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ORIGINAL ARTICLE

Effect of the COVID-19 pandemic on glycemic control in Brazilian patients with type 2 diabetes

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Abstract

Purpose To investigate the effect of restrictive measures the COVID-19 pandemic imposed on glycemic control of patients with type 2 diabetes (T2D) and its associated factors.

Methods Outpatients with T2D who had an appointment scheduled during the social distancing period were eligible for telemonitoring. Clinical and laboratorial data were collected from medical records in the last consultation before and from the first visit after the COVID-19 pandemic lockdown period.

Results From the 1241 eligible patients, 816 (65.7%) could be contacted by phone, 137 (11%) attended the unit for consultation during the social distancing period, and 1040 (83.8%) returned up to 12 months after the end of the lockdown period. We observed a meaningful reduction of glycated hemoglobin (HbA1c) (7.9 [7–9] vs. 7.7 [6.9–8.8] $p = 0.004$) and no difference in body mass index (29.5 [26–33.7] vs. 29.6 [26.2–34.1], $p = 0.17$) before and after the social distancing period. According to insulin use at baseline, the HbA1c variation was +0.6 (−0.7 to +2) and −0.6 (−2.1 to +0.7) in patients without and with insulin, respectively ($p < 0.001$). In the multivariate model, insulin therapy was the only independent significant predictor of HbA1c reduction.

Conclusion This study observed an improvement in glycemic control after the lockdown. The only independent predictor found was previous insulin use. Probably, the longer time available to perform frequent blood glucose self-monitoring at home and adjustments in insulin therapy could explain our findings.

Keywords COVID-19 · Social distancing · Lockdown · Type 2 diabetes · Glycemic control

Introduction

Since March 2020, social restrictions were imposed in several countries because of the COVID-19 pandemic. To limit the spread of the new coronavirus, several measures were established, including social distancing with consequent restrictions to physical and work activities, leading to a worsening of quality of life, eating patterns, sleep impairment, and an increase in emotional stress levels [1, 2]. Healthy lifestyle habits are the cornerstone of treating diabetes mellitus (DM) [3]. Therefore, the reduced physical activity, poor adherence to diet, and increased body weight could worsen glycemic control [4–7]. Moreover, restrictive measures could limit the access to health services as well as the public health system's distribution of supplies and medicines, making metabolic control even more difficult. On the other hand, increased spare time at home could have stimulated better eating habits, physical activity, and weight loss due to the fear of presenting serious COVID-19 complications in people at a higher risk of developing the severe form of this disease that the media widely reported.

There are few studies that address the effect of social distancing during the COVID-19 pandemic on the metabolic control of patients with DM, especially those with type 2 diabetes (T2D). Existing data are conflicting. Some studies showed that restrictive measures did not significantly affect glycemic control [8, 9] while another observed a negative impact on body weight and glycemic control in this population, especially in those using insulin [10].

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This study aimed to investigate the effect of restrictive measures the COVID-19 pandemic imposed on glycemic control of patients with T2D and its associated factors.

Material and methods

This observational study was conducted at the Diabetes Unit of State University of Rio de Janeiro. The local ethics committee approved this study and it received Plataforma Brasil's Certificado de Apresentação para Apreciação Ética (CAEE) under the number of 31780320.3.0000.5259.

Outpatients with DM receiving follow-up treatment at our unit who had an appointment scheduled during the social distancing period (March–June 2020) were eligible for telemonitoring. Those with type 1 diabetes were excluded once data had already been published elsewhere [11].

Clinical, demographic, and laboratorial data recorded in the last consultation before the COVID-19 pandemic lockdown were collected from medical records, such as: age, type and duration of diabetes, insulin use (Yes/No), glycated hemoglobin (HbA1c) (%), body mass index (BMI) (kg/m^2), systolic (sBP) and diastolic blood pressure (dBP), diagnosis of hypertension, diabetic retinopathy and neuropathy, and estimated glomerular filtration rate (eGFR) (estimated by the Chronic Kidney Disease Epidemiology Collaboration creatinine equation) [12]. Patients were considered overweight or obese if BMI ≥ 25 or ≥30 kg/m^2 in adults, respectively.

The data obtained from medical records referring to the COVID-19 pandemic lockdown were as follows: difficulties in acquiring supplies for diabetes treatment (syringes, needles, and glycemic stripes for glucose monitoring), adherence to diabetes management, including adherence to medication (0 to 10 scale) and diet (0 to 10 scale), and self-reported frequency of physical exercise. We considered ideal adherence to diet and treatment based on the self-report score when ≥8. This information could only be obtained from the subgroup of patients the medical team contacted via telephone contact or consultation.

Demographic, clinical, and laboratorial data were also collected from medical reports from the first visit after the social distancing period, including turn-around time for consultations and exams and metabolic parameters such as HbA1c, sBP, dBP, BMI, and GFR values.

Statistical analysis

The distribution of variables was tested for normality with the Shapiro–Wilk test. An exploratory analysis was performed, and data were presented as median values (interquartile range) and frequencies. Chi-square test was used to analyze categorical variables. A Mann–Whitney test was used to compare unpaired samples, and Wilcoxon's signed-rank test was used to analyze data collected before and after the social distancing period. A univariable logistic regression was performed to determine which factors were associated with improved glycemic control and were considered as dependent variables. Variables with p value < 0.1 were included in the multivariate regression analysis. The calculated odds ratio with a 95% confidence interval is expressed as indicated. The multicollinearity test between variables included in the multivariate analysis was performed. A two-sided p value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 27.0.

Results

From the 1241 patients with previously scheduled appointments during the COVID-19 pandemic lockdown,

Fig. 1 Flowchart of the studied sample selection

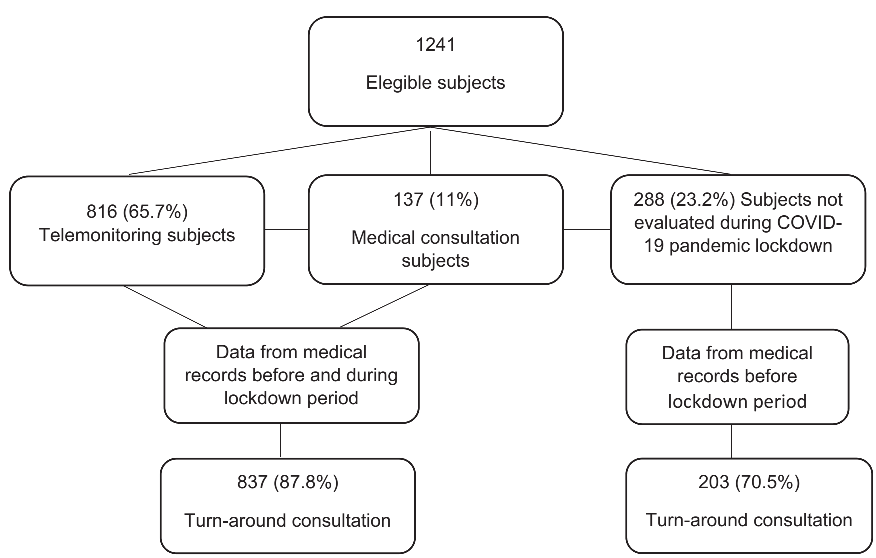

Table 1 Demographic and clinical data of the studied population

Data	$N = 1241$
Age (y)	66 (59–73)
Gender, female, *n* (%)	757 (61)
Diabetes duration (y)	16 (9–23)
Insulin use, *n* (%)	841 (67.8)
HbA1c (%)	7.9 (7–9)
BMI (kg/m^2)[a]	29.5 (26–33.7)
- Normal, *n* (%)	207 (16.8)
- Overweight, *n* (%)	434 (35.2)
- Obesity, *n* (%)	592 (48)
Hypertension, *n* (%)	1071 (86.3)
GFR (ml/min/1.73 m^2)[b]	77.8 (55.1–94)
GFR < 60 ml/min/1.73 m^2, yes, *n* (%)	369 (29.8)

HbA1c glycated hemoglobin, *BMI* body mass index, *GFR* glomerular filtration rate. Data are presented as median (interquartile range) or percentual

[a]Missing data from eight patients

[b]Missing data from five patients

816 (65.7%) were successfully contacted via phone and 137 (11%) attended the diabetes unit for consultation during the social distancing period (Fig. 1). The characteristics of the included subjects are described in Table 1.

Of the total number of patients evaluated via telemonitoring or during medical consultation (953), 153 (16%) reported performing some type of regular physical exercise, 319 (33.5%) and 841 (88.2%) reported good adherence to diet and diabetic treatment, respectively, and 127 (13.3%) patients reported difficulties in accessing supplies for DM treatment.

Three hundred and forty-one patients (27.5%) were on monotherapy, 700 (56.4%), 182 (14.7%), and 18 (1.5%) patients were taking two, three, or four antidiabetic drugs, respectively. Details on antidiabetic treatment are shown in Table 2.

Of the evaluated patients, 1040 (83.8%) returned for a medical visit up to 12 months after the end of the lockdown period. Of the group, a medical team evaluated 837 (67.4%) via telemonitoring or consultation, and 203 (16.3%) patients were not evaluated during the COVID-19 pandemic lockdown (Fig. 1). The median turn-around time for consultation was 3 (2–4) months and the median turn-around time for exams was 4 (2–5) months. HbA1c results were available in 932 (89.5%) of the 1041 patients who returned for the consultation after the COVID-19 pandemic lockdown.

We observed a significant HbA1c reduction before and after the social distancing period (7.9 [7–9] vs. 7.7 [6.9–8.8] %, $p = 0.004$), despite no difference in BMI level (29.5 [26–33.7] vs. 29.6 [26.2–34.1] kg/m^2, $p = 0.17$).

Table 2 Antihyperglycemic therapy in the evaluated population

Antihyperglycemic therapy	N = 1241
Monotherapy, *n* (%)	341 (27.5)
Diet, *n* (%)	5 (0.4)
Insulin, *n* (%)	185 (14.9)
Metformin, *n* (%)	133 (10.7)
SU, *n* (%)	13 (1.1)
DPP-IVi, *n* (%)	5 (0.4)
Dual Therapy, *n* (%)	700 (56.4)
Insulin + other drug, *n* (%)	536 (43.2)
- Insulin + Metformin	521 (42)
- Insulin + DPP-IVi	6 (0.5)
- Insulin + Pioglitazone	3 (0.24)
- Insulin + SGLT2-i	5 (0.4)
- Insulin + GLP1-RA	1 (0.08)
Two other drugs	164 (13.2)
- Metformin + SU	131 (10.6)
- Metformin + Pioglitazone	8 (0.65)
- Metformin + DPP-IVi	11 (0.9)
- Metformin + SGLT2-i	9 (0.7)
- SU + DPP-IVi	5 (0.4)
Triple Therapy, *n* (%)	182 (14.7)
Insulin + 2 other drugs, *n* (%)	110 (8.9)
- Insulin + Metformin + SU	39 (3.1)
- Insulin + Metformin + Pioglitazone	17 (1.4)
- Insulin + Metformin + DPP-IVi	23 (1.9)
- Insulin + Metformin + SGLT2-i	23 (1.9)
- Insulin + Metformin + GLP1-RA	1 (0.08)
- Insulin + Pioglitazone + DPP-IVi	7 (0.6)
Three other drugs, *n* (%)	72 (5.8)
- Metformin + SU + Pioglitazone	14 (1.1)
- Metformin + SU + DPP-IVi	40 (3.2)
- Metformin + SU + SGLT2-i	11 (0.9)
- Metformin + SU + GLP1-RA	1 (0.08)
- Metformin + SGLT2-i + GLP1-RA	1 (0.08)
Quadruple Therapy, *n* (%)	18 (1.5)
Insulin + 3 other drugs, *n* (%)	10 (0.8)
- Insulin + Metformin + SU + Pioglitazone	2 (0.16)
- Insulin + Metformin + SU + SGLT2-i	3 (0.24)
- Insulin + Metformin + DPP-IVi + Pioglitazone	2 (0.16)
- Insulin + Metformin + DPP-IVi + SGLT2-i	3 (0.24)
Four other drugs, *n* (%)	8 (0.6)
- Metformin + SU + Pioglitazone + DPP-IVi	6 (0.5)
- Metformin + SU + DPP-IVi + SGLT2-i	2 (0.24)

SU sulfonylureas, *SGLT2-i* sodium-glucose contransporter2 inhibitors, *DPP4i* dipeptidyl peptidase IV inhibitors, *GLP-1 RA* glucagon-like peptide-1 receptor agonists

The HbA1c variation observed in the subgroup of patients that reduced or maintained BMI ($n = 440$, 55.7%) and in the subgroup of patients that increased BMI

Table 3 Univariate and multivariate logistic regression analyses evaluating the determinants of HbA1c improvement after social distancing

Variable	Univariate logistic regression OR (C.I. 95%)	p value	Multivariate logistic regression OR (C.I. 95%)	p value
Age	0.98 (0.98–1.00)	0.08	0.99 (0.98–1.01)	0.39
Gender	0.84 (0.65–1.10)	0.21		
Diabetes duration	1(0.98–1.01)	0.98		
BMI's reduction	1.35 (1.04–1.75)	0.03	1.24 (0.91–1.69)	0.17
Insulin use	2.91 (2.19–3.87)	<0.001	2.53 (1.81–3.53)	<0.001
Telemonitoring or medical consultation	0.78 (0.57–1.06)	0.11		
Fear/anxiety	0.90 (0.66–1.25)	0.54		
Good adherence to diet	0.86 (0.63–1.16)	0.31		
Good adherence to medical treatment	0.94 (0.55–1.59)	0.81		
Turn-around time for consultation	1.04 (0.98–1.1)	0.19		
Turn-around time for exam	0.97 (0.92–1.01)	0.14		
Difficulties related to medical supplies	0.83 (0.56–1.25)	0.39		
Physical exercise practice	1.41 (0.97–2.04)	0.07	0.75 (0.51–1.11)	0.15

BMI body mass index, *GFR* glomerular filtration rate

($n = 469$, 50.6%) was −0.4 (−1.88 – +0.9)% and −0.05 (−1.4 – +1.4)%, respectively ($p = 0.011$).

Patients who used insulin showed a greater reduction in BMI compared to those who did not use: −0.4 (−5.4 – +5.0) kg/m^2 versus 1.6 (−3.6 – +6.2) kg/m^2. In addition, according to insulin use at baseline, the HbA1c variation was +0.6 (−0.7 – +2) and −0.6 (−2.1 – +0.7)% in patients without and with insulin, respectively ($p < 0.001$).

In the univariate analysis, there was no difference in pre- and post-pandemic weight change between patients who used or did not use SGLT2-i or GLP-1-RA.

In the univariate logistic regression, insulin therapy, self-reported physical activity practice, and reduced BMI were significant predictors of HbA1c improvement. In the multivariate model, insulin therapy was the only independent significant predictor of HbA1c reduction (Table 3).

Discussion

In our study, we observed a positive effect of restrictive measures the COVID-19 pandemic lockdown imposed on glycemic control. This result was slightly expected because the media's wide dissemination of diabetes as a risk factor for severe COVID-19 cases could have stimulated better care and adherence to treatment. However, the only independent predictor of improvement in HbA1c in our study was the use of insulin.

A study conducted in Italy with 128 patients with T2D [10] found that insulin treatment was an independent predictor of worsening metabolic control, resulting in an increase in HbA1c. However, the analysis was limited to individuals who had no medical contact during the lockdown, and consequently, the absence of an adequate insulin dose adjustment may have played a role in the worsened glycemic control. This finding conflicts with the result found in the present study, in which using insulin was significantly associated with an improvement in HbA1c. This result may seem paradoxical because insulin use is usually reserved for T2D patients with a longer duration of diabetes and inadequate glycemic control despite optimized non-insulin treatment. Our study was carried out in a public health center in which the vast majority of patients are treated only with medications supplied by the government, including metformin, sulfonylurea, and insulin. Thus, insulin is often used as a third drug or possibly as a second drug if there is contraindication or intolerance to oral drugs, justifying the large number of patients on insulin therapy. A relevant aspect of the Brazilian public health system is that supplies for self-monitoring blood glucose levels are usually provided only to patients on insulin therapy. This may have contributed to better control in patients who had tools to monitor and adjust their glycemic levels.

A cross-sectional survey of patients and physicians in eight developed and developing countries (China, France, Japan, Germany, Spain, Turkey, the UK, and the US) found that insulin omission/non-adherence was a common problem in all countries and that taking insulin at the prescribed time and frequency were the main difficulties that both patients and physicians pointed out [13]. In our study, one of the reasons that could explain the improvement in glycemic control was a better adherence to insulin therapy because patients spent more time at home due to restrictive measures the COVID-19 pandemic imposed, making it easier to respect mealtimes and insulin application.

In the present study, we did not observe a reduction in BMI, but the subgroup that reduced BMI had better levels of HbA1c. As opposed to what would be expected, patients using insulin had a greater reduction in BMI, but in the multivariate analysis, only insulin use was independently associated with improved glycemic control. This fact corroborates the hypothesis described above regarding the importance of blood glucose self-monitoring for greater motivation in relation to treatment and better glycemic control.

To our knowledge, this is the first study that analyzed the effect of the COVID-19 pandemic lockdown on glycemic control in T2D patients in Brazil. The strength of our work is the number of evaluated patients and the expressive percentage of contact achieved during the COVID-19 lockdown via either telemonitoring or in-person consultation.

Our study has some limitations. Data on medication adherence, diet, physical activity, and feelings of fear/anxiety were self-reported and collected in a non-systematized way, which could have impaired the data's accuracy. We also did not have data on these variables from the pre-pandemic period for comparison. These facts may explain the absence of a relationship found between these variables and the change in glycemic control. In addition, we did not obtain HbA1c data from the entire population that returned to the consultation after the lockdown due to difficulties in rescheduling laboratory tests. Data on lipid profiles were not reported because those data were not available for all patients before and after the lockdown.

Conclusion

The present study observed an improvement in glycemic control after the COVID-19 pandemic lockdown. The only independent predictor found was previous insulin use. Probably, the longer time available to perform frequent blood glucose self-monitoring at home and adjustments in insulin therapy could explain our findings.

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Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by L.R.M.T., R.M.Z., C.A.C., A.S.M.M., P.C.C., R.C.A-A., R.P. and R.A.C. The first draft of the manuscript was written by L.R.M.T., R.M.Z., C.A.C., A.S.M.M., R.C.A-A., R.P., and R.A.C. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Consent to participate Patient consent was waived due to the observational nature of the study and collection of medical record data.

Ethics approval The study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Universidade do Estado do Rio de Janeiro (Plataforma Brasil's Certificado de Apresentação para Apreciação Ética (CAEE) under the number of 31780320.3.0000.5259).

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