ORIGINAL ARTICLE

COVID-19 Pandemic Impact on Metabolic Control of Type 1 Diabetes in Children

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Port J Pediatr 2022;53:646-54
DOI: https://doi.org/10.25754/pjp.2022.25777

Abstract

Introduction: Coronavirus disease 2019 pandemic has led to the adoption of extreme public health measures worldwide, and many governments imposed lockdown policies during the pandemic. In Portugal, the first emergency state began in March 2020 which led to the closure of schools and gyms, depriving children of all physical activities. This study aimed to evaluate the lockdown impact on metabolic control of children with type 1 diabetes.

Methods: Children with type 1 diabetes, followed in the pediatric endocrinology unit of a tertiary care hospital were included in this study. Data were collected from 16/03/2019 to 15/12/2020 and analyzed by quarters: -Q4, -Q3, -Q2, -Q1, from 16/03/2019 to 15/03/2020, and Q1, Q2, and Q3 from 16/03/2020 to 15/12/2020. Metabolic control was evaluated by evolution of glycated hemoglobin, z-score of body mass index, and the insulin daily dose. The statistical analysis was performed using SPSS Statistics (version 23), and mean differences were considered statistically significant at $p < 0.05$.

Results: This study included a total of 203 patients with a mean age of 10.8 ± 3.2 years and a type 1 diabetes duration of 6.4 ± 3.6 years. Moreover, 57.1% of the patients were male, and 86.7% were undergoing continuous subcutaneous insulin infusion. Mean glycated hemoglobin decreased from Q1 to Q2 (7.97% to 7.51%, $p < 0.001$) in all age groups, regardless of gender and type of treatment; however, it maintained the same value for the homologous periods -Q3 to Q2. Body mass index z-score increased from -Q4/-Q3 to Q2/Q3 (0.58 standard deviation to 0.71 standard deviation, $p = 0.009$). Insulin daily dose increased from -Q3 to Q3 (0.87 U/kg/day to 0.91 U/kg/day, $p = 0.009$).

Conclusion: During the lockdown period, there was no worsening of metabolic control and parents made accurate adjustments to insulin doses, indicating a good level of knowledge regarding the treatment of type 1 diabetes.

Keywords: Adolescent; Child; COVID-19; Diabetes Mellitus, Type 1/epidemiology; Diabetes Mellitus, Type 1/therapy; Glycated Hemoglobin A/metabolism; Glycemic Control; Infant; Portugal; Quarantine

Keypoints

What is known:
- Type 1 diabetes is greatly affected by daily routines, namely physical activity, stress, diet, and sleep pattern.

What is added:
During the pandemic lockdown, pediatric patients achieved good metabolic control, due to a rise in insulin levels, despite an overall weight gain.

Introduction

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first emerged in Wuhan city of China, in December 2019.[1] The World Health Organization (WHO) declared the outbreak a public health emergency of international concern on January 30, 2020,[2] given its rapid and worldwide spread and announced it a pandemic on March 11, 2020.[3] In Portugal, a national emergency state was declared on March 18, 2020, and an almost complete lockdown was imposed for a period of one and a half months. The government decrees imposed social distancing and confinement, which led to the closure of schools, gyms, and sports clubs.

The implementation of these preventive measures allowed

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Received: 07/11/2021 | Accepted: 09/07/2022 | Published online: 01/10/2022 | Published: 01/10/2022

to keep the SARS-CoV-2 R0 (basic reproduction number that evaluates the number of second infections produced by a single person infected) low in the first months but completely affected the people health and lifestyle.

Common COVID-19 symptoms include fever, fatigue, cough, and myalgia; however, they are highly variable and can progress to shortness of breath, pneumonia, and even death.[4] Although the disease seems to be less severe in children, patients with diabetes are at higher risk of all infections compared with the general population,[5] and since the beginning of the COVID-19 pandemic, concerns were raised about patients with chronic conditions.[6]

Type 1 diabetes is one of the most common chronic diseases in children, accounting for 5% of all diagnosed cases of diabetes, and its global incidence is on the rise.[8] According to the International Diabetes Federation, it is estimated that 1.1 million children and adolescents (in the age range of 0-19 years) have type 1 diabetes worldwide, with an incidence of 128 000 new cases per year.[9] Type 1 diabetes management involves frequent blood glucose monitoring, insulin therapy, a healthy diet with carbohydrate monitoring, as well as structured physical activity, which requires complete parental dedication in the case of young patients.[10] On the other hand, parents of patients diagnosed in late childhood or adolescence tend to be less involved in diabetes care, meaning that usually, adolescents are prone to have poorer glycemic control.[10]

Children affected by type 1 diabetes were unable to continue their routine follow-up and had to adapt and modify their disease management plan with the onset of the SARS-CoV-2 pandemic. It is well known that type 1 diabetes is greatly affected by daily routines, and there have been concerns regarding the likely negative effects of this lockdown on glycemic control due to restriction of physical activities, stress, poorer diet, and irregular sleep patterns in adolescents.[11,12]

Despite these lifestyle changes, studies showed that patients of all ages with type 1 diabetes managed to keep good metabolic control during the lockdown.[13-16] At present, COVID-19 infection is clinically different in children and adolescents with type 1 diabetes, compared to adults, without an increase in morbidity and mortality.[17]

In this context, the present study aimed to assess the impact of lockdown in metabolic control in type 1 diabetes patients who were followed in a tertiary pediatric endocrinology center.

Methods

An analytical and retrospective study of all data from children and adolescents (< 18 years) with type 1 diabetes was performed in the pediatric endocrinology unit of a tertiary care hospital, between March 16, 2019, and December 15, 2020. The data were collected from the Hospital Pediátrico de Coimbra pediatric endocrinology unit database and the digital medical records of each patient.

Data were analyzed by quarters: -Q4 (16/03/2019 to 15/06/2019), -Q3 (16/06/2019 to 15/09/2019), -Q2 (16/09/2019 to 15/12/2019), -Q1 (16/12/2019 to 15/03/2020), and Q1 (16/03/2020 to 15/06/2020), Q2 (16/06/2020 to 15/09/2020) and Q3 (16/09/2020 to 15/12/2020). Demographic (age, gender, type of treatment, and disease duration) and clinical variables were registered and analyzed: evolution of glycated hemoglobin (HbA1c), body mass index (BMI) z-score, and insulin daily dose (IDD).

Normality distribution was evaluated with the Kolmogorov-Smirnov test (p value > 0.10 for all study groups, except HbA1c in -Q1 and BMI z-score in -Q1, but normal distribution was assumed considering the group dimension > 30). Moreover, paired-sample t-tests were conducted to identify the differences between means. All statistical analysis was performed using SPSS Statistics software (IBM SPSS, version 23), considering the error probability of 0.05.

Results

A total of 203 patients with a mean age of 10.8 ± 3.2 years were included during the study period, of whom 116 (57.1%) patients were male. In addition, 176 (86.7%) and 27 (13.3%) patients were undergoing continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDI), respectively. The age group distribution showed that the majority of patients were between 10 and 15 years old and had type 1 diabetes for less than 10 years, with a mean ± standard deviation (SD) age of 6.4 ± 3.6 years. Demographic data are presented in Table 1.

Evolution of glycated hemoglobin

There was a decrease in HbA1c values in Q2 (June 16, to September 15, 2020). These values reflect the glycemia in the previous three months period, from March to June 2020. When compared to other quarters, there were statistically significant differences between -Q1 and Q2 (7.83% to 7.51%, $p < 0.001$) and between Q1 and Q2 (7.97% to 7.51%, $p < 0.001$). However, compared to the homologous period (Q2 *vs* -Q3), there was no difference between values (7.51% to 7.51%). Moreover, a statistically significant increase was observed in HbA1c values (7.51% to 7.65%, $p = 0.023$) in Q3 (September 16 to December 15, 2020) after the lockdown period. Glycated hemoglobin values in all quarters and mean differences between HbA1c values in Q2, compared to other quarters, are presented in Table 2, and the evolution is presented in Fig. 1.

As far as age groups were concerned, a similar evolution was found, and a decrease was observed between -Q1 and Q2 in all age groups. As registered in Table 3, there was no statistically significant difference between Q2 and its homologous period -Q3. However, there was a decrease in HbA1c values from -Q3 to Q2 (7.60% to 7.49%, $p = 0.206$) in the group of patients older than 10 years. Although this difference is not statistically significative, it indicates better metabolic control during the lockdown period.

Glycemic control was always worse in girls (in the same period HbA1c was always higher), and there was no significant difference between -Q3 and Q2. However, a significant decrease from -Q1 to Q2 was observed in both genders ($p < 0.001$). Patients treated with continuous subcutaneous insulin infusion achieved better glycemic control than those treated with multiple daily insulin injections, continuing the trend described before. Moreover, metabolic control improved significantly during the lockdown in patients with multiple daily insulin injections compared with the homologous period in the previous year from -Q3 to Q2 (8.03 to 7.65, $p = 0.032$).

Table 1. Demographic data of the type 1 diabetes patients (n = 203)

Gender	n	%
Male	116	57.1
Female	87	42.9
Age (years)	**n**	**%**
0-5	12	5.9
5-10	65	32.0
10-15	117	57.6
15-18	9	4.4
Treatment	**n**	**%**
CSII	176	86.7
MDI	27	13.3
Duration of disease (years)	**n**	**%**
0-5	70	34.5
5-10	91	44.8
10-15	40	19.7
15-18	2	1.0

CSII - continuous subcutaneous insulin infusion; MDI - multiple daily insulin injections.

Table 2. Glycated hemoglobin values in all quarters and the mean differences between Q2 glycated hemoglobin *versus* other quarters

HbA1c ± SD (%) values in all quarters						
-Q4	-Q3	-Q2	-Q1	Q1	Q2	Q3
7.57 ± 1.02	7.51 ± 0.98	7.61 ± 1.4	7.83 ± 1.08	7.97 ± 1.08	7.51 ± 1.11	7.65 ± 1.24

HbA1c Q2 (7.512%) difference to			
-Q3 (diff / *p*)	-Q1 (diff / *p*)	Q1 (diff / *p*)	Q3 (diff / *p*)
-0.006 / 0.756	-0.345 / < 0.001	-0.463 / < 0.001	-0.149 / 0.023

diff - mean difference; HbA1c - glycated hemoglobin; SD - standard deviation.
Mean differences between quarters were calculated by paired sample t-test.

Children with shorter disease duration showed better metabolic control, although there was a significant increase in HbA1c from -Q3 to Q2 in the group with a disease duration of fewer than five years from diagnosis (7.18% to 7.38%, $p = 0.047$). On the other hand, patients with a disease duration of 5-10 years or more showed an improvement from -Q3 to Q2 (7.95% to 7.76%, $p = 0.056$ and 7.51% to 7.47%, $p = 0.098$, respectively), but this difference was not statistically significant.

Evolution of body mass index z-score

There was a significant increase in BMI z-score from the interval between -Q4 and -Q3 to the interval from Q2 to Q3 (0.58 kg/m^2 to 0.71 kg/m^2, $p = 0.009$), as presented in Table 4 and Fig. 2. These values were registered in a larger interval since patients had to attend a clinical evaluation to measure weight and height and several values were missing. Therefore, we merged the two quarters in each interval. For some reason, several BMI values in -Q2 were missing, and we had to exclude that period from this analysis.

This rise was statistically significant from the beginning to the end of this study in the age group 5-10 years (0.66 kg/m^2 to 0.90 kg/m^2, $p < 0.001$). However, statistical significance was not confirmed in the age groups below five years and adolescents.

Just as with HbA1c, male patients presented with lower BMI z-score values, with a significant rise (0.47 kg/m^2 to 0.57 kg/m^2, $p = 0.049$) from -Q4/-Q3 to Q2/Q3. However, the increase was observed in both genders and with similar magnitude. This increase happened for both treatment modalities but with no statistical significance (CSII: 0.61 kg/m^2 to 0.70 kg/m^2, $p = 0.098$; MDI: 0.33 kg/m^2 to 0.50 kg/m^2, $p = 0.057$).

Despite better metabolic control, the most affected group in terms of weight gain was the group with a disease duration of fewer than five years (0.31 kg/m^2 to 0.61 kg/m^2, $p = 0.001$), although the growing trend was verified also in the group with disease duration of 5-10 years from diagnosis (Table 5).

Table 3. Glycated hemoglobin evolution in different groups and comparison between Q2 and its homologous period -Q3

HbA1c ± SD (%) evolution in quarters -Q3, -Q1, Q2, and Q3				
	-Q3	-Q1	Q2 / (*p* value *vs* -Q3)	Q3
by age group (years)				
0-5	7.41 ± 0.15	7.83 ± 0.16	7.60 ± 0.13 / 0.246	7.69 ± 0.15
5-10	7.34 ± 0.21	7.82 ± 0.23	7.43 ± 0.20 / 0.350	7.53 ± 0.23
10-18	7.60 ± 0.13	7.86 ± 0.15	7.49 ± 0.16 / 0.206	7.65 ± 0.14
by gender				
Male	7.49 ± 0.13	7.83 ± 0.15	7.46 ± 0.16 / 0.451	7.61 ± 0.14
Female	7.73 ± 0.15	8.03 ± 0.18	7.55 ± 0.16 / 0.284	7.69 ± 0.18
by type of treatment				
CSII	7.51 ± 0.10	7.82 ± 0.11	7.55 ± 0.12/0.432	7.63 ± 0.11
MDI	8.03 ± 0.36	8.47 ± 0.39	7.65 ± 0.38/0.032	8.15 ± 0.41
by time since diagnosis (years)				
0-5	7.18 ± 0.16	7.57 ± 0.19	7.38 ± 0.22 / 0.047	7.50 ± 0.16
5-10	7.95 ± 0.14	8.18 ± 0.15	7.76 ± 0.14 / 0.056	7.96 ± 0.17
10-18	7.51 ± 0.20	7.95 ± 0.29	7.47 ± 0.23 / 0.098	7.48 ± 0.27

CSII - continuous subcutaneous insulin infusion; HbA1c - glycated hemoglobin; MDI - multiple daily insulin injections; SD - standard deviation.
Statistical significance of mean differences between quarters was tested by paired sample t-test.

Table 4. Body mass index z-score evolution by quarters and mean differences between intervals

BMI z-score ± SD (kg/m²) evolution by quarters		
-Q4 to -Q3	**-Q1 to Q1**	**Q2 to Q3**
0.58 ± 0.92	0.59 ± 0.92	0.71 ± 0.89

BMI z-score ± SD (kg/m²) Q2 to Q3 difference to	
-Q4 to -Q3 (diff / *p*)	**-Q1 to Q1 (diff / *p*)**
0.13 / 0.009	0.12 / 0.025

BMI - body mass index; diff - difference; SD - standard deviation.
Statistical significance of mean differences between quarters was tested by paired sample t-test.

Table 5. Body mass index z-score evolution in all groups

BMI z-score ± SD (kg/m²) evolution by intervals (-Q4 to Q3, -Q1 to Q1, Q2 to Q3)			
	-Q4 to -Q3	-Q1 to Q1	Q2 to Q3 / (*p* vs -Q4 to Q3)
by age group (years)			
0-5	0.94 ± 0.29	0.78 ± 0.23	0.81 ± 0.20 / 0.720
5-10	0.66 ± 0.18	0.69 ± 0.18	0.90 ± 0.17 / < 0.001
10-18	0.49 ± 0.10	0.57 ± 0.10	0.60 ± 0.10 / 0.399
by gender			
Male	0.47 ± 0.12	0.49 ± 0.12	0.57 ± 0.12 / 0.049
Female	0.73 ± 0.11	0.79 ± 0.12	0.83 ± 0.12 / 0.080
by type of treatment			
CSII	0.61 ± 0.09	0.63 ± 0.09	0.70 ± 0.09 / 0.098
MDI	0.33 ± 0.17	0.47 ± 0.19	0.50 ± 0.22 / 0.057
by time from diagnosis (years)			
0-5	0.31 ± 0.15	0.45 ± 0.14	0.61 ± 0.16 / 0.001
5-10	0.79 ± 0.14	0.85 ± 0.13	0.88 ± 0.15 / 0.180
10-18	0.42 ± 0.12	0.34 ± 0.14	0.39 ± 0.11 / 0.790

BMI - body mass index; CSII - continuous subcutaneous insulin infusion; MDI - multiple daily insulin injections; SD - standard deviation.
Statistical significance of mean differences between quarters was tested by paired sample t-test.

Table 6. Insulin daily dose mean differences between quarters

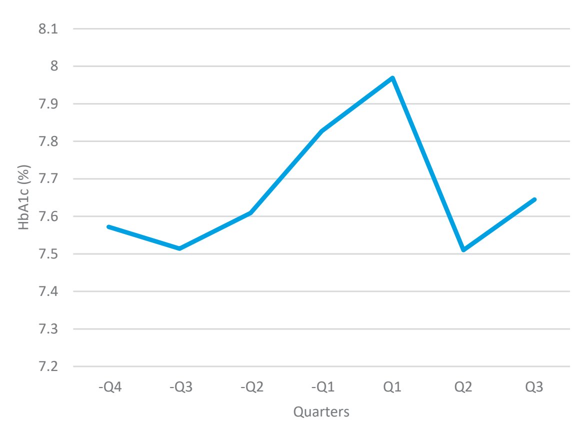
IDD ± SD (IU/kg/day) evolution by quarters						
-Q4	**-Q3**	**-Q2**	**-Q1**	**Q1**	**Q2**	**Q3**
0.86 ± 0.30	0.87 ± 0.27	0.86 ± 0.27	0.89 ± 0.27	0.86 ± 0.16	0.87 ± 0.25	0.91 ± 0.26
IDD Q3 (0.91 IU/kg/day) *versus*						
-Q4 (diff / *p*)	**-Q3 (diff / *p*)**	**-Q2 (diff / *p*)**	**-Q1 (diff / *p*)**	**Q1 (diff / *p*)**	**Q2 (diff / *p*)**	
0.05 / 0.002	0.04 / 0.009	0.05 / 0.006	0.02 / 0.157	0.05 / 0.043	0.04 / 0.013	

IDD - insulin daily dose; SD - standard deviation.
Statistical significance of mean differences between quarters was tested by paired sample t-test.

Table 7. Mean insulin daily dose differences between quarters in all groups

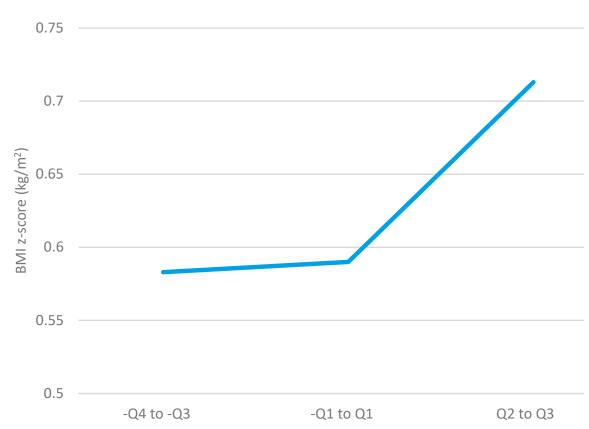
	IDD ± SD (IU/kg/day) evolution			
	-Q3	**-Q2**	**Q2 / (*p vs* -Q3)**	**Q3 / (*p vs* -Q2)**
by age group (years)				
0-5	0.81 ± 0.11	0.70 ± 0.31	0.80 ± 0.11 / 0.899	0.80 ± 0.12 / 0.434
5-10	0.79 ± 0.05	0.86 ± 0.23	0.89 ± 0.06 / < 0.001	0.89 ± 0.06 / 0.012
10-18	0.88 ± 0.04	0.89 ± 0.28	0.89 ± 0.04 / 0.976	0.94 ± 0.04 / 0.081
by gender				
Male	0.78 ± 0.04	0.84 ± 0.28	0.85 ± 0.04 / 0.028	0.88 ± 0.04 / 0.022
Female	0.94 ± 0.04	0.89 ± 0.26	0.93 ± 0.06 / 0.904	0.96 ± 0.05 / 0.109
by type of treatment				
CSII	0.84 ± 0.03	0.87 ± 0.26	0.89 ± 0.03 / 0.028	0.92 ± 0.03 / 0.006
MDI	0.74 ± 0.06	0.68 ± 0.24	0.73 ± 0.05 / 0.793	0.78 ± 0.05 / 0.516
by time from diagnosis				
0-5	0.69 ± 0.04	0.70 ± 0.22	0.81 ± 0.05 / 0.011	0.84 ± 0.05 / 0.020
5-10	0.96 ± 0.04	0.96 ± 0.21	0.98 ± 0.06 / 0.145	1.00 ± 0.06 / 0.107
10-18	0.95 ± 0.05	0.98 ± 0.30	0.91 ± 0.05 / 0.138	0.94 ± 0.06 / 0.321

IDD - insulin daily dose; CSII - continuous subcutaneous insulin infusion; MDI - multiple daily insulin injections; SD - standard deviation.
Statistical significance of mean differences between quarters was tested by paired sample t-test.



HbA1c - glycated hemoglobin.

Figure 1. HbA1c evolution in the general group of patients (n = 203).



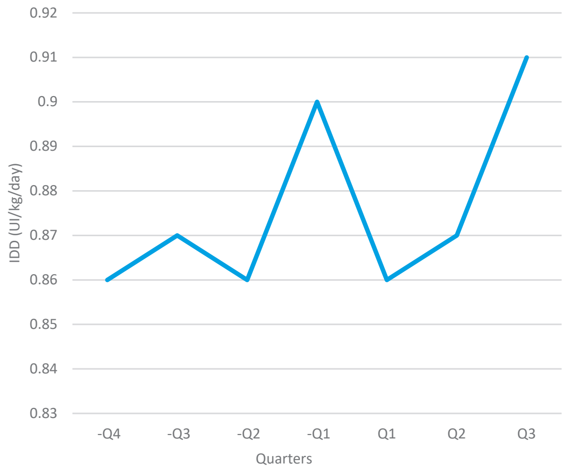
BMI - body mass index.

Figure 2. Body mass index z-score evolution in all patients (n = 203).

Evolution of insulin daily dose

During the lockdown period, insulin daily dose values were kept stable in comparison to the homologous period in the previous year (0.86 U/kg/day). However, a rising trend was observed after the lockdown (Table 2 and Fig. 3). It should be noted that -Q1 includes the winter and Christmas holidays.

In comparison with other homologous periods, no



IDD - insulin daily dose.

Figure 3. Insulin daily dose evolution in all patients (n = 203).

differences were observed, except for the rise from -Q2 to Q3 (0.86 U/kg/day to 0.91 U/kg/day, p = 0.012). As registered in Table 6, insulin daily dose (UI/kg/day) was significantly higher in Q3, compared to other periods except for -Q1.

It was in the group of patients in the age range of 5-10 years that the highest rise occurred in insulin daily dose from -Q3 to Q2 (0.79 U/kg/day to 0.89 U/kg/day, p < 0.001), and there were practically no differences between these quarters in the other age groups. There was also a significant difference in insulin daily dose from -Q2 to Q3 (0.86 U/kg/day to 0.89 U/kg/day, p = 0.012) in this age group.

The variation in insulin daily dose was higher in male patients from -Q3 to Q3 (0.78 U/kg/day to 0.88 U/kg/day, p = 0.004), and there were statistically significant differences between homologous periods -Q3 to Q2 (0.78 U/kg/day to 0.85 U/kg/day, p = 0.028) and -Q2 to Q3 (0.84 U/kg/day to 0.88 U/kg/day, p = 0.022).

This increase was verified for both types of treatment, although it was statistically significant only for continuous subcutaneous insulin infusion (0.84 U/kg/day to 0.89 U/kg/day, p = 0.028) from -Q3 to Q2 and from -Q2 to Q3 (0.87 U/kg/day to 0.92 U/kg/day, p = 0.006).

In the group with a disease duration of fewer than five years, there was a higher rise in insulin daily dose from -Q3 to Q2 (0.69 U/kg/day to 0.81 U/kg/day, p = 0.020) and from -Q2 to Q3 (0.70 U/kg/day to 0.84 U/kg (day, p = 0.011), coinciding the higher rise in BMI z-score and lower HbA1c values. However, no rise in insulin daily dose was observed in the group with disease duration more than ten years from diagnosis.

Discussion

In the analysis of the HbA1c variation through the studied time, a gradual rise was observed in the levels until Q1 and then a sudden decrease occurred in Q2. These Q2 values reflect the glycemia in the previous three months period, namely from March to June 2020, corresponding to the lockdown period.

There were statistically significant differences between -Q1 and Q2 (7.83% to 7.51%, p < 0.001) and between Q1 and Q2 (7.97% to 7.51%, p < 0.001). However, compared to the homologous period (Q2 *vs* -Q3), there was no difference between values (7.51% to 7.51%). It should be noted that -Q1 and Q1 values correspond to winter in Portugal, the season with less physical activity, and the winter and Christmas holidays. Therefore, the increase during these periods can be explained by those factors, and the decrease in Q2 values can be assigned to the normal year variation. This is because children and adolescents are in lockdown with their families, and there is more parental control over food and carbohydrate counting and more time / predisposition to adjust insulin levels, which in turn leads to better metabolic control. Considering the lack of differences between Q2 and its homologous period in 2019 (-Q3), it seemed that metabolic control did not worsen during this time despite the decrease in physical outdoor and group activities.

After the lockdown period, in Q3 (September 16, to December 15, 2020), schools reopened and there was a statistically significant increase in HbA1c values (7.51% to 7.65%, p = 0.023). This increase can be explained by less parental control and difficulty with carbohydrate counting and adjusting insulin levels in children and adolescents during school time, the return to fast-food and restaurant meals, and very limited physical activity. A similar evolution was noted regarding the age groups as well.

Glycemic control was always worse in girls (in the same period HbA1c was always higher), and although there was no significant difference between -Q3 and Q2, a significant decrease was observed in both genders from -Q1 to Q2 (p < 0.001). Patients treated with continuous subcutaneous insulin infusion achieved better glycemic rather than multiple daily insulin injections control by continuing the trend described before, and there was a significant improvement in metabolic control during the lockdown in patients with multiple daily insulin injections period compared to the homologous period in the previous year from -Q3 to Q2 (8.03% to 7.65%, p = 0.032), probably due to better parental control on insulin administration or the preference not to practice it in front of school colleagues.

Children with shorter disease duration showed better metabolic control, although there was a significant increase in HbA1c from -Q3 to Q2 in the group with a disease duration fewer than five years from diagnosis (7.18% to 7.38%, $p = 0.047$). This data may show that in this group the decrease in physical activity is the main factor in daily metabolic control. On the other hand, patients with a disease duration of more than 10 years showed an improvement from -Q3 to Q2 (7.51% to 7.47%, $p = 0.098$). Therefore, although this difference is not statistically significant, it can confirm that adolescents have more facilities to control their disease if they are in a controlled environment, probably since they have more time and the chance to practice the procedure in the absence of their friends.

There was a significant increase in BMI z-score from the interval between -Q4 and -Q3 to the interval from Q2 to Q3 (0.58 kg/m^2 to 0.71 kg/m^2, $p = 0.009$). This increase was probably related to the severe decrease in physical activity that occurred during the pandemic since many clubs and gyms remained closed even after the lockdown period and parents were afraid to let their children go out to play, for the fear of contracting the disease.

This rise was statistically significant from the beginning to the end of this study in the age group of 5-10 years (0.66 kg/m^2 to 0.90 kg/m^2, $p < 0.001$). However, no statistically significant difference was confirmed either in the group of patients younger than 5 years old or adolescents.

Just as with HbA1c, male patients presented with lower BMI z-score values, with a significant rise (0.47 kg/m^2 to 0.57 kg/m^2, $p = 0.049$) from -Q4/-Q3 to Q2/Q3, but the increase occurred in both genders and for both treatment modalities. This indicated that the weight gain was probably more related to the decreased exercise level and that the glycemic control was achieved through a rise in insulin level rather than a decrease in food intake.

Insulin daily dose values were kept stable during the lockdown period in comparison to the similar period the previous year (0.86 U/kg/day). However, a rising trend was observed after the lockdown (Table 2 and Fig. 3). It should be noted that -Q1 includes the winter and Christmas holidays.

Comparing other homologous periods there were no differences to register except for the rise from -Q2 to Q3 (0.86 U/kg/day to 0.91 U/kg/day, $p = 0.012$), probably due to continuous restrictions on physical activity in schools, sports clubs, and even outdoor.

The highest rise in insulin daily dose occurred in the age group 5-10 years from -Q3 to Q2 (0.79 U/kg/day to 0.89 U/kg/day, $p < 0.001$), reflecting less concern with food intake, more dependence on physical activity, or more screen time at this age. Moreover, there were practically no differences between these quarters in the other age groups. The increase in this age group can also be explained by the fact that parents had to telework, and these children were left on their own, while with younger children, parents had to take a leave of absence to take more care of them.

The variation in insulin daily dose was higher in male patients, from -Q3 to Q3 (0.78 U/kg/day to 0.88 U/kg/day, $p = 0.004$), and there were statistically significant differences between homologous periods -Q3 to Q2 (0.78 U/kg/day to 0.85 U/kg/day, $p = 0.028$) and -Q2 to Q3 (0.84 U/kg/day to 0.88 U/kg/day, $p = 0.022$), which was in concordance with the lower HbA1c values.

This increase was verified for both types of treatment.

In the group with a disease duration fewer than five years, there was a higher rise in insulin daily dose from -Q3 to Q2 (0.69 U/kg/day to 0.81 U/kg/day, $p = 0.020$) and from -Q2 to Q3 (0.70 U/kg/day to 0.84 U/kg/day, $p = 0.011$), which was in concordance with the higher rise in BMI z-score and lesser HbA1c values. The absence of a rise in insulin daily dose was observed only in the group with a disease duration of more than ten years from the diagnosis.

The COVID-19 pandemic presented a challenge for both type 1 diabetes patients and endocrinologists. Patients had to adapt their routines and healthcare providers had to adapt and improve telemedicine services to help patients and their careers. The imposed lockdown was initially thought to cause deterioration in glycemic control. However, our data showed no deterioration, and even improvement was observed in HbA1c values in some groups. These results are consistent with those obtained in other studies.[18-20] We attribute this improvement to full-time parental supervision, less daily life unpredictability, better nutritional quality of meals with more accurate carbohydrate counting, and more frequent insulin dose adjustments. During the pandemic, parents made accurate adjustments to insulin doses, supervised by the pediatric endocrinology unit team, showing a good level of knowledge in the treatment of type 1 diabetes. This reinforces the importance of regular education for children and caregivers that allows them to adjust treatment to daily life changes, as part of their usual activity at pediatric age. This good control also reinforces the importance of telemedicine services and allows the patients to remain in close contact with the clinical team. Maintaining regular presential follow-up remains the standard of care.

Regarding the limitations of this study, some points should be noted. Although telemedicine was extremely important during the pandemic, some data were missing, especially on anthropometric values, which made us merge data in larger periods. Glycated hemoglobin is a parameter indicating the mean glycemic values. However, it does not specify how low and how high the values for each child were. For a better understanding of real metabolic control, it would be important to analyze "time in range" and to compare it with HbA1c evolution. During the lockdown caused by the COVID-19 pandemic, there was an overall improvement in metabolic control, despite the restrictions on physical activity and an associated significant increase in insulin daily dose and BMI, compared to the similar period in the previous year.

Author Contribuitions

JNS, TB and AM participated in the study conception or design. JNS and TB participated in acquisition of data. JNS and TB participated in the analysis or interpretation of data. JNS, TB, JSC, RC, ID and AM participated in the drafting of the manuscript. JNS, JSC, RC, ID and AM participated in the critical revision of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

Funding Sources

There were no external funding sources for the realization of this paper.

Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki 2013).

Provenance and peer review

Not commissioned; externally peer reviewed

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Impacto da Pandemia de COVID-19 no Controlo Metabólico da Diabetes Tipo 1 em Crianças

Introdução: A pandemia da doença de coronavírus 2019 levou à adoção de medidas extremas de saúde pública em todo o mundo e muitos governos impuseram políticas de confinamento durante a pandemia. Em Portugal, o primeiro estado de emergência começou em março de 2020 e levou ao encerramento de escolas e ginásios, privando as crianças de todas as atividades físicas. Este estudo teve como objetivo avaliar o impacto do confinamento no controlo metabólico de diabetes tipo 1 em crianças.

Métodos: Foram incluídas neste estudo crianças com diabetes tipo 1 acompanhadas na unidade de endocrinologia pediátrica de um hospital terciário. Os dados foram recolhidos entre 16/03/2019 e 15/12/2020 e analisados por trimestres: -Q4, -Q3, -Q2, -Q1, de 16/03/2019 a 15/03/2020, e Q1, Q2, e Q3 de 16/03/2020 a 15/12/2020. O controle metabólico foi avaliado pela evolução da hemoglobina glicada, *z-score* do índice de massa corporal e dose diária de insulina. A análise estatística foi realizada recorrendo ao programa SPSS Statistics (versão 23), e as diferenças médias foram consideradas estatisticamente significativas para um valor de $p < 0,05$.

Resultados: O estudo incluiu um total de 203 doentes com uma idade média de 10,8 ± 3,2 anos e duração da diabetes tipo 1 de 6,4 ± 3,6 anos. Além disso, 57,1% eram do géenero masculino e 86,7% faziam infusão contínua de insulina subcutânea. O valor médio da hemoglobina glicada diminuiu de Q1 para Q2 (7,97% para 7,51%, $p < 0,001$) em todas as faixas etárias, independentemente do género e tipo de tratamento. No entanto, manteve o mesmo valor para os períodos homólogos -Q3 a Q2. O *z-score* do índice de massa corporal aumentou de -Q4/-Q3 para Q2/Q3 (0,58 desvio padrão para 0,71 desvio padrão, $p = 0,009$). A dose diária de insulina aumentou de -Q3 para Q3 (0,87 U/kg/dia para 0,91 U/kg/dia, $p = 0,009$).

Conclusão: Durante o período de confirnamento, não houve agravamento do controlo metabólico e os pais fizeram ajustes precisos das doses de insulina, indicando um bom nível de conhecimento sobre o tratamento do diabetes tipo 1.

Palavras-Chave: Adolescente; Confinamento; Controle Glicémico; Criança; COVID-19; Diabetes Mellitus Tipo 1/epidemiologia; Diabetes Mellitus Tipo 1/tratamento; Hemoglobina A Glicada/metabolismo; Lactente; Portugal