuous glucose monitoring. Continuous glucose monitoring data were extracted from the cloud-based platform before, during and after lockdown. Demographics and lifestyle change-related information were collected from the database or questionnaires. We compared these data before, during and after lockdown.

Results: A total of 43 children with type 1 diabetes were recruited (20 girls; mean age 7.45 years; median diabetes duration 1.05 years). We collected 41,784 h of continuous glucose monitoring data. Although time in range (3.9–10.0 mmol/L) was similar before, during and after lockdown, the median time below range <3.9 mmol/L decreased from 3.70% (interquartile range [IQR] 2.25–9.53%) before lockdown to 2.91% (IQR 1.43–5.95%) during lockdown, but reversed to 4.95% (IQR 2.11–9.42%) after lockdown ($P = 0.004$). Time below range <3.0 mmol/L was 0.59% (IQR 0.14–2.21%), 0.38% (IQR 0.05–1.35%) and 0.82% (IQR 0.22–1.69%), respectively ($P = 0.008$). The amelioration of hypoglycemia during lockdown was more prominent among those who had less time spent <3.9 mmol/L at baseline. During lockdown, individuals reduced their physical activity, received longer sleep duration and spent more time on diabetes management. In addition, they attended outpatient clinics less and turned to telemedicine more frequently.

Conclusion: Glycemic control did not deteriorate in children and teenagers with type 1 diabetes around the COVID-19 pandemic. Hypoglycemia declined during lockdown, but reversed after lockdown, and the changes related to lifestyle might not provide a long-term effect.

INTRODUCTION

Since coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, the disaster has aroused worldwide concerns¹.

To contain the outbreak of COVID-19, the Chinese government took a series of actions, such as extreme lockdown and regional quarantines. On 25 January 2020, nearly all the cities activated the first-level public health emergency response². The lockdown and other government measures, including extending the Chinese New Year holiday, postponing schools' reopening,

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closing scenic locations and halting or reducing traffic services, have curbed population flow.

As the primary focus was centered on patients infected with COVID-19, people living with chronic diseases, such as diabetes, suffered a cut back in healthcare and required support^{3–5}. Rigid restrictions on outdoor activities might imply a shortage of access to medical resources, limited attendance at diabetes clinics and restricted contact with endocrinologists⁵. Simultaneously, the lockdown also brought considerable lifestyle changes to citizens, such as less physical activity, limited nutrition intake, changed sleep cycles and stress^{6,7}, but might have resulted in a healthier lifestyle, clearer temporal planning and maybe more organized insulin administration timing. All the daily aforementioned changes are likely to affect glycemic control in people with type 1 diabetes^{8–10}. Furthermore, accumulating evidence showed that COVID-19 patients with diabetes are at higher risk of severity and mortality^{11,12}. Although children and teenagers were initially considered less affected by COVID-19 than adults¹³, severe manifestation was also reported in children^{14,15}, and comorbidities were considered as a risk factor for COVID-19 in children¹⁶. Thus, it is also vital for children and teenagers with diabetes to keep strict adherence to diabetes management and strive for sufficient glycemic control.

Currently, a few studies^{17–20} showed that glycemic control improved in children and teenagers with type 1 diabetes during lockdown. Still, there has been little discussion about the long-term effect on blood glucose control after lockdown^{21,22}. Whether the reported improvement among children and adolescents will still maintain or attenuate after lockdown remains mostly unexamined.

Therefore, the present study aimed to investigate the medium- and long-term impact of lockdown on blood glucose control in children and teenagers with type 1 diabetes.

METHODS

Type 1 diabetes China

The type 1 diabetes China Registry Study is a registration project for type 1 diabetes patients in China, and was initiated in 2014 (ChiCTR2000034642). The program aimed to estimate the incidence of type 1 diabetes in all age groups in China²³, and establish a longitudinal cohort of type 1 diabetes patients in China to describe the disease profile and assess the metabolic control and diabetes management²⁴. Participants attended at least yearly office visits for medical information and sample collection after enrollment. Additional phone or online contact was occasionally made. Furthermore, the program was ongoing with the aid of the Tangtangquan application and the Nightscout system. Tangtangquan is a Chinese mobile application designed to provide diabetes self-management education for patients with type 1 diabetes, and has been available in major mobile application stores in China since September 2015²⁵. The Web-based cloud platform relies on the Nightscout system^{26,27}, which was established and has been used since September 2019 based on a website and cloud storage service, which provides

remote online access to the continuous glucose monitoring (CGM) data in real-time. The CGM acceptors (set up on smartwatches or mobile phones) acquire glucose values every 5 min from glucose transmitters connected to the sensors through Bluetooth devices. The devices automatically upload the glucose values to the cloud platform.

Study design and participants

The present observational study was paired designed to evaluate the collected CGM data from the population in the type 1 diabetes China Registry Study. This study's eligibility criteria were listed as follows: (i) diagnosed with type 1 diabetes by an endocrinologist; (ii) aged <18 years; and (iii) wore a personal CGM device for at least 1 week before (1 November–31 December 2019), during (25 January–29 February 2020) and after (1 June–31 July 2020) lockdown, while maintaining the same device. The exclusion criteria were listed as follows: (i) severe diabetes complications, such as nephropathy, proliferative retinopathy and myocardial infarction, within the past 6 months; (ii) used the artificial pancreas system during the study; (iii) refused to participate in the study; and (iv) could not cooperate due to psychological problems or other physical problems. Electronic informed consent was obtained from a parent/legal guardian for participants before enrollment, and patient anonymity was preserved. This study was approved by the institutional review board at the third affiliated hospital of Sun Yat-sen University (IRB no: [2014]2-105-1), and it conformed to the provisions of the Declaration of Helsinki.

Data collection

We collected demographic data (including age, sex, education level, household income), medical history (including medication, diabetes duration, diabetes complications and most recent glycated hemoglobin values) from the dataset of the type 1 diabetes China Registry Study. The information related to lifestyle changes was acquired through a telephone-based questionnaire. Our questionnaire consisted of five parts: (i) dietary; (ii) physical exercise; (iii) sleep habits; (iv) diabetes management; and (v) medical access. Briefly, trained investigators in our study group contacted the parents of the children with type 1 diabetes on the telephone and interviewed the parents using a questionnaire. The questions about diet, physical exercise, sleep habits and emotions were intended for the children. Regarding diabetes management and medical accessibility, we mainly asked the parents, who were mainly responsible for the healthcare of pediatric type 1 diabetes patients. Although there might have been recall bias and unknown confounding in our data collection during the telephone questionnaire, we had tried our best to carry out quality control. In detail, before the telephone interview: (i) the questionnaire was designed with concise and easy to understand questions – most of our questions were qualitative questions; (ii) our investigators made an appointment for the interview with the parents in advance to ensure that their children were present during

the interview; and (iii) we pilot tested the questionnaire to ensure the clarity of expression, and estimated that the time required for a thorough interview would be no less than half an hour. In fact, in the present study, the time spent in the interviews ranged between half an hour to one hour. Our interviewers were experienced in data collection, and skilled in language and communications. They were blinded to the glycemic results. During the telephone interview, our interviewers avoided any comments that might induce bias. After each interview, the interviewer would make an anonymized record. For the open-ended questions, the answers were discussed in our study groups to extract the participants' intentions. The CGM system measured glucose concentrations from interstitial fluid in the range of 40–400 mg/dL every 5 min for up to consecutive 7–10 days, and it automatically connected the cloud platform and uploaded the glucose data in real-time. CGM data were donated by participants and extracted from the cloud platform database in an observation time frame of 7–14 continuous days before, during and after lockdown, respectively. The related CGM parameters were calculated by GlyCulator 2.0 software (Department of Biostatistics and Translational Medicine, Medical University of Lodz, Poland)²⁸.

Study outcomes

The outcomes were basic CGM metrics, including: (i) blood glucose control parameters, such as CGM-measured time in range 3.9–7.8 mmol/L (TIR^{3.9–7.8}), time in range 3.9–10.0 mmol/L (TIR^{3.9–10.0}), CGM-measured mean glucose concentration and the estimated glycated hemoglobin outcomes; (ii) hyperglycemia metrics: time above range >10.0 mmol/L (TAR 10.0), TAR >13.9 mmol/L (TAR 13.9) and high blood glucose index; (iii) hypoglycemia metrics, such as time below range <3.9 mmol/L (TBR <3.9), TBR <3.0 mmol/L (TBR 3.0), low blood glucose index, hypoglycemic events (CGM readings <3.0 mmol/L for at least 15 min²⁹) and prolonged hypoglycemia (CGM readings <3.0 mmol/L for >120 min²⁹); and (iv) glucose variability parameters, such as coefficient of variation, standard deviation, mean amplitude of glucose excursion and mean of daily differences.

Statistical analysis

Continuous variables are shown as the mean \pm standard deviation or presented as the median and interquartile range (IQR), if not normally distributed. Categorical variables are presented as the number and percentage of participants affected. To compare the difference between the three phases, we used repeated measures ANOVA or the Friedman rank test to analyze the CGM metrics, and McNemar's χ^2 -test to examine lifestyle changes. Statistical significance was defined as a two-tailed $P < 0.05$. Data analyses were carried out using SPSS 25.0 statistical analysis software (SPSS Inc., Chicago, IL, USA). The definition of the three phases around lockdown was as follow: (i) baseline/before lockdown (1 November–31

December 2019, at the routine before the pandemic of COVID-19 in China); (ii) during lockdown (25 January–29 February 2020, enacting the first-level public health emergency response in nearly all the provinces²); and (iii) post-lockdown (1 June–31 July 2020, all provinces had lifted the first-level public health emergency response³⁰, while most people had resumed their studies and work).

RESULTS

Demographic characteristics

In all, 43 children and teenagers with type 1 diabetes (20 girls) were included, and the selection process is shown in Figure 1. The demographic characteristics of participants are summarized in Table 1. The mean age of patients was 7.45 ± 3.23 years, the median age of onset of type 1 diabetes was 5.45 years (IQR 3.10–8.25) and the median duration of type 1 diabetes was 1.05 years (IQR 0.58–1.84). The median body mass index of participants was 16.47 (IQR 14.19–17.82). The median baseline glycosylated hemoglobin value was 6.80% (IQR 6.50–7.20). A total of 77% of the participants ($n = 33$) used flash glucose monitoring (FreeStyle Libre[®]; Abbott, North Chicago, IL, USA), and 23% of the patients ($n = 10$) used CGM (7 participants used Dexcom G5[®], 3 participants used Dexcom G6[®]). All the participants were treated with insulin, and most used continuous subcutaneous insulin infusion ($n = 30$, 69.8%), whereas others were on multiple daily insulin injections ($n = 13$, 30.2%). We collected 41,784 h of CGM data in all, with 14,448 h before lockdown (14.0 days for 1 person on average), 13,344 h during lockdown (12.9 days for 1 person on average) and 13,272 h after lockdown (13.6 days for 1 person on average), respectively. All patients stayed at home, because schools closed when CGM data were captured during lockdown, and most people returned to study when CGM data were collected after lockdown.

Changes in glycemic control

Table 2 shows the comparison of CGM metrics among baseline, lockdown and post-lockdown. We found a small, but significant, difference in hypoglycemia among the three periods. Compared with baseline, hypoglycemia improved during lockdown, shown as the decrease of TBR <3.9 mmol/L, TBR <3.0 mmol/L, low blood glucose index, and the number of hypoglycemic events and prolonged hypoglycemic events. The median TBR <3.9 mmol/L decreased from 3.70% (IQR 2.25–9.53%) before lockdown to 2.91% (IQR 1.43–5.95%) during lockdown, but reversed to 4.95% (IQR 2.11–9.42%) after lockdown ($P = 0.004$). The median TBR <3.0 mmol/L was 0.59% (IQR 0.14–2.21%), 0.38% (IQR 0.05–1.35%) and 0.82% (IQR 0.22–1.69%), respectively ($P = 0.008$). The median low blood glucose index was 1.15 (IQR 0.73–2.60), 1.03 (IQR 0.58–1.68) and 1.40 (0.81–2.36), respectively ($P = 0.020$). The median number of hypoglycemic events was 1.50 per week (IQR 0–3.50), 0.50 per week (IQR 0–2.00) and 1.27 per week (IQR: 0.5–4.00), respectively ($P = 0.020$). The median number of

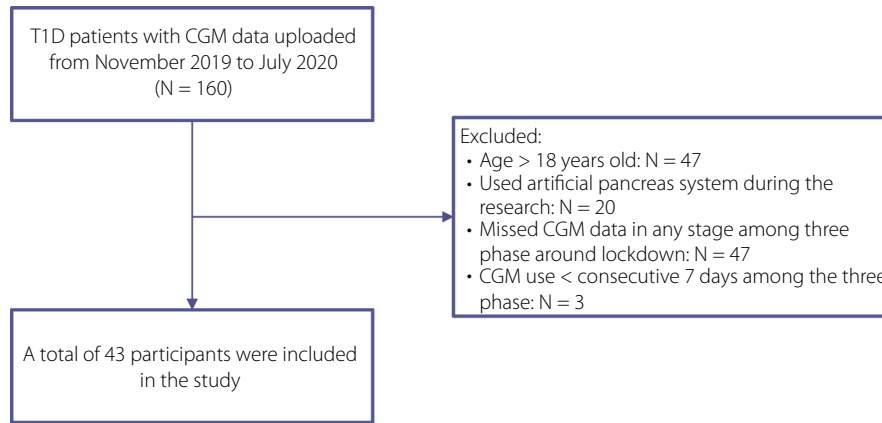


Figure 1 | Flowchart of study participants selection in the research. CGM, continuous glucose monitoring; T1D, type 1 diabetes.

Table 1 | Demographic characteristics of participants

Characteristics	Value			P-value
	Whole (n = 43)	Male (n = 23)	Female (n = 20)	
Age (years)	7.45 ± 3.23	7.60 ± 3.60	7.28 ± 2.83	0.756
Sex				
Male	23 (53.5%)	–	–	
Female	20 (46.5%)	–	–	
Body mass index (kg/m ² ; n = 36)	16.47 (14.19, 17.82)	14.80 (14.08, 18.90)	16.83 (14.42, 17.58)	0.836
Duration of register in for TTQ (years)	1.07 (0.72, 1.53)	1.11 ± 0.54	1.18 (0.60, 1.55)	0.789
Household income per year (n = 38)				
<¥30,000	2 (5.3%)	2 (9.5%)	0	0.528
≥¥30,000 a & <¥100,000	12 (31.6%)	6 (28.6%)	6 (35.3%)	
≥¥100,000	24 (55.8%)	13 (61.9%)	11 (64.7%)	
Education level (n = 33)	For parents			0.805
Primary school	0	0	0	
High school	11 (33.3%)	6 (35.3%)	5 (31.3%)	
University	22 (66.7%)	11 (47.8%)	11 (68.8%)	
Age of onset of type 1 diabetes (years)	5.45 (3.1, 8.25)	5.52 ± 2.93	5.87 ± 2.94	0.696
Duration of type 1 diabetes (years)	1.05 (0.58, 1.84)	1.16 (0.58, 2.22)	1.04 (0.50, 1.62)	0.715
Baseline HbA1c (%) (n = 32)	6.80 (6.50, 7.20)	6.93 ± 0.76	6.86 ± 0.53	0.754
Insulin treatment				
Pump	30 (69.8%)	15 (65.3%)	15 (75.0%)	0.486
Multiple daily injection	13 (30.2%)	8 (34.8%)	5 (25.0%)	
Premixed	0			
Insulin dosage (U/kg; n = 32)	0.76 (0.62, 0.95)	0.81 (0.70, 0.95)	0.70 (0.57, 0.98)	0.386

Total n = 43. Values are presented as mean ± standard deviation, median (interquartile range), or number (%). HbA1c, glycated hemoglobin; TTQ, Tangtangquan mobile application.

prolonged hypoglycemic events was 0 per week (IQR 0–0.50), 0 per week (IQR 0–0) and 0 per week (IQR 0–0.50), respectively (P = 0.039). What can be seen clearly in Figure 2 is the trend-line describing the decline and subsequent rise in hypoglycemia around lockdown. There was no significant difference in other CGM parameters (time in range, time in hyperglycemia and other glucose variability parameters).

Glycemic patterns in people with different hypoglycemia at baseline

To further observe the blood glucose profile after quarantine in the population of children and teenage with different baseline glycemic control, we attempted to explore the comparison of CGM metrics among three phases in both optimal (baseline TBR 3.9 <4%) and suboptimal control groups (baseline TBR

Table 2 | Continuous glucose monitoring metrics

	Before lockdown	During lockdown	After lockdown	<i>P</i> -value [†]
Time in range 3.9–7.8 mmol/L (%)	52.57 ± 14.42	52.18 ± 15.40	51.16 ± 15.29	0.614
Time in range 3.9–10.0 mmol/L (%)	74.28 ± 12.13	75.35 ± 12.66	73.60 ± 12.83	0.081
Mean glucose (mmol/L)	7.74 ± 1.19	7.85 ± 1.14	7.70 ± 1.20	0.368
Estimated HbA1c (%)	6.47 ± 0.75	6.54 ± 0.72	6.54 ± 0.72	0.368
Hyperglycemia				
Time >13.9 mmol/L (%)	2.95 (0.42, 5.91)	1.58 (0.69, 7.29)	1.80 (0.71, 3.86)	0.862
Time >10.0 mmol/L (%)	18.68 (12.05, 27.92)	15.39 (12.16, 27.67)	15.84 (11.78, 26.71)	0.404
High blood glucose index	41.54 (31.27, 54.69)	41.20 (33.49, 57.78)	40.74 (31.23, 52.61)	0.298
Hypoglycemia				
Time <3.9 mmol/L (%)	3.70 (2.25, 9.53)	2.91 (1.43, 5.95)	4.95 (2.11, 9.42)	0.004
Time <3.0 mmol/L (%)	0.59 (0.14, 2.21)	0.38 (0.05, 1.35)	0.82 (0.22, 1.69)	0.008
Low blood glucose index	1.15 (0.73, 2.60)	1.03 (0.58, 1.68)	1.40 (0.81, 2.36)	0.020
Hypoglycemic events (per week)	1.50 (0, 3.50)	0.50 (0, 2.00)	1.27 (0.50, 4.00)	0.020
Prolong hypoglycemia (per week)	0 (0, 0.50)	0 (0, 0)	0 (0, 0.50)	0.039
Glucose variability				
CV (%)	35.48 ± 7.17	34.06 ± 6.51	35.20 ± 6.38	0.242
SD (mmol/L)	2.77 ± 0.81	2.70 ± 0.75	2.72 ± 0.69	0.911
MAGE (mmol/L)	7.17 ± 2.04	7.01 ± 1.85	6.99 ± 1.76	0.975
MODD (mmol/L)	3.02 ± 1.00	2.89 ± 0.87	2.87 ± 0.99	0.086

Total *n* = 43. Data are expressed as mean ± standard deviation or median (interquartile range). CV, coefficient of variation; HbA1c, glycated hemoglobin; MAGE, mean amplitude of glucose excursion; MODD, mean of daily differences; SD, standard deviation. [†]ANOVA of repeated measures or the Friedman rank test.

3.9 ≥4%). Figure 3 shows the changing progress of hypoglycemia. Individuals who spent more time <3.9 mmol/L at baseline consistently had worse hypoglycemia than the optimal control group (Figure 3a–d). Consistent with expectations, similar amelioration of hypoglycemia was found in the optimal control group (Table S1), but the improvement did not occur in the suboptimal control group. Although the suboptimal control group appeared to show a trend of improvement of hypoglycemia in the chart, there was no statistical difference. Furthermore, TIR^{3.9–10.0} also gradually worsened in the suboptimal group (Figure 3e). There was no significant difference in other CGM parameters (time in hyperglycemia and other glucose variability parameters). It seemed that people who spent less time <3.9 mmol/L at baseline were more likely to benefit from confinement.

When dividing the participants into two groups based on whether they had hypoglycemic events at baseline, we found a different phenomenon (Table S2). There was no improvement in hypoglycemia during lockdown among people without hypoglycemic events at baseline. However, those with baseline hypoglycemic events achieved a reduction in TBR <3.0 mmol/L (*P* = 0.016) and the number of hypoglycemic events (*P* = 0.005; Figure S1).

Changes related to lifestyle during lockdown

There was no denying that massive changes related to lifestyle would occur due to hard lockdown and home quarantine. Changes in lifestyle and medical resources are shown in

Table 3. Notably, there was a sharp increase in the number of snacks, sleep duration and time for diabetes management during lockdown (in 32.4% children [*P* = 0.018]; in 41.2% children [*P* = 0.024]; in 67.6% children [*P* < 0.001], respectively). A total of 44.1% of children reduced physical exercise during lockdown, and the primary exercise type changed from outdoor activities, such as cycling and basketball, to indoor activities, such as pacing and rope skipping. A total of 52.9% of individuals reduced their studying time (*P* < 0.001), 23.5% of people ate less regularly (*P* = 0.029), 55.9% of patients went to bed later and 58.8% of patients woke later. The patients claimed self-perceived hypoglycemia decreased during lockdown (in 70.6% children, *P* < 0.001), consistently with the improved hypoglycemia detected by CGM, and no hyperglycemia or hypoglycemia coma occurred. Only a minority of patients (3 individuals) did experience a temporary shortage of insulin during lockdown. Still, insulin doses did not change during all three periods (Table S3). Meanwhile, the patients acquired less access to outpatient clinics (in 64.7% children, *P* = 0.002) and turned to online medical services more frequently (in 29.4% children, *P* = 0.011), whereas nearly no stress and anxiety changed.

Further analysis of the data showed different lifestyle changes through the lockdown in the optimal control group and suboptimal control group (Table S4) or people with and without hypoglycemic events (Table S5). The results of pairwise comparisons are shown in Table S6). The optimal control group (TBR 3.9 <4% at baseline) reduced total physical activity during

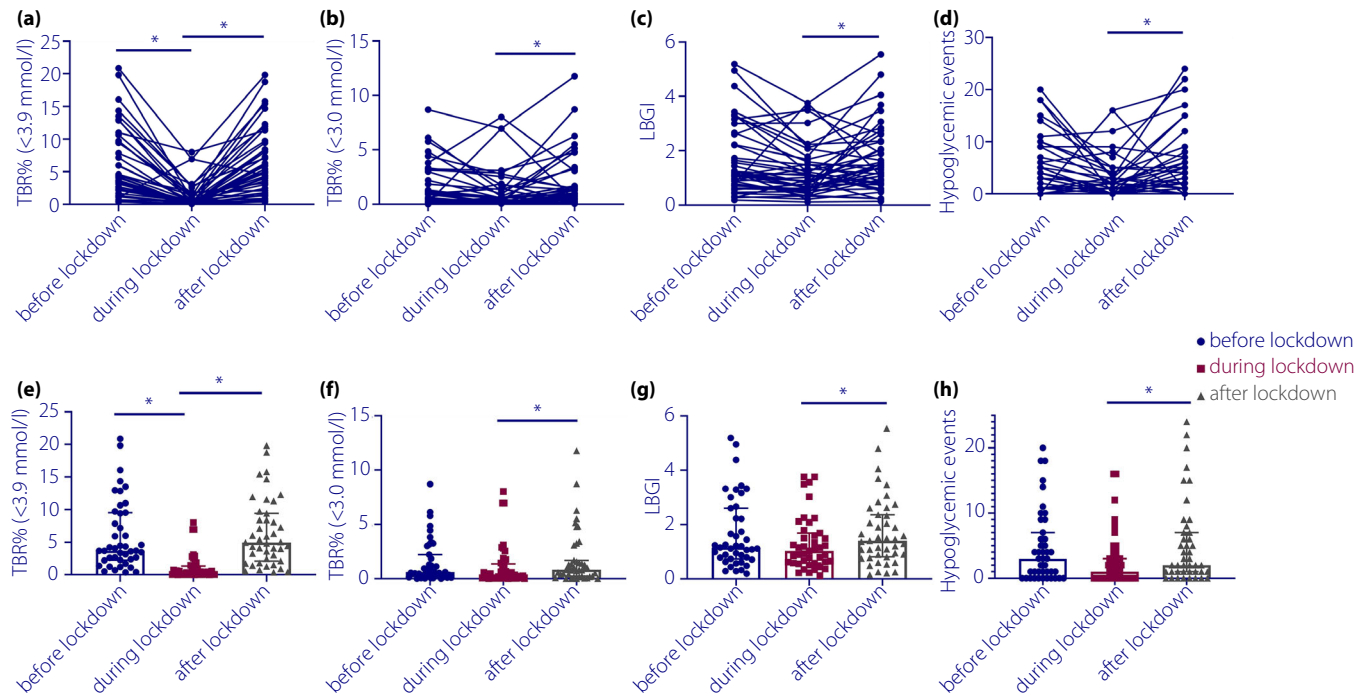


Figure 2 | Changes in hypoglycemia among children and teenagers ($n = 43$). (a–d) Trend line of changes of individual patients. (e–h) Box scatterplots based on the median value. (a,e) Time below range (TBR) <3.9 mmol/L significantly decreased during lockdown ($P = 0.011$) and reversed after lockdown ($P = 0.011$). (b,f) TBR <3.0 mmol/L trended downward during lockdown ($P = 0.093$) and elevated after lockdown ($P = 0.008$). (c,g) Low blood glucose index (LBGI) declined during lockdown ($P = 0.053$) and rose again after lockdown ($P = 0.039$). (d,h) The number of hypoglycemic events decreased during lockdown and reversed after lockdown ($P = 0.039$).

lockdown ($P = 0.011$), whereas the suboptimal control group remained mostly unchanged in exercise. For people with baseline hypoglycemic events, there was a considerable decrease in physical activity, and a sharp increase in the number of snacks, sleep duration and time for diabetes management during lockdown, whereas there were no significant changes in people without baseline hypoglycemic events.

DISCUSSION

The present data showed that during the COVID-19 pandemic and lockdown, glycemic control in children and adolescents with type 1 diabetes did not deteriorate. Contrarily, improved hypoglycemia occurred during lockdown, suggested by a reduction in TBR 3.9, TBR 3.0, low blood glucose index, and the number of hypoglycemic events and prolonged hypoglycemic events, but reversed after lockdown, which was more prominent in those with less time spent <3.9 mmol/L. Meanwhile, lockdown and quarantine brought enormous changes to type 1 diabetes patients' routines, characterized by less physical exercise, study time and outpatient visits, but more sleep duration and diabetes management time. Nevertheless, the lifestyle-related change in glycemic control did not show medium- and long-term effects.

The COVID-19 pandemic has imposed a tremendous challenge to the people and government of China^{31,32}. The public healthcare system has carried more immense burdens, which has caused a significant reduction in care services for chronic diseases, such as diabetes³³. During the outbreak, rigid quarantine forced people to change their daily routines by shutting down work, reducing physical activities, confining nutrient intake, and limiting outpatient services and even essential medicine. Rapid lifestyle changes and a shortage of medical resources are likely to worsen glycemic control in people with type 1 diabetes^{9,34}. Nevertheless, our observation that the amelioration of blood glucose control occurred during lockdown is reassuring.

One possible explanation is that the calmer routine enabled children and adolescents to maintain longer sleep duration and less studying time. Most parents were at home during confinement, keeping in contact with and closely monitoring their children. Patients had more enough time to carry out self-management for diabetes, to take care of glycemic control and to respond quickly to hypoglycemia under parental supervision. In the period after lockdown, the time patients spent on blood glucose management decreased, and the improvement in glycemic control disappeared, which suggests that patients should

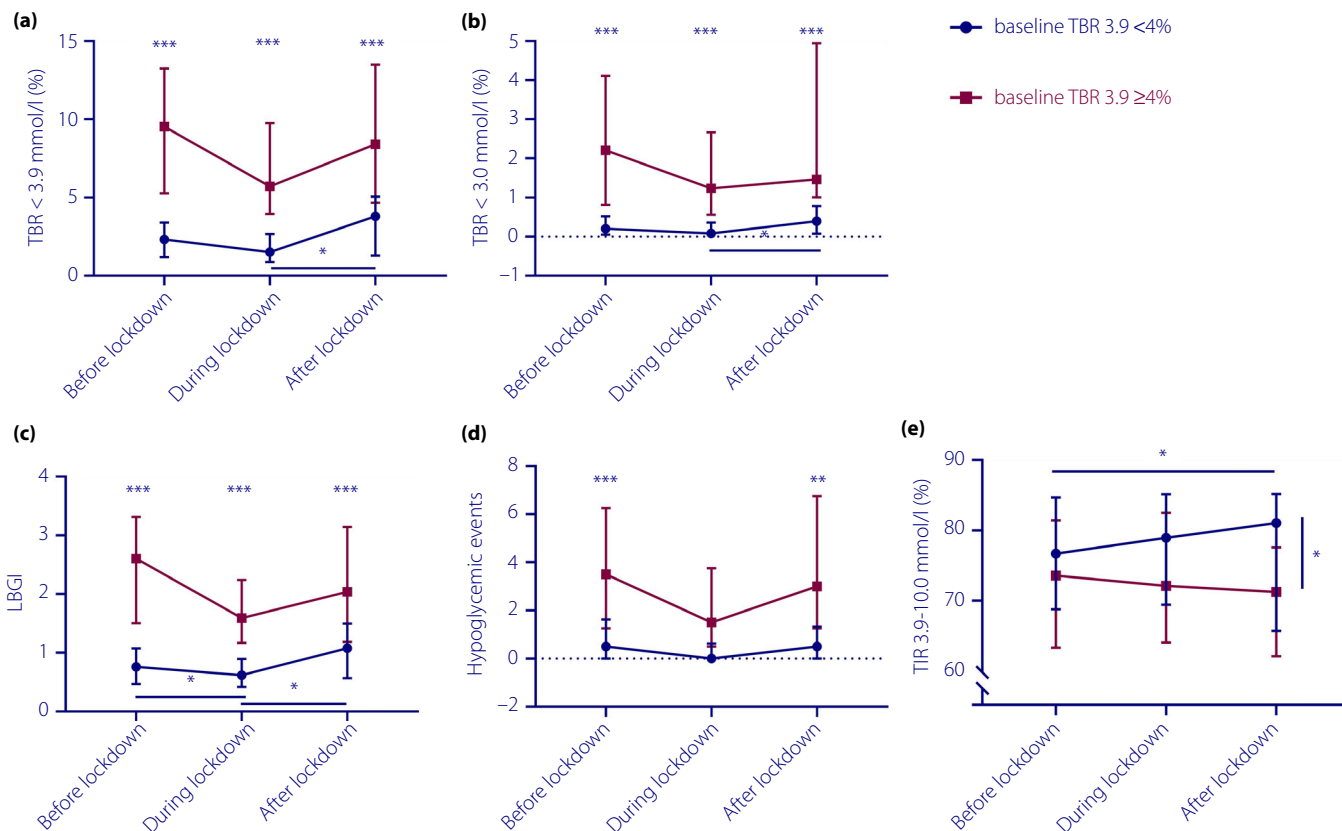


Figure 3 | Hypoglycemia and time in range time in range 3.9–10.0 mmol/L ($TIR^{3.9-10.0}$) in the optimal ($n = 22$) and suboptimal ($n = 21$) glycemic control group among children and teenagers. Optimal control group refers to baseline time below range (TBR) <3.9 mmol/L (TBR 3.9) <4%, whereas the suboptimal group refers to baseline TBR 3.9 \geq 4%. (a–c) Hypoglycemia (TBR <3.9 mmol/L, TBR <3.0 mmol/L and LBGi) in the optimal control group showed better control in all three periods compared with the suboptimal control group. (a) TBR <3.9 mmol/L decreased during lockdown ($P = 0.100$) and reversed significantly after lockdown ($P = 0.023$) in the optimal group. (b) TBR <3.0 mmol/L trended downward during lockdown ($P = 0.326$) and elevated after lockdown ($P = 0.048$) in the optimal group. (c) The low blood glucose index (LBGi) declined during lockdown ($P = 0.033$) and rose again after lockdown ($P = 0.023$). (d) The number of hypoglycemic events in the optimal and suboptimal group. (e) $TIR^{3.9-10.0}$ in the optimal group gradually improved as time went on ($P = 0.033$), and after lockdown $TIR^{3.9-10.0}$ in the optimal group was significantly better than that in the suboptimal group ($P = 0.031$).

insist on diabetes management. Furthermore, the present participants had relatively good glycemic control at baseline, shown by low glycosylated hemoglobin (<7%) and high TIR (>70%). Parents of children with type 1 diabetes had a high education level in our research. Therefore, they maintained effective management of diabetes before the pandemic. The susceptibility and severity of diabetes complicated with COVID-19 might also concern parents and improve adherence to strict blood glucose management.

Another reason for the amelioration of blood glucose control during lockdown is likely due to the development of remote glucose monitoring and online healthcare assistance services. CGM use is beneficial to adolescents and young adults for glycemic control³⁵. Remote access to CGM data supported by Nightscout has enabled parents to be involved in glycemic control in a more timely and convenient manner. Notably, the technological development of online medical

resources, such as mobile health applications and telemedicine, in recent years has provided a convenient and effective impact on self-management and blood glucose control of type 1 diabetes patients^{36–38}. In response to the outbreak, the Chinese government strongly advocated and implemented virtual care technologies³⁹. In our research, most parents claimed that their children had difficulty going out to clinics or doing physical exercise. The parents also worried about children becoming infected, with SARS-CoV-2 being present in hospitals during lockdown. Therefore, families of children with type 1 diabetes in the present study hoped to acquire assistance in purchasing insulin and systematic knowledge about diabetes management. Meanwhile, they suggested that telemedicine could provide targeted, timely, and long-term consultations and services. During the unprecedented lockdown with restriction of outdoor activities, telemedicine has played an essential role in providing healthcare services and medical

Table 3 | Questionnaire-derived lifestyle and medical data around lockdown in the study participants

Lifestyle changes compared with pre-lockdown (<i>n</i> = 34)	During lockdown			After lockdown			<i>P</i> -value [†]
	More	Same	Less	More	Same	Less	
Total physical activity [‡]	4 (11.8%)	15 (44.1%)	15 (44.1%)	4 (11.8%)	28 (82.4%)	2 (5.9%)	0.004
Food amount	6 (17.6%)	25 (73.5%)	3 (8.8%)	1 (2.9%)	31 (91.2%)	2 (5.9%)	0.142
Regularity of mealtimes	0	26 (76.5%)	8 (23.5%)	3 (8.8%)	31 (91.2%)	0	0.029
No. snacks	11 (32.4%)	22 (64.7%)	1 (2.9%)	3 (8.8%)	30 (88.2%)	1 (2.9%)	0.018
No. midnight snacks	3 (8.8%)	31 (91.2%)	0	0	34 (100.0%)	0	0.317
Sleep duration	14 (41.2%)	19 (55.9%)	1 (2.3%)	4 (11.8%)	27 (79.4%)	3 (8.8%)	0.024
Bedtime [§]	19 (55.9%)	13 (38.2%)	2 (5.9%)	5 (14.7%)	26 (76.5%)	3 (8.8%)	0.003
Waking time [§]	20 (58.8%)	13 (38.2%)	1 (2.9%)	3 (8.8%)	28 (82.4%)	3 (8.8%)	<0.001
Study time	5 (14.7%)	11 (32.4%)	18 (52.9%)	6 (17.6%)	26 (76.5%)	2 (5.9%)	<0.001
Stress	1 (2.9%)	33 (97.1%)	0	2 (5.9%)	32 (94.1%)	0	0.317
Anxiety	1 (2.9%)	33 (97.1%)	0	2 (5.9%)	32 (94.1%)	0	0.317
Self-perceived hypoglycemia	1 (2.9%)	9 (26.5%)	24 (70.6%)	5 (14.7%)	29 (85.3%)	0	<0.001
Time in glycemic management	23 (67.6%)	11 (32.4%)	0	0	34 (100.0%)	0	<0.001
Access to outpatient clinics	0	12 (35.3%)	22 (64.7%)	1 (2.9%)	22 (64.7%)	11 (32.4%)	0.002
Use of online medical service	10 (29.4%)	23 (67.6%)	1 (2.9%)	1 (2.9%)	30 (88.2%)	3 (8.8%)	0.011
Insulin purchase	2 (6.1%)	26 (78.8%)	5 (15.2%)	3 (9.1%)	29 (87.9%)	1 (3%)	0.172
	Yes	No		Yes	No		
Hyperglycemic coma	0	34 (100.0%)		0	34 (100.0%)		>1.000
Hypoglycemic coma	0	34 (100.0%)		0	34 (100.0%)		>1.000
Shortage of insulin	3 (8.8%)	31 (91.2%)		0	34 (100.0%)		0.002
Online shopping for insulin	5 (14.7%)	29 (85.3%)		5 (14.7%)	29 (85.3%)		1.000

Data are expressed as the number of participants (%). [†]McNemar's χ^2 -test. [‡]Based on the frequency and duration of physical activity. [§]In bedtime and waking time, 'more' and 'less' referred to 'later' and 'earlier'.

advice to children with type 1 diabetes and their families, enabling patients to adhere to diabetes management and promote the further progress of telemedicine.

In the present study, individuals with different hypoglycemia situations at baseline showed diverse glucose profiles through the lockdown. We suspected that people who spent less time <3.9 mmol/L at baseline had achieved reasonable glycemic control with low TBR 3.9 (2.32%) and high TIR 3.9–10.0 (76.71%) before lockdown. A good awareness of diabetes management and stable routines might enable them to benefit from the lockdown. Furthermore, people with more hypoglycemic events before lockdown showed relatively poor glycemic control at baseline. They underwent a relaxed and calmer lifestyle during lockdown, with less physical activity, study time and longer sleep duration, resulting in improved glycemic control.

Our study's strength is that it described the blood glucose profiles and lifestyle changes of children with type 1 diabetes before, during and after lockdown, which reflected a medium- and long-term effect of lockdown to some extent. Furthermore, our CGM cloud platform has provided remote access to the blood glucose value in real-time. The limitation of the present study was the relatively small sample size and mainly qualitative lifestyle information. However, we captured an extended time frame of CGM data, reflecting the phases before, during

and after lockdown. The information related to lifestyle could roughly indicate the change through the three periods. A larger population should be used to confirm the results, especially in people with worse glycemic control and those who do not use continuous glucose monitoring. The findings indicated that children and teenagers with type 1 diabetes might go through the COVID-19 lockdown and quarantine safely with no deterioration in glycemic control with remote telemedicine assistance, which would provide a new form of diabetes management and enable us to prepare for disease-related restrictions more sufficiently.

The present results showed that glycemic control did not deteriorate in children and adolescents with type 1 diabetes in China around the COVID-19 pandemic. Hypoglycemia improved during lockdown, but reversed after lockdown, and those with better control at baseline were more likely to achieve amelioration in hypoglycemia. A more stable and slowed down rhythm might lead to better glycemic control, but lifestyle changes could not provide a long-term effect.

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DISCLOSURE

The authors declare no conflict of interest.

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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 | Hypoglycemia and time in range 3.9–10.0 mmol/L (TIR^{3.9–10.0}) in people without hypoglycemic events ($n = 11$) and with hypoglycemic events ($n = 32$) among children and teenagers.

Table S1 | Continuous glucose monitoring metrics in people with different time below range <3.9 mmol/L at baseline ($n = 43$).

Table S2 | Continuous glucose monitoring metrics in people with or without hypoglycemic events at baseline ($n = 43$).

Table S3 | Changes in insulin administration.

Table S4 | Pairwise comparisons of metrics with significant difference in ANOVA of repeated measures or the Friedman rank test.

Table S5 | Questionnaire-derived lifestyle and medical data around lockdown in people with different time below range <3.9 mmol/L at baseline.

Table S6 | Questionnaire-derived lifestyle and medical data around lockdown in people with or without hypoglycemic events at baseline.