

SHORT COMMUNICATION

The Impact of COVID-19 Lockdown on Patients with Type 2 Diabetes Mellitus: A Brief Report

Alfredo Vozza¹, Erasmo Porfido¹, Alessandra Delvino¹, Carlo Custodero¹, Giuseppe Lisco^{1,*}, Vincenzo Triggiani¹, Cosimo Tortorella¹ and Giuseppina Piazzolla¹

¹Interdisciplinary Department of Medicine, University of Bari "Aldo Moro", School of Medicine, Policlinico, Piazza G. Cesare 11, 70124 Bari, Italy

Abstract: Background: The Italian population's habits changed dramatically during the "COVID-19 lockdown" due to physical distancing and self-isolation. Moreover, medical consultations of patients with chronic diseases, such as type 2 diabetes (T2D), were suspended or postponed, unless urgent or semi-urgent, for several consecutive months. Thus, it is expected that the lockdown could have affected glucometabolic control in T2D.

Purpose: The aim of the study was to assess changes in glucometabolic control in a cohort of T2D patients before (T1) and after (T2) the COVID-19 lockdown (March-May 2020).

Methods: The study was approved by the Ethics Committee of the University of Bari, and all patients provided informed written consent to participate. Medical history, complete physical examination, and laboratory assessment were conducted as real-life clinical practice. Changes in clinical and laboratory variables between T1 and T2 were calculated.

Results: In detail, 13 patients were on metformin as monotherapy, 36 on GLP-1RA, 12 on sodium-glucose transporter 2 inhibitors (SGLT-2i), and 2 on dipeptidyl-peptidase 4 inhibitors (DPP4i). The mean age was 65.3 years (43-83). Study participants were mainly men (73%). The body weight (BW) ranged from 56 to 145 kg, and the waist circumference ranged from 88 to 146 cm. The mean HbA1c was 51.0 mmol/mol. At T2, no statistically significant changes were observed from baseline except for BW [-1.6 (-2.60 to -0.62)] and HbA1c [-2.90 (-4.69; -1.12)].

Conclusion: We evaluated the effects of the COVID-19 lockdown on glucometabolic control in patients with background well-controlled T2D. We found that the lockdown had no adverse effects on metabolic profile regardless of background clinical characteristics and antihyperglycemic management. Despite limitations due to the nature of this study (sample size, retrospective observation, lack of data on lifestyle changes in our patients' everyday lives), T2D patients managed in our Diabetes Centers faced the lockdown-related restrictions without any detrimental consequence.

Keywords: COVID-19, lockdown, diabetes mellitus, glycosylated hemoglobin, body weight, GLP-1RA, SGLT2 inhibitors.

1. BACKGROUND

On 11th March, 2020, the World Health Organization declared the state of a pandemic due to Coronavirus Disease 2019 (COVID-19), a highly human-to-human transmissible viral disease [1]. To contain the spread of COVID-19, the Italian Government decided upon more stringent containment measures leading to the so-called #iorestoacasa (#stayathome) decree. The decree included several constraints, such as physical distancing and self-isolation, leading to the "COVID-19 lockdown". The "COVID-19 lockdown" was imposed from

10th March to 18th May, 2020, abruptly changing habits and lifestyles with relevant consequences on everyday activities. For some examples, eating habits and social life have changed significantly [2]. Carbohydrates consumption increased, especially high-glycemic-index carbohydrates, homemade products (pizza, cakes, sweets), and junk foods [3, 4]. Tea consumption was found to increase remarkably, too [5]. The leading causes of this attitude would be better elucidated, but they could be related to boredom, stress, and anxiety due to home confinement and stressful reports from the mass media [6-8]. In addition to pharmacological therapy, a healthy lifestyle is essential to promote insulin sensibility and weight loss, both conditions considered highly relevant for obtaining and maintaining adequate glycemic control [9].

*Address correspondence to this author at the Interdisciplinary Department of Medicine, University of Bari "Aldo Moro", School of Medicine, Policlinico, Piazza G. Cesare 11, 70124 Bari, Italy; E-mail: giuseppe.lisco@uniba.it

Moreover, healthcare facilities were rigidly reorganized to cope with the COVID-19 epidemic, and access to care was also restricted to urgent or semi-urgent essentials. In-presence follow-up medical consultations were discontinued or postponed, posing real challenges for managing chronic diseases, such as type 2 diabetes (T2D). Considering this issue, it is expected that the lockdown could have detrimental consequences on glucometabolic control in T2D.

In this brief report, we have analyzed data on 63 consecutive patients (46 males and 17 females, mean age 65.3 ± 9.3 years) with an established diagnosis of T2D, attending the Diabetes Centre of the Department of Internal Medicine "C. Frugoni" at the University of Bari. Patients underwent at least two in-person visits during the study period, one before and one after the lockdown.

2. METHODS

We retrospectively analyzed data referring to two periods to assess any relevant changes in glucometabolic, clinic, and anthropometric parameters in T2D due to restrictive measures observed through the lockdown. More precisely, baseline visits were carried out between December 2019 and February 2020, corresponding to T1; short-term follow-up visits were carried out after the lockdown (from May to July 2020, T2). The study was approved by the Ethics Committee of the University of Bari (ethical approval number 6468, version 2, 14th September, 2020). All patients provided written informed consent to participate. Experimental procedures were carried out according to the ethical standards for clinical research in humans by the Helsinki Declaration. At both times (T1 and T2), medical history and a complete physical examination were carried out for each patient. Laboratory parameters were also collected. Mean changes in clinic, anthropometric and

biochemical parameters, including body weight (BW), waist circumference (WC), body mass index (BMI), systolic and diastolic blood pressure, glycated hemoglobin (HbA1c), and lipids, were also calculated. All medications were registered at baseline. Changes in clinical and laboratory variables between T1 and T2 were analyzed using separate mixed models, applying an unstructured parameterization matrix for repeated measures. The statistical models were adjusted for GLP-1RA treatment [GLP-1RA (Coded 1) or other antidiabetic medications (Coded 0) in partially adjusted models, Models 1], and age and gender (in fully adjusted models: Model 1 plus age and gender, Models 2). All statistical analyses were performed using STATA 17 statistical software (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

3. RESULTS

At T1, 13 patients were on metformin as monotherapy, 36 on GLP-1RA, 12 on sodium-glucose transporter 2 inhibitors (SGLT-2i), and 2 on dipeptidyl-peptidase 4 inhibitors (DPP4i). Only one patient (in the SGLT-2i group) was on insulin therapy. Medications and posology remained unchanged from T1 to T2. The study population characteristics at T1 and T2 and the mean statistically significant changes are summarized in Table 1. The mean age was 65.3 years. Study participants were mainly men (73%). Anthropometrical parameters varied considerably at T1. The body weight (BW) ranged from 56 to 145 kg, and the waist circumference (WC) ranged from 88 to 146 cm. At T2, no statistically significant changes were observed compared to baseline except for BW and HbA1c (Table 1). Changes in HbA1c levels and BW were found to be significant, regardless of gender, age, and ongoing medications (Table 2).

Table 1. Mean difference in glucometabolic and anthropometric variables between T1 (before the lockdown) and T2 (after the lockdown).

-	T1	T2	Mean Difference
Age (years)	65.31 \pm 9.33	-	-
Gentlemen (n; %)	46 (73%)	-	-
GLP-1RA (n; %)	36 (57%)	-	-
Metformin (n; %)	13 (20%)	-	-
SGLT2i	12 (19%)	-	-
DPP-IVi	2 (3%)	-	-
HbA1c (mmol/mol)	51.0 \pm 12.34	48.09 \pm 10.09*	-2.90 [-4.69; -1.12]
Total cholesterol (mmol/L)	3.77 \pm 0.99	3.68 \pm 0.94	-
LDL (mmol/L)	1.95 \pm 0.85	1.85 \pm 0.76	-
HDL (mmol/L)	1.21 \pm 0.33	1.26 \pm 0.34	-
Triglycerides (mmol/L)	3.6 \pm 2.15	3.46 \pm 2.07	-
Body weight (kg)	83.56 \pm 17.0	81.95 \pm 15.95*	-1.6 [-2.60 to -0.62]
Waist circumference (cm)	106.72 \pm 12.18	105.49 \pm 11.58	-

Note: Data are expressed as mean \pm SD, frequency, and percentages.

Abbreviations: HbA1c = glycated hemoglobin; LDL = low density lipoprotein; HDL = high density lipoprotein.

*p=0.0025

Table 2. Post-lockdown changes in HbA1c and body weight in the study population.

-	Partially Adjusted † [Model 1]		Fully Adjusted ‡ [Model 2]	
	β	95% CI	β	95% CI
Change in HbA1c (mmol/mol)	-2.90	-4.69 to -1.12	-2.90	-4.69 to -1.12
Time*GLP-1RA	-1.63	-5.21 to 1.95	-1.63	-5.21 to 1.95
Change in body weight (kg)	-1.61	-2.60 to -0.62	-1.61	-2.60 to -0.62
Time*GLP-1RA	-0.36	-2.36 to 1.64	-0.36	-2.36 to 1.64

Note: †) **Partially adjusted models:** change over time of parameters of interest adjusted for treatment with GLP-1RA or other antidiabetic medications.

‡) **Fully adjusted models:** change over time of parameters of interest adjusted for parameters in Model 1 plus age and gender.

Abbreviations: HbA1c = glycated hemoglobin; GLP-1RA = glucagon-like peptide-1 receptor agonists.

4. DISCUSSION

Our findings displayed patients to have a baseline optimal glucose control and exhibit a slight but statistically significant improvement in HbA1c. A slight but statistically significant reduction in body weight was also observed. The improvements occurred irrespective of background characteristics (*i.e.*, age and sex) and treatments, including GLP-1 RA. GLP-1RA was expected to provide more relevant weight loss and to contrast a potential weight gain or deterioration of glucose control because of COVID-19-related constraints and lifestyle changes.

As we assumed that unhealthy habits due to the epidemic-related constraints, such as increased time spent in sedentary activities and possibly excessive dietary intake, had occurred, our brief report suggests that the lockdown did not affect glucometabolic control in T2D. An Italian study focusing on the role of telemedicine in replacing in-person visits during the COVID-19 lockdown found a similar reduction in BW [10]. Self-reported data on BW changes in 119 T2D British patients before and after the lockdown confirmed our results [11]. These data suggest that the lack of follow-up for a few months (5 in our study) did not affect the effectiveness of background treatment. However, other reports showed different results. More precisely, a high pre-existing BMI was associated with further weight gain and body composition worsening during the lockdown [12]. Italian patients with type 1 diabetes (T1D) exhibited a slight weight gain, which was ascribed to the lack of physical activity during the lockdown [13].

Despite that the home confinement could have increased caloric intake, worsened the quality of ingested meals (*i.e.*, high-glycemic-index carbohydrates), and enhanced sedentary behaviors in the general population, the COVID-19 lockdown probably made patients with T2D more prone to keep better control of meal quality, carbohydrate counting, and glucose monitoring [14]. These attitudes were perhaps driven by the fact that diabetes mellitus, especially in the case of poor glycemic control, severe and comorbid obesity, male hypogonadism, and re-organization of healthcare facilities were becoming some of the leading risk factors associated with worse progression of COVID-19 [15-19].

Regarding the HbA1c, our findings contrast with the results of a single-center Italian study [20] but align with a Greek study [21]. Biamonte *et al.* [12] came to conflicting conclusions depending on the type of diabetes since glycemic control worsened in T2D and improved in T1D individuals. This dimorphism may reflect that T1D individuals spend more "free time" carrying out structured glycemic control and carbohydrate management. As Sutkowska *et al.* [14] suggested, family support was another relevant factor that improved glycemic control and facilitated better weight management.

The role of chronic assumption of usual medications represented a relevant issue in that period. The lack of evidence of explicit protective action or serious or non-serious concerns about using certain medications (*e.g.*, GLP-1RA, DPP-IVi, and SGLT2i) posed a real matter in the management of T2D [15]. Nevertheless, considering the glycemic and extra-glycemic (contrasting weight gain and inducing weight loss) effects of incretin-based therapy and SGLT2i, these medications appeared to be effective and safe during the first wave of the pandemic.

CONCLUSION

We found that lockdown did not negatively affect glucometabolic control in T2D. Our results were independent of the effectiveness of specific antihyperglycemic medications, such as GLP-1RA, thus suggesting that adherence to background treatment in a short time (a few months) could have protected patients from possible detrimental consequences due to the temporary discontinuation of follow-up visits that occurred through the lockdown. Other coincident factors may also explain this phenomenon. However, the lack of direct control of changes in lifestyle habits (physical activity, time, quality of disease management at home, and eating behaviors) leads us not to provide a specific conclusion and generalize our findings.

LIST OF ABBREVIATIONS

BMI = Body Mass Index

BW = Body Weight

COVID-19 = Coronavirus Disease 2019

DPP-4i	=	Dipeptidyl Peptidase 4 inhibitors
GLP-1RA	=	Glucagon-Like Peptide 1 Receptor Agonists
HbA1c	=	Glycated hemoglobin
HDL	=	High Density Lipoprotein
LDL	=	Low Density Lipoprotein
SGLT2i	=	Sodium-Glucose Transporter 2 inhibitors
T1D	=	Type 1 Diabetes
T2D	=	Type 2 Diabetes
WC	=	Waist Circumference

AUTHORS' CONTRIBUTIONS

All authors contributed significantly to conceptualization, data collection, analyses, manuscript drafting, and critical reviewing. All the authors gave feedback and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ethics Committee of the University of Bari (Ethical approval number 6468, version 2, 14th September, 2020).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committee and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

All patients provided written informed consent to participate.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

CONFLICT OF INTEREST

Vincenzo Triggiani is the Associate Editor of the journal *Endocrine, Metabolic & Immune Disorders-Drug Targets*.

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