Impact of COVID-19 on glycaemic control in a Spanish cohort of patients with type 2 diabetes

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Abstract

The purpose of this study was to investigate the impact of COVID-19 lockdown on monitoring and glycaemic control of people with type 2 diabetes (T2DM) in a Spanish population.

This prospective cohort study focused on patients with T2DM from a Spanish cohort followed since 2017, with at least one HbA_{1c} determination since the start of the pandemic.

A total of 246 patients was included; 45.9% (113) had at least one HbA_{1c} measurement during the pandemic and, in this case, we used the most recent one. The HbA_{1c} mean value increased from 7.37% before the pandemic to 7.43% ($p=0.63$). Those patients with previous HbA_{1c} ≥8.5% were the ones whose glycaemic controlled worsened: uncontrolled patients increased from 10.5% to 28.6% ($p<0.05$), relative risk 1.65.

In conclusion, nine months after the pandemic start, less than a half of the T2DM patients in our Spanish cohort had at least one HbA_{1c} measurement. Glycaemic control was similar when comparing before versus after the pandemic start, although those patients who were previously poorly controlled had a 1.65 higher risk of worsening their glycaemic control compared to the rest. Copyright © 2022 John Wiley & Sons.

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Key words

type 2 diabetes mellitus; glycaemic control; COVID-19; infectious diseases; primary care

Introduction

Since the end of 2019, when the first case of severe acute respiratory syndrome (SARS-CoV-2) caused by the new coronavirus appeared in Wuhan (China), numerous situations have occurred which before were difficult to imagine. Following the rapid spread of the infection in numerous countries, on 11 March 2020 it was declared a pandemic disease and exceptional measures were taken by different governments and public health authorities to minimise its spread. Thus, in Spain, on 14 March 2020 a state of emergency was declared, accompanied by an almost complete blockade of the country.[1–3] During this confinement period, activities considered as essential were the only ones authorised, and the mobility of most of the people was limited to the acquisition of food and medicine. The Spanish government recommended people remain in their houses and, later, mask use and social distancing were also recommended. While hospitals were at saturation point and health professionals were treating hundreds of patients with COVID-19, the health centres focused on the follow-up of infected patients, doing most of the work by telemedicine, remotely, allowing face-to-face access only to patients with urgent pathology.

Today, millions of people have been affected by COVID-19 infection and it has cost thousands of lives. Most of the deceased are elderly or people with chronic diseases such as diabetes, hypertension, obesity, chronic kidney disease (CKD), cardiovascular disease and cancer.[4] Type 2 diabetes (T2DM) is responsible for a significant mortality increase related to COVID-19; optimal glycaemic control could strengthen the immune system and reduce the severity of the disease, since the persistent rise in glycaemia favours the predisposition to infectious processes and their poor prognosis.[5–9] Containment measures adopted to prevent the spread of the virus have undoubtedly affected the

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lifestyle of people with T2DM and their emotional state, which in turn can influence their glycaemic control. On the other hand, the lower accessibility to health centres – either due to lack of direct access or even due to fear of contagion – has led to an interruption in the follow-up of these patients and a delay in the performance of recommended control tests. Likewise, circumstances derived from isolation such as less physical activity and possible dietary changes without the family members' and caregiver's supervision have been able to influence the degree of glycaemic control of people with T2DM.[10]

While there are several studies on the effects of the pandemic in the control of type 1 diabetes mellitus (T1DM), there are only a few publications which show results in those with T2DM.[11–15] The aim of this work was to evaluate the impact of the COVID-19 pandemic, and the measures that have been taken to reduce its spread, both in monitoring and in glycaemic control of people with T2DM in a Spanish cohort.

Methods

A prospective, longitudinal, fixed cohort study was conducted based on a previous descriptive study, the objective of which was to assess the degree of glycaemic control in patients with T2DM in the jurisdiction of the health centre in Spain. The study comprises two clinics that serve an urban population of 18,481 people.[16] The study was approved by the Local Ethics Committee, and the ethical requirements expressed in the Declaration of Helsinki and its subsequent amendments were met. It also complied with the Spanish data protection law.

For this study, the data from T2DM patients registered in January 2017 were considered and were re-evaluated 48 months later (December 2020), coinciding with the end of the second wave of the COVID-19 pandemic in Spain. The total number of patients was 1229, and a randomised sampling was performed including 297 T2DM patients (95% CI: margin of error <5%).

Factor	Worsening of glycaemic control after the onset of the pandemic		P-value
	No n=57 (50.4%)	Yes n=56 (49.6%)	
Sociodemographic data			
Age in years, mean ± SD (min–max)	64.35±9.6 (38–82)	66.87±8.8 (42–89)	p=0.20
Sex, n (%) – Male – Female	 33 (57.9%) 24 (42.1%)	 28 (50%) 28 (50%)	p=0.40
Clinical conditions			
Years of diabetes duration ± SD	12.07±4.7	10.9±4.9	p=0.20
Uncontrolled hypertension, n (%)	11 (19.3%)	14 (25.0%)	p=0.26
Previous HbA_{1c}, n (%) – <8.5% (<69.4mmol/mol) – ≥8.5 % (≥69.4mmol/mol)	 51 (89.5%) 6 (10.5%)	 40 (71.4%) 16 (28.6%)	p<0.05
Lipid levels ± SD – Total cholesterol mg/dL – LDL cholesterol mg/dL – HDL cholesterol mg/dL	 162.1±47.1 91.1±44.2 47.8±10.8	 181.1±43.5 105.9±36.2 50.6±11.35	 p<0.05 p<0.05 p=0.22
Chronic kidney disease, n (%)	12 (21.1%)	20 (35.7%)	p=0.08
Smoking, n (%)	7 (12.3%)	11 (19.6%)	p=0.28
Obesity, n (%)	26 (45.6%)	24 (42.9%)	p=0.98

SD: standard deviation; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

Table 1. Variables of glycaemic deterioration after the onset of the pandemic in a cohort of 113 patients

Deceased patients (45) and administrative misplacements (six) which occurred during the follow-up period were excluded. From the 246 remaining patients, those who had at least one glycated haemoglobin (HbA_{1c}) measurement after the onset of the pandemic were selected (n=113).

The study variables collected from the computerised history were demographic data, HbA_{1c}, lipid profile, blood pressure (BP), body mass index (BMI), glomerular filtration rate (GFR), duration of diabetic illness, and iatrogenesis related to hypertension, lipids and T2DM. To calculate the GFR, we used the MDRD/CKD-EPI formula, considering CKD when the GFR was <60ml/min/1.73m^2. With regard to BP, we considered uncontrolled those patients with figures greater than 140mmHg systolic or 90mmHg diastolic. We defined as obese those with a BMI ≥30kg/m^2. The patients studied were divided into two groups based on whether their HbA_{1c} worsened or not after the onset of the pandemic; the different variables associated with this deterioration were analysed (Table 1).

For data collection, a standardised protocol was developed and volunteer physicians from the primary

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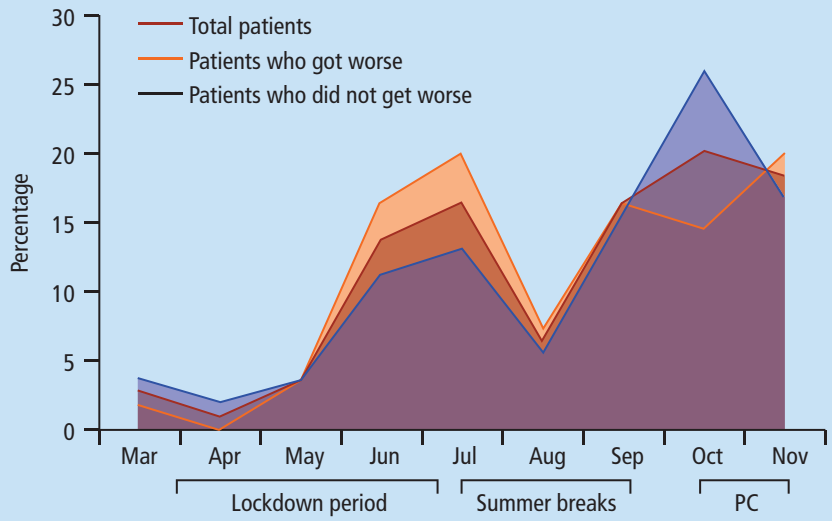
care area were trained. The data of the last observation were collected during the last week of December 2020. In addition to the variables examined in a previous study conducted by our research group, in those patients who had HbA1c records after the onset of the COVID-19 pandemic in Spain, the determination prior to that date was also considered.[16] Confinement measures in Spain lasted just over three months (15 March to 21 June 2020). Also in our region there was a period of perimeter mobility confinement that was decreed in October until December 2020 (Figure 1).

The quantitative variables were expressed with their mean, standard deviation (SD) and range (minimum-maximum), and qualitative variables were presented as the number of patients and the frequency distribution. To compare quantitative variables, the Student's t-test was performed. To verify the applicability of this test, normality was previously checked with the Lilliefors normality test, and Levene's test of equality of variances was also performed. In the comparison of independent qualitative variables, the Chi-square test (χ^2) was used when less than 20% of the expected frequencies were 5 or less, and Fisher's exact test was performed when more than 20% of the expected frequencies were 5 or lower. In contrast, to compare dependent qualitative variables (changes over time), the McNemar test was used. The complete analysis of the data was carried out using the statistical package R (R Foundation for Statistical Computing, Vienna, Austria), specifically Rcmdr 4.0.3. For all hypothesis tests, a risk (α) of 0.05 was set.[17]

Results

Only 45.9% of the 246 patients that made up the study's follow-up cohort had any HbA1c data recorded after the onset of the pandemic; therefore, the analysed sample was 113 patients. There was a decrease in the number of HbA1c analysis requests of between 76% and 94% during the months of confinement (Figure 1).



PC = perimeter confinement. The Y-axis relates to the numerical value (in percentages) of the study subjects registered. The X-axis represents the months in which the HbA1c control tests were performed. The total number of patients and the 2 study groups (patients whose glycaemic control got worse and those whose glycaemic control did not get worse) are analysed in the graph.

Figure 1. Percentage of HbA1c analysis requests studied after COVID-19 pandemic start

The average patient age was 65.6±9.2 years (range 38–89); 55.8% were aged ≥65 years, and just over half were men (54%). The mean time for the duration of T2DM was 11.5±4.8 years and 61.95% of the patients studied had T2DM of more than 10 years' duration. The clinical situation at the beginning of the study reflected that 69.6% had uncontrolled dyslipidaemia, 44.2% obesity, 28.3% CKD, 22.1% uncontrolled hypertension, and 16% were smokers.

Regarding glycaemic control, the mean HbA1c value prior to the pandemic (7.37±1.7% [57mmol/mol]) was similar (p=0.63) to that found after the blockade period (7.43±1.6% [57.7mmol/mol]).

Considering different variables associated to glycaemic deterioration (Table 1), the study patients were split into two groups based on whether their HbA1c worsened or not after social isolation due to the pandemic. Patients whose previous HbA1c level was ≥8.5% (≥69.4mmol/mol) worsened significantly after the onset of the pandemic (p<0.05) with a relative risk (RR) of 1.65 (95% CI 1.05–2.59). In those patients, elevations in total cholesterol (181mg/dL vs 161mg/dL; p<0.05) and in LDL cholesterol (106mg/dL vs 91mg/dL; p<0.05) were also found.

In the group of patients whose degree of control worsened, no differences between men and women were found, and the average age was two years older. On the other hand, the length of duration of T2DM was two years shorter, and there were more patients with uncontrolled hypertension, CKD, and/or were smokers and obese. They also consumed a greater number of diabetes medications than those whose glycaemic control did not get worse. We did not find significant differences in all of the above mentioned characteristics (p>0.05).

Discussion

Nine months after the pandemic start, only 45.9% of patients in our Spanish cohort had some analytical data regarding HbA1c/glycaemic control; this is insufficient considering that, as recommended by the American Diabetes Association, at least two annual measurements must

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be made.[18] According to recent research by Wright *et al.*, during the months of confinement the request for control tests in T2DM was reduced by 81–90% in a population of Tennessee (USA).[19] A similar situation has occurred in our population, with a decrease of between 76% and 94% in HbA1c tests (Figure 1). After the test reduction occurred during the exceptional confinement measures, we consider the recovery in the subsequent months from delayed tests has not been sufficient, since less than a half of our patients with T2DM had an HbA1c test after the start of the pandemic.

Our data show a minimal, non-significant increase in HbA1c levels of 0.06 points: from 7.37±1.7% before confinement to 7.43±1.6% after it (57 to 57.7mmol/mol); (p=0.63). This is consistent with the only two other studies with T2DM that we have found. One of them was in Turkey with a slightly lower sample (n=101), where HbA1c increased by 0.44 points in the period studied: from 7.67±1.76 to 8.11±2.48 (60.3 to 65.1mmol/mol); (p=0.253).[14] And another one was in China with 50 elderly patients, over 65 years old, where the increase in HbA1c was 0.2 points: from 7.2±1.7% to 7.4±1.8% (55.2 to 57.4mmol/mol); (p=0.158).[15] The minimal alteration in the degree of glycaemic control in our T2DM population could be explained in part by the fact that during confinement moderate-to-vigorous activity decreased by 66% in men and 52% in women and the quality of food worsened, according to a Spanish study at the beginning of the pandemic.[20]

In contrast, the subgroup of patients who previously had poorer glycaemic control (those with HbA1c ≥8.5%) suffered greater worsening; they had a 1.65 higher risk of worsening during this period compared to the rest (28.6% vs 10.5%; p<0.05). These data may suggest people with poorly controlled glycaemia are the most vulnerable to confinement measures and so closer follow-up should be prioritised for them. These patients are the ones who could suffer the worst consequences of poor control during the decreed social isolation. In the same way, we found patients whose glycaemic control worsened had higher levels of lipids, both total cholesterol and LDL, compared to those who did not. It is well known that lipid levels, especially LDL, correlate with a healthy lifestyle, so we could explain this lipid increase by poor adherence to diet and less physical activity.[21]

According to three studies, two from Spain and another one from Italy, patients with T1DM had different behaviour profiles. They showed a significant decrease in HbA1c levels during confinement.[13,22,23] Possibly, the stability of the household routine, the absence of the usual daily stress levels, the increased hours of sleep and more time for self-monitoring could have surpassed the negative aspects derived from pandemic directives in this patient profile. This suggests that people with T1DM and T2DM, who have different pathophysiology, also demonstrated different behaviour during lockdown measures.

The main limitation of our work is that the measurements have been made at two different time points, and it is difficult to establish a strict causality between the study results and the direct influence of the pandemic. Additionally, the nine-month follow-up interval and the small number of patients could have interfered with the results. Our study has been limited by the decrease in controls in our patients, which corresponds to a real life situation in the pandemic. To compare those results with previous values to the pandemic, the HbA1c immediately prior to the onset of the pandemic was chosen and this could be in a period of up to three years; this can be an important bias since in these three years the physical, personal, medical and professional situations of participants could have changed. As the analysis is exploratory, the study does not have the power to find out between-group differences; this can be seen in Table 1 in which the anthropometric characteristics are different in the group of patients whose glycaemic control worsened: older age, a high percentage of women and of comorbidities (obesity, CKD, uncontrolled hypertension, smoking and higher lipids values). Finally, the present study is limited to a specific health area, so the results may not be extrapolated to other populations. To reaffirm our results in future studies, it would be necessary to increase the number of patients and expand the studied health area.

In conclusion, it is worrying that less than a half of our T2DM Spanish cohort study population had at least one HbA1c measurement after nine months from the beginning of the pandemic, which could seriously affect their subsequent health. As in other countries, the COVID-19 pandemic has influenced the glycaemic control of the T2DM population. Among those whose glycaemic control worsened were those people whose glycaemia status had previously been already poorly controlled, so we consider this group has been the most vulnerable and could present more long-term consequences; consequently, we should prioritise them when it comes to resuming delayed glycaemic control measurements. It is essential to contact them proactively, as soon as possible, so it will be necessary to provide primary care with adequate resources to carry out this task.

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Declaration of interests

There are no conflicts of interest declared.

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KEY POINTS

- During the state of emergency due to the COVID-19 pandemic, the number of HbA_{1c} analysis requests from patients with type 2 diabetes in a Spanish cohort had been reduced
- The confinement measures did not generally affect the glycaemic control of the patients with type 2 diabetes in the Spanish cohort studied
- Patients who had poor glycaemic control before the start of the COVID-19 pandemic were the ones whose glycaemic control worsened the most during the pandemic
- Those patients whose glycaemic profile worsened during the COVID-19 pandemic had higher levels of total cholesterol and LDL cholesterol

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