Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
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ORIGINAL RESEARCH

The Impact of COVID-19 Lockdown on Glycemic Balance in Romanian Patients with Type 1 Diabetes Mellitus

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Introduction: The COVID-19 pandemic has brought major changes not only at the economic and social level but especially in the medical system.

Objective: To evaluate the impact of COVID-19 lockdown on the quality of glycemic control in Romanian patients with type 1 diabetes mellitus (T1DM).

Material and Method: Our study group included 102 Romanian volunteers' patients with T1DM from both urban and rural areas. Data were collected during an interview, based on a structured questionnaire with multiple-choice questions about diabetes management during lockdown, how they interact with their diabetologist, how they accessed the treatment and what other factors influenced their diabetes management during the lockdown.

Results: Blood glucose levels were significantly higher in the MDII group as a consequence of delayed administration of insulin corrections due to inadequate insulin dosing (60% vs 31.81%; $\chi^2 = 5.51$, $p = 0.018$). In addition, insulin pump users had improved response to stress and anxiety (ie, additional therapeutic safety being provided by use of insulin pump; in some devices, blood glucose being continuously monitored, leading to premature detection of important blood glucose excursions) compared to insulin pen users ($\chi^2 = 5.09$, $p = 0.024$). In the context of hypoglycemia, we observed that in the pen MDII group, more users have administered an excess of insulin, compared with the pump users (80% vs 45.45%; $\chi^2 = 10.34$; $p = 0.001$).

Conclusion: A lower impact of COVID-19 lockdown on glycemic control was observed in patients with T1DM treated using insulin pumps compared to patients with T1DM who administered their insulin using insulin pens. Telemedicine and online consultations have brought significant improvements in diseases management. Stress, emotions, and anxiety were among the main reasons that led to increases in blood sugar levels, suggesting that the psychological impact may have long-term complications.

Keywords: COVID-19, lockdown, type 1 diabetes mellitus, insulin pumps, diabetes management

Introduction

Association between COVID-19 and diabetes is controversial, the latter bringing challenges and new concerns in the management of SARS-CoV-2 infection, especially for type 1 diabetes mellitus (T1DM). It is well known that patients with diabetes need a well-established routine, both in terms of diet, treatment, and daily physical activity, as well as increased attention to possible long-term complications. At the same time, the increased susceptibility to infections (even higher in type 1 diabetes than in type 2 diabetes)[1] makes these patients affected, in the context of the pandemic, on several levels.

COVID-19 is an infectious-contagious disease which is thought to have appeared in December 2019 in Wuhan, China, has spread rapidly and, according to the World Health Organization (WHO), has killed more than 1,000,000

Received: 22 August 2022
Accepted: 22 October 2022
Published: 2 November 2022

people globally, of which approximately 6200 in Romania (reports 24.10.2020) within 11 months. The disease was declared a pandemic on March 11, 2020.[2]

In Romania, 168 cases were confirmed until 16th March 2020, and in the context of the epidemiological situation and the rapid transmission of the infection, a state of emergency was established in the country.[3] The epidemiological status is constantly changing and despite the protection measures, the social distance imposed by the pandemic, respected, of the overwhelmed health system, the number of cases increased, reaching 7 months later (October 23, 2020), 201,032 confirmed cases (total) of which 6245 deaths and 144,429 patients declared cured, affecting 218 countries.[4] The lack of information and preparation for such a crisis, together with the fear of an impending global economic crisis, has led to an increase in the need to understand the pathogenesis of the SARS-CoV-2 virus to find therapeutic strategies as soon as possible.

Due to the rapid spread of the disease, as well as the large number of cases affecting most countries around the world, the studies performed differ depending on the region and the number of patients they had. The data obtained suggested that the virus predominantly affects the population with comorbidities such as diabetes, hypertension, and cardiovascular disease, increasing the mortality rate of these diseases.[5] From a collection of 10 studies conducted in China (with a group of 2209 patients) on the characteristics of comorbidities of patients with COVID-19, Singh et al reported a 7% prevalence of diabetes, a percentage supported by other studies conducted in this region. In contrast, in Italy, a study by Onder et al reported a prevalence of almost 36% of diabetes (a study conducted on a group of 335 patients), while researchers at the CDC (Center of Disease Control and Prevention), USA, showed a prevalence of 10.9% among patients (group of 7162 patients).[6]

Several affected countries have introduced a few restrictions (even a total lockdown) and measures to limit the spread of the SARS-CoV-2 virus, including the mandatory isolation of those at high risk of infection (including people with diabetes). Given this context, an issue arises regarding the possible impact of COVID-19 lockdown measured on T1DM, how much the patient's daily routine was affected and, consequently decreasing the quality of the glycemic control, by limiting movement and physical activities, or by the psychological stress exerted by the restrictions and social distancing.[7]

This paper studied the impact that the COVID-19 pandemic had on patients with T1DM, what it meant for them and how their therapeutic follow-up was influenced by the State of Emergency declared in Romania on 16 March 2020, due to the rapid spread of the infection. According to the protocol, the admission of patients in the hospital was restricted, free only to medical emergencies and cases in which a delay in admission cannot be postponed, leading thus to an increased remotely follow-up of patients using telemedicine solutions.

Materials and Methods

Study Design and Patients

This non-interventional, consecutive-case, population-based study, was conducted between April and December 2020, and enrolled 102 patients with T1DM, volunteers, from all over the country, aged between 18 and 80 years. The studied sample was stratified according to the method of insulin delivery: multiple daily insulin injections (MDII) or continuous subcutaneous insulin infusion (insulin pumps) and analyzed accordingly. All patients with type 1 diabetes are trained to calculate the amount of carbohydrates and adjust their insulin doses depending on what they eat.

The study was conducted according to the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the "Pius Brinzeu" Emergency Hospital Timisoara. All patients included in the study signed an informed consent.

The inclusion criteria in the study were

- patients with T1DM in treatment with different types of insulin therapy (insulin pump, or basal-bolus patients).

The exclusion criteria from the study were

- patients with type 2 diabetes

- pregnant or lactating T1DM patients
- the presence of mental illness.

At the basis of this retrospective observational study (case-control), it was an original questionnaire, with grid-type questions with several answers. This method was chosen because, given the restrictions imposed, it was considered a much more accessible way to get in touch with patients and get concrete answers.

Questionnaire

The questionnaire was published online, on social networks, through the Google Forms program. It included a series of questions, including blood glucose values (values reached in hyperglycemia or hypoglycemia), values of HbA1c, how they got in touch with the diabetologist, how they had access to treatment and what influenced the management of glycemic control. The questionnaire was completed anonymously, and the answers are strictly confidential. To be able to objectively analyze the level of glycemic control, the questionnaire included questions about glycemic level and HbA1c values measured during the lockdown by the patients themselves. The values were then compared with the criteria corresponding to hypoglycemia and diabetic ketoacidosis, according to the DM Management Guide developed by the National Society of Diabetes, Nutrition and Metabolic Diseases in Romania[8] and American Diabetes Association (ADA).[9]

For each patient, we recorded the used type of blood glucose monitoring: Self-Monitoring of Blood Glucose (SMBG) or subcutaneous glycemic sensor by Continuous Glucose Monitoring (CGM). HbA1c was assessed using capillary blood.

Other parameters used were demographic data (age, gender, origin), type of insulin therapy, how they kept in touch with the diabetologist, how they had access to the health system during the lockdown, how they managed the episodes of hypoglycemia, respectively hyperglycemia, physical activity performed during this period, and how glycemic control was hampered during the restrictions.

Telemedicine consists in messages, e-mails, voice, and video calls to those who were their attending physicians. Also, we collected the data about their lifestyle during lockdown, focusing on the change in eating habits and daily hours of physical activity.

The questionnaire was approved by the Research Committee of the Timisoara County Emergency Hospital for use with the Romanian population (see Supplementary Material).

Statistical Analysis

The collected data were analyzed using the EpiInfo software (version 7.2.4), and OpenEpi program (version 3.01). Continuous data with normal distribution were described as mean and standard deviations (SDs), while continuous variables without normal distribution were described as median and interquartile range (IQR). The categorical data were presented as percentage (absolute frequency). The distribution of continuous data was tested for normality using the Shapiro–Wilk test and for equality of variances by using Levene's test.

To analyze the differences between the patients with basal-bolus and the patients using insulin pumps, we applied the chi-square tests. When at least one expected value was less than 5, Fisher's exact test or Mid-P exact test were applied.

A p-value of 0.05 was considered as the threshold for statistical significance, and a confidence level of 0.95 was considered for estimating intervals.

Results

The study group included 102 patients with T1DM, with a mean age of 25.5 ± 0.7 years. Of these, 75 were women and 27 men. Among them, only 14 (18.66%) answered "Not always" when asked if they tried to strictly follow the insulin therapy regimen. There were 9 men (33.33%) who answered ($\chi^2 = 2.17$; $p < 0.078$). A much higher percentage of patients from urban areas (n = 81, 79.4%) answered the questionnaire, compared to those from rural areas (n = 21, 20.6%), which may suggest a more among those from the urban environment, the restrictions imposed affecting more the way they carried out their daily activities (shopping, sports, service, etc.) and procured their food.

The mean duration of diabetes was 19 (±0.12) years. The glycemic balance expressed by the mean value of HbA1c was 6.5 (±0.56)%. The general characteristics of the studied group are listed in Table 1.

Table 1 Characteristics of the Studied Group

Parameters	N=102
Age (years)[a]	25.5 ± 0.7
Gender[b]	
F	75 (73.5%)
M	27 (26.5%)
Environment[b]	
Urban	81 (79.4%)
Rural	21 (20.6%)
DM duration (years)[a]	19 ± 0.12
HbA1c (%)[a]	6.5 ± 0.56
Type of treatment[b]	
Basal bolus (4–5 injections)	80 (78.43%)
Insulin pumps	22 (21.56%)

Notes: [a]Continuous variables (with distribution) are indicated by their mean ± SD. [b]Categorical variables are presented by percentage (absolute frequency) in the sample.
Abbreviation: DM, diabetes mellitus.

To objectively quantify the level of glycemic control, the patients were asked if they noticed an increase in the number of episodes of hyperglycemia or increased glycemic values compared to periods prior to the restrictions and how they managed this increase. It was considered an increased number of episodes of hyperglycemias when more than 2 episodes/month appeared.

The majority, 55 patients (53.92%) noticed an increase in the number of hypoglycemia episodes, but 47 (46.08%) claimed that they did not notice an increase of hypoglycemia. Most patients (69.61%) reported that stress, emotions, and anxiety caused by the pandemic led to higher blood glucose levels, while 56 (54.9%) had claimed that the lack of a regular diet was the cause, respectively 34 (33.33%) did not comply with the insulin dose. Also, 6 patients mentioned other reasons, such as insulin pump errors, and SARS-CoV-2 virus infection, in which blood glucose levels tripled, while 3 patients claimed that they did not have access to their insulin doses.

We observed a significant increase of hyperglycemias in patients basal-bolus therapy in comparison with patients carrying an insulin pump (60% vs 31.81%; $\chi^2 = 5.51$, $p = 0.018$). In terms of response to stress and anxiety caused by the pandemic, we observed a significant difference between patients carrying an insulin pump and those with basal-bolus therapy. A percent of 50% patients carrying insulin pumps found increases in glycemic values in this context, compared to 75% patients using pens ($\chi^2 = 5.09$; $p = 0.024$). These data indicate a better management of T1DM in the case of insulin pump users, the management being facilitated by the device and blood glucose sensors, as well as a lower anxiety, since patients relied on corrections made directly by the sensor. Other reasons were irregular meals or non-compliance with main meals, lack of sports/physical activity, irregular snacks, miscalculation of carbohydrates and insulin requirements, infections (other than COVID-19) or even infection with SARS-CoV-2, in which the required insulin dose tripled (Table 2).

Regarding episodes of hypoglycemia, 62 patients (60.78%) claimed that they did not observe significant increases in the number of hypoglycemia, in contrast to 40 patients (39.21%) who did observe ($\chi^2 = 9.49$; $p = 0.002$). Of these, 7 patients (31.81%) were pump bearers, and 33 patients (41.25%) were pen users. We observed that 74 patients (72.54%) administered too many insulin units, from which 80% were patients with basal therapy and 45.45% were patients with insulin pumps ($\chi^2 = 10.34$; $p = 0.001$) (Table 2).

In both hyperglycemic and hypoglycemic episodes, patients reported irregular meals and snacks, miscalculation of carbohydrates, and insulin requirements. A percent of 28.4% stated that they increased the number of meals during the

Table 2 Comparison of the Two Groups Regarding the Number of Hypoglycemia/Hyperglycemia Episodes and the Context in Which These Episodes Appeared

Parameters[a]	Basal Bolus (n = 80)	Insulin Pumps (n = 22)	*p*-value[b]
Increased number of hyperglycemias	48 (60%)	7 (31.81%)	0.018
Context of hyperglycemia			
Stress, emotions, and anxiety caused by the pandemic	60 (75%)	11 (50%)	0.024
Lack of a regular diet	46 (57.5%)	10 (45.45%)	0.316
No comply with the insulin dose	27 (33.75%)	7 (31.81%)	0.864
Increased number of hypoglycemia	33 (41.25%)	7 (31.81%)	0.422
Context of hypoglycemia			
Too many units of insulin	64 (80%)	10 (45.45%)	0.001
Excessive physical exertion	17 (21.25%)	6 (27.27%)	0.549
Irregular meals	38 (47.5%)	6 (27.25%)	0.089
Connection error	0 (0%)	15 (68.18%)	<0.001

Notes: [a]Values are expressed as counts (percentage). [b]Chi-square test or Fisher's exact test.

lockdown, staying more at home, and 22 (21.6%) that, on the contrary, the number of meals low due to stress and worries. In addition, 50% patients claimed that their number remained the same.

Patients were also asked how they managed the hyperglycemic episodes and whether they needed hospital intervention (in the case of diabetic ketoacidosis). Their response ranged from the case when they made the necessary correction by administering a few extra units of insulin (in most hyperglycemic events), but there were 5 patients (4.9%) who claimed to have had at least one event who required emergency care. The 5 patients were all on basal-bolus therapy, 4 of them admitted that they did not always follow the insulin dose and diet (3 due to negligence, 2 due to lack of physical activity), 4 had values of fasting blood glucose higher than 300 mg/dl, 3 of them were infected with the SARS-CoV-2 virus, and one had another type of infection.

To be able to determine if there were any changes in insulin requirements, patients were asked if they noticed significant increases in the units used and if they had access to more doses if needed. Only 10 patients (9.8%) considered that the insulin requirement increased, compared to 92 (90.2%) who did not notice significant changes ($\chi^2 = 131.84$; $p < 0.001$). Of those who answered that they had not always access, only 1 (0.9%) was a carrier of insulin pump. He said that he did not contact any diabetologist, and he went only to the family doctor for treatment, who adjusted the doses according to the number of carbohydrates ingested and physical activity performed. His glycemic values were even over 300 mg/dL, and HbA1c ranged from 7 to 8. The other nine patients blamed the increase in insulin requirements due to lack of physical activity and regular meals (including snacks), non-compliance with insulin doses and stress, emotions, and accumulated anxiety.

Regarding the increase in insulin requirement during the lockdown period, 50 patients (49%) claimed that the need increased, 6 patients (5.9%) said that it decreased, while 46 patients (45.1%) considered that the need remained the same. The necessary changes were attributed to the lack of regular physical activity, improper diet, anxiety caused by the context of the pandemic. Comparison between the two groups of patients (pump carriers and basal-bolus type insulin therapy), 44 pen users (43.1%) considered that the need for insulin increased, as opposed to 6 patients (5.8%) who are pump carriers. This may be due to the increased need for corrections made by those who used pens. Of those who did not notice changes in need, 30 (29.4%) are on basal-bolus therapy, and 16 (15.6%) are pump carriers.

Table 3 Comparisons of the Two Groups Regarding the Fast Glucose Level and HbA1c

Parameters[a]	Basal Bolus (n=80)	Insulin Pump (n=22)	*p*-value[b]
Fast glucose level			
126–200 mg/dL	5 (6.25%)	1 (4.54%)	0.763
200–300 mg/dL	16 (20%)	6 (27.27%)	0.472
>300 mg/dL	59 (73.75%)	14 (63.63%)	0.351
HbA1c			
<6.5%	16 (20%)	14 (63.63%)	<0.001
6.5–7%	21 (26.25%)	3 (13.63%)	0.217
7–8%	25 (31.25%)	3 (13.63%)	0.101
>8%	15 (18.75%)	0 (0%)	0.019

Notes: [a]Values are expressed as counts (percentage). [b]Chi-square test or Fisher's exact test.

An objective way to see if there was adequate glycemic control was to analyze fasting blood glucose and HbA1c. The results obtained are presented in Table 3. The increase of HbA1c level present in the first group of patients suggests a better glycemic control in insulin pump users.

Another topic addressed with the patients in the questionnaire were infections (other than those with SARS-CoV-2 virus) and how they treated it. There were 21.5% of the patients who presented an infection. The types of infections they mentioned were respiratory tract infection (9 patients, 40.9%), dental infection (22.7%), genital infection (22.7%), and panaritium (3 patients 13.6%). Only 27.27% of the patients did not contact the physician, for fear of going to the hospital for treatment, compared to 16 people who asked for specialized treatment, either to the family physician (22.7%), or to another specialist (50%).

Regarding HbA1c (April–December 2020), only 29.41% of the patients reported a value lower than 6.5, of which 16 were patients with pens and 14 were pump carriers (20% vs 63.63%, $\chi^2 = 15.19$; $p < 0.001$). A number of 24 patients (23.52%) had the value between 6.5 and 7, 28 patients (27.4%) between 7 and 8, respectively, 15 patients (14.7%), all on basal-bolus therapy, above 8. This increase present in the first group of patients suggests a better glycemic control in insulin pump users.

A series of statements that patients were asked about were related to the psychological damage caused by the pandemic context. Each statement was rated with 1 (disagree), 2 (neutral opinion) and 3 (agree) (Table 4).

We observed an increased number of patients who agreed with most of the statements. Of these, 59 (57.8%) claimed that they were afraid to go to the hospital when their general condition was altered, for fear of being infected with the SARS-CoV-2 virus (59 vs 43, $\chi^2 = 5.01$; $p = 0.025$), and 72 (70.5%) stated that the stress increased during the restrictions (73 vs 30, $\chi^2 = 34.58$; $p < 0.001$), due to the panic established (n = 5; 4.9% disagreed with this statement and n = 25; 24.6% had a neutral opinion). Only 55 patients (53.9%) felt overwhelmed by the multitude of information about their disease, which they had to manage on their own (55 vs 47, $\chi^2 = 1.25$; $p = 0.262$) and only 38 (37.2%) measured their blood glucose more often being afraid of hyperglycemia/hypoglycemia events (38 vs 64, $\chi^2 = 13.25$; $p < 0.001$). However, 53 patients (51.9%) stated that they were able to contact the diabetologist more often via telemedicine, WhatsApp, e-mail, or other social media (53 vs 49, $\chi^2 = 0.31$; $p = 0.575$) and only 39 people (38.2%) said that they did not encounter difficulties in managing T1DM during the pandemic, compared to 25 (24.5%) who had difficulties, and the 38 (37.2%) who chose to have a neutral opinion.

Due to the restrictions established, both travel and the physician–patient relationship were limited. Physicians were using special platforms (telemedicine)/WhatsApp/phone to monitor the evolution of patients' disease. Only 23 (22.5%)

Table 4 Distribution of Patients According to the Psychological Damage Caused by the Pandemic Context

Statements[a]	Basal Bolus (n = 80)	Insulin Pump (n = 22)	*p*-value[b]
When I felt sick, I was afraid to go to the hospital, not to be infected			
1 (disagreement)	9 (11.25%)	10 (45.45%)	<0.001
2 (neutral opinion)	18 (22.5%)	6 (27.27%)	0.640
3 (agreement)	53 (66.25%)	6 (27.27%)	0.001
Emotional stress increased during the pandemic due to the established panic			
1 (disagreement)	4 (5%)	1 (4.54%)	0.995
2 (neutral opinion)	13 (16.25%)	12 (54.54%)	<0.001
3 (agreement)	63 (78.75%)	9 (40.91%)	<0.001
I started measuring my blood sugar more often, for fear of complications			
1 (disagreement)	20 (25%)	11 (50%)	0.024
2 (neutral opinion)	32 (40%)	6 (27.27%)	0.275
3 (agreement)	28 (35%)	5 (22.72%)	0.277
I became anxious and overwhelmed by the multitude of information about my illness that I had to manage on my own.			
1 (disagreement)	41 (51.25%)	14 (63.63%)	0.304
2 (neutral opinion)	16 (20%)	4 (18.18%)	0.881
3 (agreement)	23 (28.75%)	4 18.18 (%)	0.319
We did not encounter any difficulties in managing diabetes during the pandemic			
1 (disagreement)	30 (37.5%)	8 (36.36%)	0.922
2 (neutral opinion)	23 (28.75%)	2 (9.09%)	0.057
3 (agreement)	27 (33.75%)	12 (54.54%)	0.075
I contacted my diabetologist more often (WhatsApp, telemedicine, other media) than before			
1 (disagreement)	14 (17.5%)	0 (0%)	0.025
2 (neutral opinion)	41 (51.25%)	12 (54.54%)	0.784
3 (agreement)	25 (31.25%)	10 (45.45%)	0.214

Notes: [a]Values are expressed as counts (percentage). [b]Chi-square test or Fisher's exact test.

patients considered that they did not have access to the health system, compared to 37 (36.2%) who did not agree with this statement. Also, a major disagreement can be observed in the statement that they could not contact the diabetologist, 76 patients (74.5%) compared to 7 patients (6.8%) who agreed ($\chi^2 = 96.7$; $p < 0.001$). The proportions were similar in case of access to treatment, 57 (55.8%) disagreeing with the statement "I did not have access to treatment as before", and 13 (12.7%) agree with it ($\chi^2 = 42.1$; $p < 0.001$). So, we can state that, although limited, access to the health system, diabetologist and treatment was not significantly affected.

Patients were also asked how the medical consultation took place and how they kept in touch with the diabetologist during the restrictions. Several 55 patients contacted the diabetologist either through social media/WhatsApp/e-mail or by phone (53–54%). At the same time, 13 (12.7%) of them went only to the family doctor for the prescription, and 7 (6%)

did not keep in touch with any physician. Regarding the way the consultation was carried out, only 31 (30%) of the patients were physically present at the consultation (in a diabetes center, private clinic, etc.), compared to 42 (41.1%) who send their daily glycemic values. Also, 25 (24.5%) patients claim to have had a conversation with the diabetologist, through whom he made a brief history (general condition, insulin therapy), and 14 (13.7%) contacted the physician only in case of emergencies in their control of glycemic values. As the regular consultations were limited to the online meetings/phone calls, it was decided that the prescription of treatment, as well as the list of consumables for the management of T1DM (depending on the type of therapy – basal bolus or insulin pump) can be transmitted by e-mail. This reduced the patients' exposure to a possible infection with the SARS-CoV-2 virus and facilitated the treatment process. A number of 58 patients (56.8%) claimed that this method was helpful, raising insulin doses and consumables from pharmacy, with prior appointment and a reduced waiting time. In comparison, 16 patients (15.6%) disagreed with this statement ($\chi^2 = 37.4$; $p < 0.001$). A number of 50 patients (49%) patients, of whom 43 patients (86%) on a basal-bolus regimen and 7 (14%) of insulin/artificial pancreas users answered "Yes" when were asked if they considered that the restrictions imposed made it difficult for them to manage the disease. In comparison, 51% considered that the restrictions did not allow adequate glycemic control (49% vs 51%, $\chi^2 = 0.07$; $p = 0.799$).

Discussion

The aim of this study was to follow the impact that the pandemic with COVID-19 had in the management of glycemic control in patients with T1DM, how they were affected by the restrictions and lockdown established at national level.

However, studies have shown the opposite. Either the glycemic control was not affected, or, on the contrary, the lockdown favored a better management of T1DM. A possible explanation could be the lack of stress in the workplace (many companies had to continue the activity online, at home) or at school (in the case of children and adolescents), the existence of regular meals taken at home, with a more accurate and implicit calculation of carbohydrates of insulin units. Also, the fear of SARS-CoV-2 infection and the complications that may occur has made possible a better adherence to the treatment and recommendations of diabetologists.[10] For example, in a study conducted in Italy and published in May 2020, an improvement in glycemic control was observed in the first 7 days of lockdown. It was performed in a group of 20 patients whose blood glucose decreased from 177 ± 45 mg/dl (before 1 week of lockdown) to 160 ± 40 mg/dl (first week of lockdown). Also, the time spent in a state of hyperglycemia decreased from 42.3% to 31.6%, but there was no significant change in the number of tests performed (on the test strip). The results of the study suggested that a moderation of daily activities could have a beneficial effect in the management of T1DM.[11]

Another study, also conducted in Italy, in three stages (before the pandemic, at the beginning of the imposition of restrictions and, respectively, during the lockdown), on a group of 13 patients carrying an insulin pump, showed a higher increase of time spent in hyperglycemia in stage 3 (72%) compared to stage 2 (66%), as well as an increase in periods of hypoglycemia in stage 3. However, the results showed that the restrictions did not adversely affect the glycemic control of these patients, much less those who continued to play sports at home. Moreover, the maintenance of most physical activities in a safe and controlled environment has been essential for the proper management of T1DM.[12]

On the same principle, of the stages (before, at the beginning, in the middle and after the lockdown), another Italian study reinforced these statements, highlighting a significant improvement in glycemic control immediately after the imposition of restrictions. The study was performed on a group of 63 patients with T1DM, of whom 52 (82%) used the glucometer to measure blood glucose levels and 11 (18%) insulin sensors. An improvement was observed in the value of glycemia (from 165 mg/dL to 158 mg/dL) as well as in that of HbA1c (from 7.2% to 7.0%) which suggests a longer time in normoglycemic status.[13]

Dalmazi et al[14] underlined that within the pandemic period glycemia can be influenced by age, lower physical activity, and stress. Given the restrictions imposed in Romania, patients claimed in this study that they either tried to exercise at home, thus maintaining better glycemic control and lowering insulin requirements, or did not perform intense physical activities due to travel limits. Lockdown policies established to avoid SARS-CoV-2 spread may favor deterioration of control in people with diabetes due to difficulties in accessing the health system, lack of physical

activity and increased stress or anxiety associated with lockdown.[15–17] Anxiety in people with T1D has been associated with less frequent BG monitoring and suboptimal glycemic control.[18]

Non-compliance with the diet, to a greater extent, than the stress and anxiety caused by the pandemic (to a lesser extent), led to the occurrence of hyperglycemic episodes. In time, these hyperglycemic episodes will determinate the occurrence of chronic diabetes complications.[19] The current study was performed in a group of patients on basal bolus therapy and insulin pump users, and it was observed that the latter managed to better manage T1DM. At the same time, more than a half of pump users' patients did not notice a significant increase in the number of hyperglycemias. In the case of pen users, the glycemic values were higher than 300mg/dL in 73.75% of the patients. They all made the necessary corrections and only five needed specialized emergency medical help. Three of them were infected with SARS-CoV-2, and their blood sugar tripled.

On the other hand, a study in India in a group of 52 patients reported an increase in blood glucose levels from 212.3 ±57.9 mg/dL to 276.9±64.7 mg/dL, either due to negligence in insulin administration (26.9%) irregular blood glucose monitoring (36.5%) or non-compliance with diet (17.4%). Patients attributed these reasons to insufficient insulin doses/ glucometer strips.[20]

In the current study, only 10 patients claimed that they did not always have access to insulin doses, and the reason was the increase in glycemic values based on stress and anxiety as well as non-compliance with diet (several snacks between meals, neglected calculation of carbohydrates). Among those who answered that they "not always" had access, only 1 (0.9%) is a carrier of an insulin pump and declared that he did not keep in touch with any diabetologist, he only went to the family doctor for the prescription medical, adjusted the doses according to the number of ingested carbohydrates and physical activity, had glycemic values even above 300 mg/dl, and HbA1c was in the range of 7–8. An increase in insulin requirements was reported by half of the patients (of which only 6 users of insulin pump), suggesting that a greater number of corrections made by pen users and implicitly more events of hyperglycemia and better control of pump wearers.

Regarding the increased risk of developing diabetic ketoacidosis in the case of an infection, the reported cases showed a late diagnosis of a newly installed T1DM presented as severe ketoacidosis. A study in India, conducted between May and October 2020 on a group of 102 patients infected with the SARS-CoV-2 virus, showed an increase in blood glucose levels in 21 of them, but with an HbA1c value of ≥6.5%, suggesting that before of infection, they had undiagnosed diabetes. Hyperglycemic status was present in all 21 patients, but without acute metabolic complications. On the other hand, cases have been reported in which the blood glucose value was in the range of 353–940 mg/dL, and of HbA1c between 12% and 15.1% which subsequently developed ketosis or ketoacidosis, suggesting poor glycemic control before infection.[21] One explanation for these cases could be the fear of patients seeking specialist medical care when their general condition worsens, the fear of being infected in hospital. Another factor would be the restriction of physical consultations and access to the health system.

The number of hypoglycemic episodes was not significantly altered than the period before the lockdown. Only 40 patients reported increases in events, of which 33 were pen users and 7 were pump users. The context of the occurrence of hypoglycemia was largely due to the overdose of administered insulin and irregular meals.

Different studies also shown that using CGM in patients with T1DM improved glycemic balance and reduced risk of hypoglycemia during lockdown.[22–24] Many studies conducted on T1DM patients using continuous glucose monitoring (CGM), show an improvement in glycemic control may be due to improved disease self-management and getting more time for diabetes management. Also, CGM usage facilitated a good adaptation to the changing reality.

What slightly alleviated the problems in managing the disease, along with the pandemic, was the development of telemedicine and the computer system in terms of medical consultation and access to the health system.

Although a global worsening in metabolic control secondary to a dramatic reduction in access to medical services and laboratory testing was expected during COVID-19, surprisingly, most of the studies published throughout the pandemic have demonstrated significant improvements of glucose metrics either in adults or in children affected by T1DM, and telemedicine application surely contributed to these results. Remote consultations and the possibility to access frequent data on glucose trends through telemedicine have permitted to reach encouraging results in T1DM population, demonstrating that remote consultations and commonly shared data access can improve clinical outcomes

and the patients' quality of life.[25–28] Furthermore, it helped to limit the spread of infection through implicit distancing, reduced costs, waiting time and inconvenience to patients, although it led to increased anxiety in patients with T1DM, to limited consultation and of access to it due to the lack of internet network infrastructure in some regions.[29]

Regarding the health system, there was a small percentage of patients who claimed that they did not have access to it and a major disagreement about access to a diabetologist, suggesting that, although limited consultations, patients were able to receive medical help, specialized to a greater or lesser extent.

Recent data from literature show a better adherence to treatment using telemedicine especially in patients with suboptimal control.[30,31] Because of the good results obtained with using telemedicine in the pandemic period, this can be used also in routine follow-up for patients with lower compliance or with a poor metabolic control, who require a strict follow-up with frequent and regular contacts with medical team.[32]

Conclusions

Contrary to expectations, but similarly with other studies conducted in different countries, we observed that either the glycemic control was not significantly impacted by the COVID-19 lockdown measures, in patients with T1DM. Telemedicine and online consultations brought significant improvements both in terms of time allocated to each patient and communication with the physician, who remotely monitored the evolution of the disease. Regarding the differences between pen users and insulin pump users, the latter showed better glycemic balance and coped better with the stress and anxiety caused by the pandemic, with fewer hyperglycemic episodes probably due to continuous glycemic monitoring system.

Consent for Publication

All participants signed a document of informed consent.

Disclosure

The authors report no conflicts of interest in this work.

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