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Impact of COVID-19 lockdown on glucose control of elderly people with type 2 diabetes in Italy

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ABSTRACT

Aims: to evaluate the effect of home confinement related to COVID-19 lockdown on metabolic control in subjects with T2DM in Italy.

Methods: we evaluated the metabolic profile of 304 individuals with T2DM (65% males; age 69 ± 9 years; diabetes duration 16 ± 10 years) attending our Diabetes Unit early at the end of lockdown period (June 8 to July 7, 2020) and compared it with the latest one recorded before lockdown.

Results: There was no significant difference in fasting plasma glucose (8.6 ± 2.1 vs 8.8 ± 2.5 mmol/L; $P = 0.353$) and HbA1c (7.1 ± 0.9 vs $7.1 \pm 0.9\%$; $P = 0.600$) before and after lockdown. Worsening of glycaemic control (i.e., $\Delta\text{HbA1c} \geq 0.5\%$) occurred more frequently in older patients (32.2% in > 80 years vs 21.3% in 61–80 years vs 9.3% in < 60 years; $P = 0.05$) and in insulin users (28.8 vs 16.5%; $P = 0.012$). On multivariable analysis, age > 80 years (OR 4.62; 95%CI: 1.22–16.07) and insulin therapy (OR 1.96; 95%CI: 1.10–3.50) remained independently associated to worsening in glycaemic control.

Conclusions: Home confinement related to COVID-19 lockdown did not exert a negative effect on glycaemic control in patients with T2DM. However, age and insulin therapy can identify patients at greatest risk of deterioration of glycaemic control.

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1. Introduction

Since its first recognition in Wuhan, China, in December 2019, the COVID-19 pandemic caused by the novel Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV2) has rapidly spread across the globe. In the absence of effective treatments or vaccines, measures have been deployed to slow the spreading of the viral infection by implementing social distancing and lockdowns of large sections of the society. In

Italy, a nationwide lockdown was imposed from March 9th through May 3rd, 2020. For people with diabetes the lockdown can be expected to exert a negative impact on the management of the disease due to the anxiety and depression that can be generated by the concern about the risk of infection for them and their relatives as well as because of the uncertainties about medical and pharmacologic supply and the possibility to access regularly consultation with health care providers. In spite of this view, data in people with type 1 dia-

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betes (T1DM) have been reassuring showing no worsening of glycaemic control and in some case a modest improvement [1–3]. These subjects, however, are generally young, trained to manage their insulin therapy often on the basis of continuous/flash glucose monitoring. The population of those with type 2 diabetes (T2DM) is more heterogeneous and generally older. Interesting enough, while several reports are available for the former, little is still available for the latter, so that it is still unclear to which extent the lockdown could have impacted on diabetes management and metabolic control in individuals with T2DM [4]. To address this issue, we have evaluated changes in metabolic control before and after lockdown in a group of patients with T2DM regularly attending our outpatient diabetes clinic.

2. Materials and methods

2.1. Participants and procedures

Subjects with T2DM referring to the Diabetes Clinic of our University Hospital were included in this survey only if they had no modification of anti-hyperglycaemic therapy in the 6 months before lockdown, no presence of severe systemic illness, and no treatment with drugs known to induce hyperglycaemia. Furthermore, none of the patients had SARS-CoV2 infection nor were quarantined for close contact with infected people.

Anthropometric (body mass index, BMI and waist circumference, WC) and metabolic parameters (fasting plasma glucose, FPG; glycated haemoglobin, HbA1c; creatinine; estimated glomerular filtration rate, eGFR; total, LDL-, HDL-cholesterol and triglycerides) were then obtained from 304 patients with T2DM at the end of lockdown period, between June 8 to July 7, 2020. The same parameters obtained at the time of the last visit before lockdown were retrieved from electronic medical records for comparison. Biochemical determinations were performed in the central laboratory of our Hospital during the time of the study. HbA1c was measured by high-performance liquid chromatography using DCCT-aligned methods [5]. The study protocol was approved by the Ethics Committee of University of Pisa and all subjects provided voluntary consent to their data analysis.

2.2. Statistical methods

Continuous variables are expressed as mean with standard deviation (SD) and median with interquartile range (IQR); categorical variables are expressed as percentages. Normality was checked using the Shapiro–Wilk test. Paired Student's *t*-test was used to compare paired continuous variables with normal distribution, while the Wilcoxon Rank test was used for not-normally distributed paired variables. A uni- and multivariable logistic regression analysis was applied to evaluate the association of age, sex, BMI, diabetes duration, presence of micro- and macrovascular complications with glycaemic control potentially associated with a worsening of HbA1c defined as an increase $\geq 0.5\%$. Finally, a sensitivity analysis including only those subjects with the last visit within three months before lockdown was performed. Statistical signifi-

cance was accepted at two-tailed $P < 0.05$. Data were analysed using SPSS version 25 (IBM SPSS Statistics).

3. Results

Out of 1250 patients referred to the Diabetes Unit in the selected period, 946 were excluded due to change in therapy at the last visit before lockdown or because of missing HbA1c data. The main clinical characteristics of the remaining 304 patients with T2DM are shown in Table 1.

The mean time between the pre- and post-lockdown visit was 6.5 ± 1.6 months (median 6.2 months [IQR, 5.6–7.3]). On average, pre-lockdown visit was carried out 3.1 ± 1.5 months (median 2.9 months [IQR, 2.0–4.0]) before lockdown. Table 2 shows the anthropometric and biochemical data of the whole cohort before and after lockdown.

Overall, minor numerical changes were apparent for almost all parameters considered, though BMI, WC, and creatinine were significantly higher while eGFR, total, LDL- and HDL-cholesterol were lower after lockdown compared to baseline. No statistically different changes were found as far

Table 1 – Clinical characteristics of the entire cohort at baseline.

Variable	N°	
Age, years	304	69.1 \pm 9.2
Sex, male	304	198 (65.1)
Smoking habit	214	
Never		99 (32.6)
Current		31 (10.2)
Former		84 (27.6)
Unknown		90 (29.6)
Hypertension	304	229 (75.3)
Dyslipidemia	304	205 (67.4)
CKD	304	134 (44.1)
Microalbuminuria	304	81 (26.6)
Macroalbuminuria		10 (3.3)
DR	304	61 (20.1)
DN	304	64 (21.1)
CVD	304	52 (17.1)
Stroke	304	10 (3.3)
HF	304	5 (1.6)
PAD	304	37 (12.2)
AHAs	304	
Lifestyle management		4 (1.3)
Insulin		104 (34.2)
MDI		57 (18.7)
Basal		47 (15.5)
Metformin		261 (85.9)
Sulphonylurea		44 (14.5)
DPP4i		103 (33.9)
GLP1-RA		70 (23)
SGLT2i		47 (15.5)
Pioglitazone		20 (6.6)
Acarbose		8 (2.6)

Abbreviations: AHA, anti-hyperglycaemic agents; CKD, chronic kidney disease; CVD, established cardiovascular disease; DN, diabetic neuropathy; DR, diabetic retinopathy; GLP1-RAs, GLP1 receptor agonists; HF, heart failure; MDI, multiple daily injections insulin therapy; PAD, peripheral artery disease. Data are expressed as mean \pm SD or frequency (%).

Table 2 – Clinical, anthropometric, and biochemical features of T2DM patients before and after the COVID lockdown.

	N°	Before lockdown		After lockdown		P
		Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
BMI, kg/m ²	303	29.2 ± 5	28.8 (25.7–32.4)	29.3 ± 5.2	28.7 (25.5–32.7)	0.032 [§]
Weight, kg	303	81.5 ± 15.9	82 (71–91)	81.8 ± 16.3	82 (70–92)	0.023 [§]
WC, cm	244	104.4 ± 12.4	103 (97–113)	105 ± 13.9	104 (97–114)	0.001 [§]
HbA1c, %	304	7.1 ± 0.9	7 (6.4–7.6)	7.1 ± 0.9	7 (6.4–7.6)	0.600*
HbA1c, mmol/mol	304	53.7 ± 10.1	53 (47–60)	54.7 ± 10.4	52.5 (47–59.7)	0.931*
FPG, mmol/l	301	8.6 ± 2.1	8.3 (7.1–9.8)	8.8 ± 2.5	8.4 (7.3–9.7)	0.353*
Creatinine, mg/dl	301	1 ± 0.36	0.92 (0.77–1.14)	1.1 ± 0.6	0.96 (0.79–1.23)	0.005 [§]
eGFR, ml/min/1.73 m ²	301	79 ± 23.9	80 (61–95)	76 ± 25.8	75 (58–94)	0.001*
TC, mmol/l	297	4.2 ± 0.8	4.2 (3.6–4.6)	4.0 ± 0.8	3.9 (3.4–4.5)	0.021*
HDL, mmol/l	297	1.3 ± 0.3	1.2 (1.0–1.4)	1.2 ± 0.3	1.2 (1.0–1.4)	0.008 [§]
LDL, mmol/l	295	2.2 ± 0.7	2.1 (1.7–2.6)	2.1 ± 0.7	2.0 (1.5–2.5)	0.006 [§]
TG, mmol/l	244	1.5 ± 0.9	1.3 (1.0–1.8)	1.6 ± 0.9	1.3 (1.0–1.9)	0.379 [§]

Abbreviations: BMI, body mass index; WC, waist circumference; HbA1c, glycated haemoglobin; eGFR, estimated glomerular filtration rate; TC, total-cholesterol; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol, TG, triglycerides.

* Student's t-test.

§ Wilcoxon Rank test.

as FPG, HbA1c, and triglycerides are concerned. When considering only patients with last follow-up visit up to 3 months before lockdown (n = 193; age 68.5 ± 9.3 years; 68.4% male), these results were confirmed (Suppl. Table 1). Upon stratification by age, a worsening in HbA1c (defined as an increase ≥ 0.5% compared to baseline value) was more common in older patients (<60 years: 9.3%; 61–79 years: 21.3%; ≥80 years: 32.2%; P < 0.05) while there were no differences across BMI categories. Similarly, no significant differences were observed between males and females (23.6 vs 19.2%; P = 0.368). Finally, HbA1c worsening occurred more commonly among those on insulin therapy as compared to those not using insulin (28.8 vs 16.5%, p = 0.012). The effect of age and insulin therapy was fully apparent in a multivariable analysis showing that those > 80 years had 4-fold higher risk of worsening HbA1c (OR 4.62; 95% CI, 1.22–16.07) compared to those < 60 years, while the risk associated with insulin therapy was 2-fold higher (OR 1.96; 95% CI, 1.10–3.50), independently of other factors (Table 3). Similar associations were found in a sensitivity analysis including only individuals with last visit before lockdown within the prior 3 months (Suppl. Table 2).

4. Discussion

In the present study, we report data on the impact of the recent lockdown period related to the COVID-19 pandemic in Italy on metabolic control of individuals with T2DM, showing that minor, though statistically significant changes were detected for some parameters but not for HbA1c, despite a slight weight gain. The robustness of our data is also confirmed by the sensitivity analysis including only patients with a strict follow-up (last visit ≤ 3 months before lockdown), thus minimizing the time-dependency of the results here reported. Our results are at variance with those reported by Khare et al. in a study involving 143 patients with T2DM in whom glycaemic control, as determined on self-monitoring, worsened during the first 3 weeks of lockdown mainly because of higher post-prandial glucose levels [6]. The

authors interpreted those results as the effect of changes in diet and less physical activity occurred during the lockdown. On the contrary, Anjana et al. in a survey including 205 patients with T2DM found a significant improvement in HbA1c after lockdown (7.7 ± 1.7 vs 8.2 ± 1.9%, P < 0.001) [7]. More recently, in a series of 114 individuals with T2DM, Biancalana et al. reported no significant change in glucose control, although a 0.3% increase in HbA1c was found in 26% of them [4]. In summary, a certain degree of heterogeneity has been found as far as changes in glycaemic control are concerned in people with T2DM throughout the lockdown imposed to prevent the spreading of Sars-Cov-2 pandemic.

Several reasons may contribute to such heterogeneous results, including differences in ethnicity, baseline glycaemic control and access to diabetes consultation during lockdown. Baseline HbA1c value in the study by Anjana et al. was higher compared to that of our population (8.2 vs 7.1%). Furthermore, our patients may not reflect a more general diabetic population as all of them regularly attended a tertiary care Diabetes Unit that continued providing teleconsultation during the lockdown period.

Although overall no changes were detected in glycaemic control, a closer look revealed that glucose deterioration could occur in some subgroups. Thus, the percentage of the patients who had, over the lockdown, an increase of HbA1c ≥ 0.5% was greater among the elderly and those on insulin therapy. These two parameters, age > 80 years and insulin therapy, were independently associated with significant glycaemic worsening in a multivariable analysis and, as such, they could help identifying subjects for whom it may be necessary to ensure sufficient contact and surveillance during challenging time as it was the case in the lockdown and as it has been suggested in a recent survey by Bonora et al. [8]. These authors compared accesses to the diabetes centre before and during lockdown to suggest that are the elderly patients with T2DM, i.e. those with more severe burden of complications and often requiring more complex treatment, who are likely to encounter more difficulties in stay in touch with their diabetes clinics. For these people it

Table 3 – Logistic regression analysis for predictors of worsened HbA1c (Δ HbA1c \geq 0.5 mmol/mol) during lockdown.

	Univariate			Multivariate (Backward conditional)		
	OR	95% CI	P	OR	95% CI	P
Male sex	0.77	0.43–1.36	0.369			
Age class						
< 60	Ref	Ref		Ref	Ref	Ref
61–80	2.64	0.90–7.74	0.077	2.36	0.79–6.99	0.121
>80	4.64	1.30–16.6	0.018	4.62	1.22–16.07	0.024
BMI class						
Normal w	Ref	Ref				
Over w	0.72	0.34–1.54	0.396			
Obese	1.10	0.53–2.28	0.796			
Microvascular Complications						
No	Ref	Ref	Ref			
1	1.16	0.61–2.22	0.656			
2	1.93	0.90–4.12	0.089			
3	1.26	0.32–4.91	0.735			
Macrovascular Complications, Yes	1.36	0.70–2.26	0.363			
Insulin therapy, Yes	2.05	1.17–3.61	0.013	1.96	1.10–3.50	0.022
DD, 1 year	1.00	0.97–1.03	0.903			

Abbreviations: BMI, body mass index; DD, diabetes duration.
Values in bold are statistically significant.

may be more difficult to get acquainted to telematic visit and monitoring systems due to poorer familiarity with modern technologies. Insulin use also was an independent predictor associated with 2-fold higher odds of glycaemic worsening compared with use of other glucose lowering agents. This may well reflect the increased complexity of the management of this therapeutic approach, particularly for those with T2DM, since evidence currently available for patients with T1DM on continue glucose monitoring show that glycaemic control did not worsen or even improved during lockdown [1,9–12]. The latter, however, are younger, on continuous or flash glucose monitoring and more intensively instructed how to handle multiple dose insulin therapy or even continuous subcutaneous glucose infusion.

Although ours as well as other results so far available may suggest a limited impact of the lockdown on metabolic control of people with T2DM, the duration of the lockdown may have been too short to fully appreciate what could be the impact of a relaxation of diabetes management that may occur under such circumstance. In line with this caution is the modest yet statistically significant increase in body weight and waist circumference that may well reflect the initiation of a trajectory that may lead to more substantial weight gain and, ultimately, deterioration of glycaemic control. Recently published surveys showed that roughly 22% of people reported gaining weight during self-quarantine along with reduced physical activity and worse eating behaviours during the COVID-19 lockdown [13,14]. Unfortunately, due to the retrospective design of the study, data about the change in daily diet and physical activity during lockdown were not available. Nevertheless, since our patients displayed an overall stable glycaemic control, we may assume that the effect of lifestyle modifications during lockdown was negligible.

Some limitation of our study needs to be acknowledged. This includes the relatively small number of participants, although ours is the largest cohort of T2DM so far reported. Also, as already pointed out, we have recruited patients regularly attending a specialized diabetic clinic thus limiting the generalizability of our results to a broader diabetic population. Finally, the duration of the lockdown may not be sufficiently long to allow a more careful assessment of the potential impact of longer lockdown and its psychological and logistic implications.

In conclusion, the home confinement related to the COVID-19 lockdown, at least with the duration our patients have been exposed to, doesn't seem to have exerted a negative effect on glycaemic control of patients with T2DM, despite slight weight gain. Nonetheless, some clinical features, in particular advanced age and insulin therapy, seem to be identify subgroups of patients with greater risk of glucose control deterioration. These characteristics may help in addressing patients requiring more attention - if not special protection - by developing special programmes at the time of challenging societal situations.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.diabres.2021.108750>.

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