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ORIGINAL RESEARCH

Effects of Two COVID-19 Lockdowns on HbA1c Levels in Patients with Type 1 Diabetes and Associations with Digital Treatment, Health Literacy, and Diabetes Self-Management: A Multicenter, Observational Cohort Study Over 3 Years

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ABSTRACT

Introduction: Short-term studies reported improved glycemic control and a decrease in eHbA1c (estimated hemoglobin A1c) in patients with type 1 diabetes during COVID-19 lockdown, but long-term changes are unknown. Therefore, the main objectives are to (1) analyze whether laboratory-measured HbA1c changed during and after two lockdowns and (2) investigate potential variables influencing HbA1c change.

Methods: In this cohort study, 291 adults with type 1 diabetes were followed over 3 years including the prepandemic phase and two lockdowns. The data from medical records and validated questionnaires assessing health literacy (HLS-EU-Q16), diabetes self-management (DSMQ-R27), general self-efficacy (GSE), and social support (F-SOZU-K14) were used to analyze associations with HbA1c levels ($N=2370$) by performing multivariable linear regressions.

Results: The median age was 54 (38–63) years and 159 (54.6%) were male. All phases of the COVID-19 pandemic were associated with a significant increase in laboratory-measured HbA1c levels in percent (e.g., during first lockdown $\beta=0.23$, 95% confidence interval (CI) 0.07–0.39, $p=0.005$; during the second lockdown, $\beta=0.27$, 95% CI 0.15–0.38, $p<0.001$). HbA1c change during lockdowns was significantly affected by the number of checkups ($\beta=-0.03$, 95% CI –0.05 to –0.01, $p=0.010$), the value of HbA1c at previous observation ($\beta=0.33$, 95% CI 0.29–0.36, $p<0.001$), educational level (secondary versus tertiary: $\beta=0.22$, 95% CI 0.06–0.38, $p=0.008$; primary versus tertiary: $\beta=0.31$, 95% CI 0.10–0.52, $p=0.004$), health literacy score (for each point: $\beta=-0.03$, 95% CI –0.05 to – 0.002, $p=0.034$), and diabetes self-management score (for each point: $\beta=-0.03$, 95% CI –0.04 to –0.02, $p<0.001$). The use of continuous glucose monitoring or insulin pump had no effect on HbA1c change.

Conclusions: Lockdowns can lead to worsening glycemic control in patients with type 1 diabetes. Particularly patients with few check-ups, poor blood glucose values, deficits in diabetes self-management, low health literacy, and a low level of education seem to be at greater risk of worsening glycemic control during lockdowns

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and, therefore, require special medical care, e.g., through telemedicine.

Trial Registration: ClinicalTrials.gov identifier, NCT04821921.

Keywords: Type 1 diabetes; COVID-19; HbA1c; Health literacy

Key Summary Points

Why carry out the study?

Previous research showed conflicting results about the impact of COVID-19 lockdown on HbA1c levels in patients with type 1 diabetes (T1D), mostly relying on short-term data from continuous glucose monitoring. Correlations with patient characteristics, such as digital treatment, were rarely investigated

What was learned from the study?

Both lockdowns were significantly associated with worsening glycemic control in patients with T1D. A low number of check-ups, poor blood glucose values, deficits in diabetes self-management, low health literacy, and low educational attainment were risk factors for worsening glycemic control during lockdowns

INTRODUCTION

During the recent coronavirus disease 2019 (COVID-19) pandemic, nationwide lockdowns were imposed in most countries to contain the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1–4]. Patients with diabetes mellitus (DM) and patients with hyperglycemia showed a higher risk of COVID-19 infection, intensive care unit admission, and death [5, 6]. Angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) are the two major cofactors required by SARS-CoV-2 to enter human cells [7]. Both cofactors were found to be more expressed in cardiomyocytes of patients with DM than in patients without DM [8]. Increased expression of ACE2 is thought to increase susceptibility to COVID-19 infection in patients with DM by favoring cellular entry of SARS-CoV-2 [8]. During the pandemic, every second hospitalized patient with DM who was infected by SARS-CoV-2 developed myocardial damage [8].

As many patients were afraid of the high infection rate and the associated mortality risk, they stayed at home and used less outpatient healthcare during COVID-19 lockdowns [1, 9, 10]. Physical inactivity and lack of follow-up consultations can lead to adverse health outcomes, so lockdowns resulted in worsened glycemic control in patients with DM [1, 2]. As systematic reviews revealed, glycosylated hemoglobin A1c (HbA1c) levels increased significantly during lockdown in patients with type 2 diabetes (T2D) [1, 2], but surprisingly, this was not observed in patients with T1D [1]. In patients with T1D, most studies even reported increased time in range and decreased HbA1c levels during lockdown [11–26], while a few reported no change [27–30] or worsened glycemic control [31–33]. In Germany, around 341,000 adults are affected by T1D [34].

However, it should be noted that most studies examining the glycemic effects of lockdown in patients with T1D [11–33, 35–39] had methodological limitations, such as the relatively short observation period. Additionally, in many studies [11, 12, 16, 17, 19, 21–24, 26], blood HbA1c concentration was not measured in the laboratory but was estimated using the continuous or flash glucose monitoring (CGM) data, which can differ widely from actual HbA1c values [3, 40]. Furthermore, it should have been considered that HbA1c levels may be influenced by other variables besides lockdowns, such as patients' educational level [41], health literacy [42], diabetes self-management [43], self-efficacy [44], perceived social support [45], comorbidities (e.g., depression [46]), and, especially, diabetes therapy [13, 17, 19, 26]. Previous lockdown studies did not examine most of these parameters.

Therefore, we conducted this study to examine the glycemic effects of two lockdowns on adults with T1D. The objective of this study is (1) to analyze whether the lockdown phases of the COVID-19 pandemic were associated with changing laboratory-measured HbA1c levels and (2) examine if patients' diabetes digital treatment (e.g., continuous glucose monitoring and insulin pump), comorbidities, perceived social support, health literacy, diabetes self-management, general self-efficacy, and sociodemographic data were mediating the change in HbA1c levels.

METHODS

Study Design and Study Population

For this retrospective study, we used data from the longitudinal observational study entitled "Impact of the COVID-19 pandemic on DIAbetes Management" (CoDiaM), which was conducted by extracting data from patient records in diabetes practices and through a postal survey. The Local Psychological Ethics Committee at the Center for Psychosocial Medicine of the University Medical Center Hamburg-Eppendorf approved the CoDiaM study on 19 January 2021 (approval number LPEK-0243), and the study was registered at ClinicalTrials.gov (NCT04821921). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. For the CoDiaM study, patients were recruited from three diabetes practices with a total of 14 physicians. All patients were screened for eligibility. Patients were included if they were at least 18 years old, had a documented diagnosis of diabetes mellitus in their medical records and had been treated at the participating practice at least once in 2019 and 2020. Patients who had died before recruitment were excluded. Further exclusion criteria for the CoDiaM study were gestational diabetes, the absence of a postal address or a change of treating diabetologist. In addition, patients were excluded if they were unable to read, write, or had insufficient German language skills, were unable to provide informed consent, or had functional limitations that precluded participation in the survey (e.g., arm paresis).

Eligible patients were invited by mail to participate in the CoDiaM study. They received an informed consent form, patient information about the study and a standardized questionnaire. Patients were able to choose when and where to complete the questionnaire. For the first practice, patient recruitment and postal surveys were conducted between 22 February and 6 April 2021, for the second practice between 2 June and 4 August 2021, and for the third practice between 30 November 2021 and 5 April 2022. After patients had given their written consent, their data between 1 January 2019 and 31 December 2021 were extracted from the medical records. Patients with type 2 diabetes or pancreoprive diabetes were excluded retrospectively.

Dependent and Independent Variables

The dependent variable was the laboratory-measured HbA1c level extracted from patient records. Independent variables comprised pandemic phases including two lockdowns, age, sex, educational level, comorbidities, patients' diabetes digital treatment (CGM and insulin pump), perceived social support, perceived health literacy, perceived diabetes self-management, and perceived self-efficacy. The endpoint of the study was the change in HbA1c levels.

Sociodemographic data, social support, health-literacy, self-efficacy, and diabetes self-management were assessed in the survey. Age was measured in years, and sex was recorded as female or male. Based on the education data, patients were assigned to three hierarchical levels of education according to the Comparative Analysis of Social Mobility in Industrial Nations (CASMIN) classification, i.e., tertiary, secondary, and primary education or below [47]. Following the manuals, the short version of the European Health Literacy Questionnaire (HLS-EU-Q16, ranging from 0 to 16 points) was used to measure perceived health literacy [48], and the revised Diabetes Self-Management Questionnaire (DSMQ-R27, ranging from 0 to 60 points) was applied to assess diabetes self-management behaviors [43, 49]. The DSMQ-R27 includes 27 questions focusing on five subscales: dietary control, blood glucose monitoring, medication adherence, physical activity, and physician contact [43, 49]. In addition, the General Self-Efficacy Scale (GSE, ranging from 10 to 40 points) was used to evaluate perceived self-efficacy [50] and the Social Support Questionnaire (F-SOZU-K14, ranging from 0 to 5 points) was applied to assess perceived social support [51] during lockdown.

The diagnosis of T1D had already been made by treating diabetologists due to positive autoantibodies. Documented prediagnoses and prescriptions for diabetes digital treatment (i.e., CGM or insulin pump accessories) were extracted from the medical records. Documented prediagnoses included depression, cardiovascular risk factors (such as hypertension), atherosclerotic cardiovascular disease (such as chronic ischemic heart disease), end-organ damages (such as retinopathy) and cardiovascular events (such as myocardial infarction).

Statistical Analyses

The descriptive data of the sample were described by fractions and medians with interquartile ranges. In this study, median HbA1c values were reported for each phase of the COVID-19 pandemic with a total of 2370 HbA1c observations. We defined the phases as (1) before the first lockdown in Germany (from 1 January 2019 to 21 March 2020), (2) during the first lockdown (from 22 March 2020 to 6 May 2020), (3) after the first lockdown (from 7 May 2020 to 12 December 2020), (4) during the second lockdown (from 13 December 2020 to 30 June 2021), and (5) after the second lockdown (from 1 July 2021 to 31 December 2021).

We analyzed the associations between the independent variables (pandemic phases including two lockdowns, age, sex, educational level, comorbidities, patients' diabetes digital treatment, perceived social support, perceived health literacy, perceived diabetes self-management, and perceived self-efficacy) and the dependent variable (HbA1c level) by longitudinal mixed-effects multivariable linear regression. We controlled the analysis for random effects on physician and patient within practice level, adjusted for the patient's HbA1c level in the measurement directly before the analyzed observation and controlled for number of the respective measurement and phase of COVID-19 pandemic. In addition, we performed unadjusted longitudinal analyses for the above independent variables. These analyses were also controlled for practice- and patient-level random effects, adjusted for prior HbA1c levels, and controlled for number of measurements and pandemic phase. An alpha level of 5% ($p < 0.05$) was considered statistically significant. Statistical analyses were conducted using Stata 15.1.

RESULTS

The recruitment of participants is shown in Supplementary Fig. 1. Of 1,503 patients who returned a questionnaire, 241 could not be included in the analysis because of incomplete data. Of 1,262 participating patients with complete data set (19.4% of eligible patients), 971 were retrospectively excluded because they had type 2 or pancreoprive diabetes. Finally, 291 patients with type 1 diabetes could be included in our data analysis.

The patient characteristics are presented in Table 1. The median age was 54 (38/63) years, 159 (54.6%) were male, and 145 (49.8%) had secondary educational level. CGM was used by 195 (67%) patients and 111 (38.1%) had an insulin pump. Among our study participants, the median score was 13 (10/15) on the short version of the European Health Literacy Questionnaire (HLS-EU-Q16), 46 (40/50) on the revised Diabetes Self-Management Questionnaire (DSMQ-R27), 30 (28/33) on the General Self-Efficacy Scale (GSE), and 4.3 (3.9/4.8) on the Social Support Questionnaire (F-SOZU-K14).

Prior to the first lockdown on 22 March 2020, 151 (51.9%) patients had cardiovascular risk factors, 91 (31.3%) end organ damages, 22 (7.6%) atherosclerotic cardiovascular disease, 11 (3.8%) cardiovascular events, and 20 (6.9%) depression (Supplementary Table 1).

For the sample of this study, 2370 HbA1c measurements were documented during the observation period, which covered the time between 17 January 2019 and 23 December

Table 1 Patient characteristics ($n = 291$)

Characteristic	Distribution
Age: median (interquartile range)	54 (38/63) years
Sex:	
Male	159 (54.6%)
Female	132 (45.4%)
Educational level (pursuant to CASMIN)	
Inadequately completed, general elementary or basic vocational	61 (21.0%)
Secondary school certificate or "A" level equivalent	145 (49.8%)
Higher or lower tertiary education	85 (29.2%)
F-SozU K14 score: median (interquartile range)	4.3 (3.9/4.8)
General self-efficacy score: median (interquartile range)	30 (28/33)
HLS-EU-Q16 score: median (interquartile range)	13 (10/15)
DSMQ score: median (interquartile range)	46 (40/50)
Use of CGM	195 (67.0%)
Use of an insulin pump	111 (38.1%)

n number of participants, *CASMIN* Comparative Analysis of Social Mobility in Industrial Nations, *F-SozU K14* the Social Support Questionnaire, *HLS-EU-Q16* the European Health Literacy Questionnaire including 16 items, *DSMQ-R27* the revised Diabetes Self-Management Questionnaire including 27 items, *CGM* continuous glucose monitoring

Table 2 HbA1c values during observation time ($n = 291$, $N = 2370$)

Characteristic	Distribution	N
HbA1c values overall: median (interquartile range)	7.3 (5.3/8.0)	2.370
Change in HbA1c values compared to first measurement		
Before first lockdown (from 1 January 2019 to 21 March 2020)	0 (−0.4/+0.4)	783
During first lockdown (from 22 March 2020 to 6 May 2020)	+0.3 (−0.2/+0.7)	50
After first lockdown (from 7 May 2020 to 12 December 2020)	+ 0.2 (−0.3/+0.6)	577
During second lockdown (from 13 December 2020 to 30 June 2021)	+0.2 (−0.3/+0.7)	513
After second lockdown (from 1 July 2021 to 31 December 2021)	+0.1 (−0.3/+0.6)	447

n number of participants, *N* number of observations, *HbA1c* glycosylated hemoglobin A1c

2021. The change in HbA1c values during the observation period is presented in Table 2. At first measurement, median HbA1c level (in %) was 7.3 (5.3/8.0). During the first lockdown (from 22 March 2020 to 6 May 2020), HbA1c levels increased compared with the first measurement, and a peak value of +0.3 (−0.2/+0.7) was observed (cf. Fig. 1). After the first lockdown (from 7 May 2020 to 12 December 2020) and during the second lockdown (from 13 December 2020 to 30 June 2021), these values stabilized at +0.2 (−0.3/+0.6)

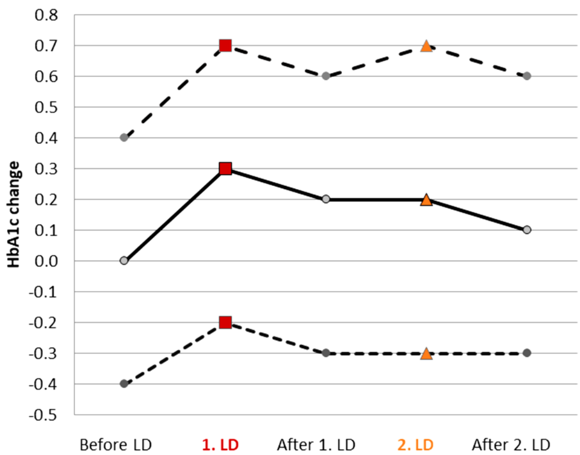

Fig. 1 Median and interquartile range of change in HbA1c (in percent) during the COVID-19 pandemic ($n=291$; $N=2370$). n number of participants, N number of HbA1c observations, *LD* lockdown. Before LD: from 1 January 2019 to 21 March 2020. First LD: from March 2020 to 6 May 2020. After first LD: from 7 May 2020 to 12 December 2020. Second LD: from 13 December 2020 to 30 June 2021. After second LD: from 1 July 2021 to 31 December 2021

and +0.2 (–0.3/+0.7), respectively. After the second lockdown (from 1 July 2021 to 31 December 2021), they converge to the baseline with a decline to +0.1 (–0.3/+0.6). During the observation time, only few diabetic events like ketoacidosis, acute renal failure or hypo- and hyperglycemic episodes were documented in the patient records (Supplementary Table 2).

Table 3 presents associations between patient characteristics and changes in HbA1c levels. Compared with the period before the first lockdown, all phases of the COVID-19 pandemic were associated with an increase in HbA1c levels, i.e., during the first lockdown (β = 0.23, 95% CI 0.07–0.39, $p=0.005$), after the first lockdown (β = 0.20, 95% CI 0.11–0.28, $p<0.001$), during the second lockdown (β = 0.27, 95% CI 0.15–0.38, $p<0.001$), and after the second lockdown (β = 0.22, 95% CI 0.07–0.37, $p<0.001$).

A higher number of HbA1c measurements, i.e., more frequent check-ups, was associated with lower HbA1c values (β = –0.03, 95% CI –0.05 to –0.01, $p=0.010$). A higher HbA1c value at previous observation was associated with a greater increase in HbA1c during lockdowns (β = 0.33, 95% CI 0.29–0.36, $p<0.001$).

The change of HbA1c levels was not significantly affected by patient age (for every year: β = 0.004, 95% CI –0.001 to 0.01, $p=0.151$), sex (for male: β = –0.02, 95% CI–0.16 to 0.12, $p=0.745$), and comorbidities (e.g., depression: β = 0.08, 95% CI–0.20 to 0.35, $p=0.592$). The use of CGM (β = 0.14, 95% CI –0.02 to 0.31, $p=0.087$) and the use of an insulin pump (β = 0.07, 95% CI –0.08 to 0.21), $p=0.373$) were also not significantly related to the change in HbA1c values (Table 3).

Compared with patients with tertiary education, we found an increase of HbA1c levels in patients with secondary (β = 0.22, 95% CI 0.06–0.38, $p=0.008$) and primary education (β = 0.31, 95% CI 0.10/0.52, $p=0.004$). There also was an increase in HbA1 in patients with worse perceived health literacy (HLS-EU-Q16) (change for each point: β = –0.03, 95% CI –0.05 to –0.002, $p=0.034$) and worse self-reported diabetes self-management (DSMQ-R27) (change for each point: β = –0.03, –0.04 to –0.02, $p<0.001$), whereas we found no association with general self-efficacy expectations (GSE) and perceived social support (F-SOZU-K14) (Table 3). Figure 2 shows the comparison between the effect sizes of the independent variables in the main analysis.

The results of the unadjusted analyses of our independent variables were consistent with those of the multivariable models. They can be found in Supplementary Tables 3–11. Compared with patients with tertiary education, the increase in HbA1c was 0.31 higher in patients with secondary (β = 0.31, 95% CI 0.14–0.48, $p<0.001$) and 0.4 higher in those with primary education (β = 0.40, 95% 0.19–0.61, $p<0.001$) (Supplementary Table 5). Worse health literacy was significantly associated with an increase in HbA1c levels (change for each point: β = –0.05, –0.07 to –0.03, $p<0.001$) (Supplementary Table 10). Worse self-reported diabetes self-management was also associated with an increase in Hba1c levels (change for each point: β = –0.03, 95% CI –0.04/–0.02, $p<0.001$) (Supplementary Table 11).

Table 3 Association between patient characteristics and change in HbA1c levels (in percent): results from multilevel mixed effects linear regression analysis (*n* = 291; *N* = 2370)

Characteristic	β (95% CI)	*p*-Value
Phase of COVID-19 pandemic		
Before first lockdown (from 1 January 2019 to 21 March 2020)	*Reference*	
During first lockdown (from 22 March 2020 to 6 May 2020)	*0.23 (0.07–0.39)*	*0.005*
After first lockdown (from 7 May 2020 to 12 December 2020)	*0.20 (0.11–0.28)*	*< 0.001*
During second lockdown (from 13 December 2020 to 30 June 2021	*0.27 (0.15–0.38)*	*< 0.001*
After second lockdown (1 July 2021 to 31 December 2021)	*0.22 (0.07–0.37)*	*0.005*
Measurement number	*−0.03 (−0.05 to −0.01)*	*0.010*
HbA1c at previous measurement	*0.33 (0.29–0.36)*	*< 0.001*
Age	0.004 (−0.001 to 0.01)	0.151
Sex		
Female	Reference	
Male	−0.02 (−0.16 to 0.12)	0.745
Educational level (pursuant to CASMIN):		
Higher or lower tertiary education	*Reference*	
Secondary school certificate or "A" level equivalent	*0.22 (0.06–0.38)*	*0.008*
Inadequately completed, general primary or basic vocational	*0.31 (0.10–0.52)*	*0.004*
Comorbidity before first lockdown (22 March 2020):		
No ASCVD, no end organ damage, and low cardiovascular risk	Reference	
No ASCVD, no end organ damage, and high cardiovascular risk	−0.12 (−0.30 to 0.06)	0.183
No ASCVD and at least one end organ damage	0.07 (−0.13 to 0.27)	0.482
ASCVD and no cardiovascular event	−0.21 (−0.55 to 0.12)	0.212
ASCVD and at least one cardiovascular event	−0.02 (−0.39 to 0.36)	0.936
Depression	0.08 (−0.20 to 0.35)	0.592
Diabetes treatment:		
CGM	0.14 (− 0.02/0.31)	0.087
Insulin pump	0.07 (−0.08 to 0.21)	0.373
F-SozU K14 score	0.03 (−0.06 to 0.12)	0.559
General self-efficacy score	0.01 (−0.01 to 0.03)	0.194
HLS-EU-Q16 score (for each point)	*−0.03 (−0.05 to −0.002)*	*0.034*
DSMQ score (for each point)	*−0.03 (−0.04 to −0.02)*	*< 0.001*

n Number of participants, *N* number of observations, *CI* confidence interval, *COVID-19* corona virus disease 2019, *HbA1c* glycosylated hemoglobin A1c, *ASCVD* atherosclerotic cardiovascular disease, *CASMIN* Comparative Analysis of Social Mobility in Industrial Nations, *F-SozU K14* the Social Support Questionnaire, *HLS-EU-Q16* the European Health Literacy Questionnaire including 16 items, *DSMQ-R27* the revised Diabetes Self-Management Questionnaire including 27 items

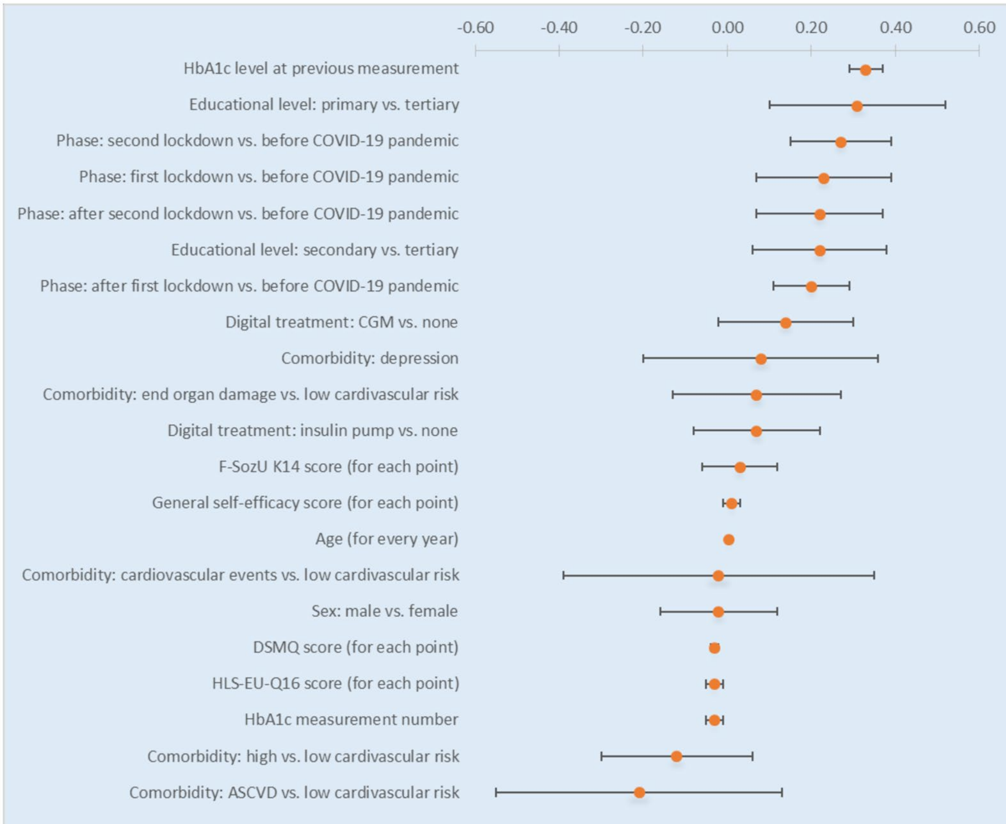

Fig. 2 Comparison between effect sizes of independent variables in main analysis (in percent; $n=291$; $N=2370$) *ASCVD* atherosclerotic cardiovascular disease

DISCUSSION

Statement of Principal Findings

Both COVID-19 lockdowns led to a significant increase in HbA1c levels in patients with T1D. The median HbA1c levels (in %) increased by up to +0.3 during the first lockdown, and in 25% of the study population, this increase was even up to +0.7 or more.

Few check-ups, poor blood glucose values, deficits in diabetes self-management, low health literacy, and a low level of education were associated with a greater increase in HbA1c during lockdowns. The use of diabetes digital treatments such as CGM, or insulin pump, had no effect on HbA1c change.

Comparison with Literature

Two meta-analyses revealed that time in range increased significantly during and after lockdown, but no significant change in HbA1c levels could be found in patients with T1D [3, 4]. The meta-analysis by Eberle et al. found a mean difference in HbA1c of –0.05% due to lockdown [1]. One explanation for these conflicting results could be that the observation period of the previous studies was too short to affect the HbA1c level, which changes slowly over a period of up to 12 weeks [52]. Another could be the substantial heterogeneity of the previous studies, as reported in a systematic review [3].

We found 28 studies that examined the effects of lockdown on glycemic control in patients with T1D [11–33, 35–39], and almost half of them ($n = 13$) were conducted in children and adolescents [14, 15, 18, 20, 25, 27, 30, 31, 35–39]. Of the 15 studies including adults [11–13, 16, 17, 19, 21–24, 26, 28, 29, 32, 33], 10 reported a decline in estimated HbA1c or GMI (glucose management indicator) due to lockdown [11, 12, 16, 17, 19, 21–24, 26]. It should be taken into account that the estimated HbA1c and GMI are calculated from CGM data only and are based on short-term average glucose values [40]. Therefore, they are not suitable for long-term assessment of glycemic control. It is also evident that both the estimated HbA1c and the GMI may differ greatly from the laboratory-measured HbA1c, which correlates with the risk of long-term complications and is, therefore, the gold standard for evaluating glycemic control in patients with DM [3, 40]. Therefore, all HbA1c values in our study were measured in the laboratory to accurately examine the glycemic effects of the COVID-19 lockdowns in patients with T1D.

In addition, all prior lockdown studies that reported a decrease in HbA1c in adults with T1D included only patients using CGM; thus, the reported HbA1c levels were estimated [11, 12, 16, 17, 19, 21–24, 26]. Therefore, some authors suggested that digital treatments such as CGM or insulin pump may have caused the decrease in HbA1c levels [1, 19, 26]. However, we found that neither the use of CGM nor the use of an insulin pump affected the change in HbA1c during lockdowns (cf. Figure 2).

It is evident that low education is associated with worse glycemic control in patients with type 1 diabetes [41]. In our study, the increase in HbA1c in percentage during the pandemic was 0.31 points higher in patients with primary education than in patients with tertiary education (Table 3). Comorbidities such as depression can be linked to higher HbA1c levels in patients with T1D [46], but we found no significant association between the change of HbA1c levels during the pandemic and patients comorbidities.

To the best of our knowledge, there is no published longitudinal study examining the impact of patients' perceived health literacy and diabetes self-management on HbA1c change during the COVID-19 pandemic. However, low health literacy is associated with behaviors that increase the risk of blood glucose deterioration, such as an inactive lifestyle and poor dietary habits [53–55]. Conversely, higher health literacy is associated with lower HbA1c in patients with DM, including T1D [42]. In line with these findings, we observed that lower health literacy was significantly associated with greater increase in HbA1c during lockdowns.

Higher scores on the Diabetes Self-Management Questionnaire (DSMQ-R27) are associated with better HbA1c levels, indicating optimal diabetes self-management [43]. In our study, Hba1c levels increased significantly less during lockdowns in patients with a higher diabetes self-management score (Figure 2).

Implications for Clinical Practice

Patients with T1D that have few check-ups, poor blood glucose values, deficits in diabetes self-management, low health literacy, and low educational levels seem to be at higher risk of worsening glycemic control during lockdowns and, therefore, need special medical care, e.g., through telemedicine. Telemedicine makes it possible to record patient data via a telecommunications system and transmit it to the healthcare provider for analysis and decision making [56]. The healthcare provider could then contact the patient via phone call, video conference, chat app, or email to provide regular advice even during lockdowns.

STRENGTHS AND LIMITATIONS

Compared with previous studies examining the association between the first COVID-19 lockdown and glycemic control in adults with T1D, our study has a long observation period of 36 months, allowing the glycemic effect of two lockdowns to be examined. While other studies included only adults with CGM [11, 12, 16, 17, 19, 21–24, 26], our study includes patients with and without CGM so that both groups can be compared.

Most of the studies examining the lockdown effect in adults with T1D had sample sizes of $n < 100$, ranging from 30 to 92 participants [11, 12, 19, 21, 23, 26, 28, 29, 33]. Our study has a large sample size of 291 participants with T1D, and it is based on multilevel, multivariable analyses, which allow for cluster effects on the level of healthcare providers and include important covariates, such as diabetes digital treatment. A median of four measurements of the dependent variable per patient with high data quality (laboratory-measured HbA1c instead of estimated HbA1c), and a complete data set without missing values are further strengths of this study. In addition, analyses that examined the unadjusted effect of the independent variables on the outcome confirmed the robustness of the results.

The limitation of the study area to a metropolitan region in Germany (i.e., the city of Hamburg), and the small number of participating physicians ($n = 14$) may have affected the representativeness of our study. The relatively low participation rate of 19.4% is another limitation of our study, which could be associated with a larger number of participants with higher education and healthier lifestyle. The changes during lockdowns may therefore have been underestimated. Although effects on the representativeness of the samples are possible, low participation rates usually have no influence on the associations found in the data set [57–60]. However, many COVID-19 studies usually have low participation rates, such as 12% in Ayoubkhani et al. 2022 [61].

We did not conduct a sample size calculation. Therefore, it is possible that some association in the data could not be detected due to low statistical power. Although the CoDiaM study included patients with T1D and T2D, only participants with T1D were included in our analyses, as T2D differs from T1D in many aspects, such as treatment options [1]. However, the results of the CoDiaM study for T2D have been published elsewhere [62]. Additionally, some independent variables only have been assessed at one time during the pandemic and some of them could therefore have changed during observation time without our knowledge. However, the frequency of changes within these indicators is usually not very high.

CONCLUSIONS

Lockdowns can lead to worsening glycemic control in patients with T1D. Particularly, patients with few check-ups, poor blood glucose values, deficits in diabetes self-management, low health literacy, and a low level of education seem to be at greater risk of worsening glycemic control during lockdowns and, therefore, require special medical care, e.g., through telemedicine.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Daniel Tajdar, Dagmar Luhmann, Laura Walther, Lasse Bittner, Martin Scherer, and Ingmar Schafer declare that they have no conflict of interests.

Ethic Approval. The "Local Psychological Ethics Committee at the Center for Psychosocial Medicine of the University Medical Center Hamburg-Eppendorf" approved the CoDiaM study on January 19, 2021 (approval number LPEK-0243) and the study was registered at ClinicalTrials.gov (NCT04821921). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

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