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The Impact of Partial Lockdown During COVID-19 Pandemic on Metabolic Control in People with Type 2 Diabetes Mellitus

COVID-19 Dönemindeki Kısmi Kapanmaların Tip 2 Diyabet Hastalarının Metabolik Kontrolü Üzerine Etkisi

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Abstract

Aim In this study, it was aimed to investigate the effects of lockdown due to COVID-19 on the metabolic control in people with type 2 diabetes mellitus.

Material and Method This cross-sectional study (Ecological trend study) was conducted based on the medical records of patients with type 2 diabetes between September 20, 2019 and September 20, 2020. The metabolic control parameter changes were evaluated as differences of haemoglobin A1c (HbA1c), fasting plasma glucose (FPG), creatinine (Cr), fasting triglyceride (FTG) and low-density lipoprotein-cholesterol (LDL-C) values during pre-lockdown and lockdown periods. The stratified analysis based on age (due to partial closure measures applied over the age of 65) and gender was also performed.

Results There are statistically significant increases between FPG levels and FTG levels in the "during lockdown" group compared to the "pre-lockdown" group (p=0.036 and p=0.013 respectively) while the differences between HbA1c, LDL-C and creatinine levels are not significant. In subgroup analysis, increases in FPG and FTG levels remained in both <65 years and male groups, but no significant difference in any parameter was found in both ≥65 years and female groups.

Conclusion COVID-19 partial lockdown period negatively impacts metabolic control parameters in people with type 2 diabetes mellitus according to our study results. Although FPG significantly increased, this increase was not found in HbA1c levels. The worsening was more pronounced in the males and patients <65 years than in females and patients ≥ 65 years probably because they were more affected by partial lockdown measures conducted in Turkey

Keywords COVID-19, Diabetes Mellitus, Type 2, Metabolic Control, Partial Lockdown

Özet

Amaç *Bu araştırmada, COVID-19 dönemindeki kısmı kapanma uygulamalarının tip 2 diyabet mellitus hastalarının metabolik kontrolü üzerine etkisinin incelenmesi amaçlanmıştır.*

Gereç ve Yöntem *Kesitsel tipte (Ekolojik trend araştırması) yapılan bu araştırma 20 Eylül 2019 ve 20 Eylül 2020 tarihleri arasındaki tip 2 diyabetes mellitus hastalarının tıbbi kayıtlarına dayalı olarak yürütülmüştür. Metabolik kontrol parametrelerindeki değişim, kapanma öncesi ve sonrası dönemdeki Hemoglobin A1c (HbA1c), açlık plazma glikoz (FPG), Kreatinin (Cr), açlık trigliserit (FTG) ve düşük yoğunluklu kolesterol (LDL-C) değerlerinin arasındaki farklılık incelenerek tespit edilmiştir. Yaş (65 yaş üzerine uygulanan kısmı kapanma önlemleri nedeniyle) ve cinsiyete dayalı tabakalı analizler de yapılmıştır.*

Bulgular *Kapanma öncesine döneme kıyasla açlık plazma glikoz (FPG) ve trigliserit (FTG) seviyelerinde kapanma sonrası dönemde istatistiksel olarak önemli artış tespit edilirken (sırasıyla, p=0.036 ve p=0.013), HbA1c, LDL-C ve kreatinin seviyelerinde önemli farklılık bulunamamıştır. Alt grup analizlerinde, <65 yaş ve erkek grupta açlık plazma glikoz ve trigliserit seviyelerindeki artış devam ederken, ≥65 yaş ve kadın grupta hiçbir parametrede değişiklik tespit edilememiştir.*

Sonuç *Çalışmamızın sonuçlarına göre, COVID-19 dönemindeki kısmı kapanma dönemi tip 2 diyabetes mellitus hastalarının metabolik kontrol parametrelerini olumsuz etkilemiştir. Bununla birlikte, açlık plazma glukoz seviyelerindeki artışa rağmen HbA1c değerlerinde bir değişme tespit edilememiştir. Parametrelerdeki kötüleşme, muhtemelen Türkiye'deki kısmı kapanma önlemlerinden daha fazla etkilenmeleri nedeniyle erkek ve <65 yaş grubunda, kadın ve ≥65 yaş grubuna kıyasla, daha belirgin olarak ortaya çıkmıştır.*

Anahtar Kelimeler *COVID-19, diyabetes mellitus, tip 2 diyabetes mellitus, metabolik kontrol, kısmi kapanma*

INTRODUCTION

In late 2019, a new variation of Coronavirus was discovered which led to a global pandemic.[1] Extraordinary measures have been taken by governments to prevent the transmission of COVID-19 infection and forestall healthcare systems worldwide.[2,3] In line with this purpose, the Turkey's Ministry of the Interior established intermittent lockdown starting from 20 March for approximately 3 months to increase social distancing and restrict population movement. During this period, public places including schools, restaurants, sport centers and places of entertainment were closed. People under 18 years and over 65 with chronic diseases were prohibited from going out.[4] These necessary lockdown policies have created an unprecedented and unique opportunity to examine the impact of lifestyle changes on diabetes control in the real life.

During COVID-19 pandemic, changes in lifestyle behaviors such as alcohol consumption, snacking behavior, body weight control, physical activity have been reported by systematic reviews.[5-7] American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) guidelines indicate that healthy lifestyle is the keystone of Type 2 Diabetes Mellitus (T2DM) management.[8,9] Therefore, these changes may have introduced obstacles in management of diabetes challenging to keep glycemic levels under control.

A systematic review demonstrated that lockdown resulted in a significant increase in HbA1c, Fasting Plasma Glucose (FPG) and Body Mass Index (BMI) values in patients with T2DM.[10] Another systematic review that based on data predominantly from high-income countries reported that multiple outcomes of glycemic control in diabetic patients improved during the pandemic period, although results for other outcomes, including HbA1c, were not statistically significantly different.[11] Wafa et al. reported significant worsening in FPG among patients with T2DM. Lipid parameters, particularly triglyceride, were deteriorated.[12] Despite the lockdown measures, several studies have shown improved glycemic control in people with T1DM diabetes. These results can be interpreted as patiens having more time for self-management may facilitate glycemic control in a good way.[12,13] Rastogi et al. reported an improvement in glycemic control during lockdown period in individuals with T2DM.[14] A study conducted in Turkey, reported weight gain in both non-diabetic and diabetic patients during lockdown. In diabetic patients' glucose regulation worsened and FTG level increased as well.[15]

Due to the insufficient number of studies in Turkey this cross-sectional study is conducted to investigate the effects of lockdown due to COVID-19 on the metabolic control in people with T2DM.

MATERIALS and METHODS

Study design

We conducted a cross-sectional study (Ecological trend study) based on the medical records with T2DM patients (ICD code E.11) who have attended an university hospital (Istanbul – Turkey) between September 20, 2019 and September 20, 2020.

The study period was divided up according to the timing of the partial lockdown enforcement in Turkey (March 20, 2020). Data of the patients who have attended 6 months prior to enforcement (pre-lockdown group, n=321), were compared with the data of the patients who have attended during 6 months of the partial lockdown period (lockdown group, n=168).

A total of 489 patients with a history of T2DM, aged above 18 years, who have complete data in our patient record system were included in the study. Gender, age, biochemical parameters including serum haemoglobin A1c (HbA1c), fasting plasma glucose (FPG), creatinine (Cr), fasting triglyceride (FTG) and low-density lipoprotein-cholesterol (LDL-C) levels were collected from the medical records of the study group. The metabolic control changes were evaluated as differences of HbA1c, FPG, FTG, Cr and LDL-C

values during pre-lockdown and lockdown periods.

The study was approved by the Ethics Committee of Non-interventional Clinical Trials of Istanbul Medipol University (17/02/2022-145), and the data of patients' identity was not shared in the study in order to protect patient privacy.

Statistical analysis

Data analysis was performed using SPSS version 28.0 software. The changes in HbA1c, LDL-C, FTG, FPG, Cr measurements during the lockdown were considered as dependent variables while the age, gender, research periods were independent variables. Descriptive analyses were expressed as numbers (n), percentages (%), mean, standard deviation (SD), median, and interquartile range (IQR). Normality was examined using the Shapiro–Wilk test. Chi Square Test were used to analyze the similarity of the distribution of age and gender values of the patients during pre-lockdown and during lockdown periods. The biochemical values before and during the lockdown were compared using the Mann Whitney U Test. The p-value ≤ 0.05 was considered significant. Due to the stricter quarantine policies were applied to people aged ≥ 65 years in Turkey and continuation of men's active business life, a stratified analysis based on age and gender was performed using the Mann Whitney U Test to evaluate the differences in between pre-lockdown and during-lockdown values.

RESULTS

Demographic characteristics of the "pre-lockdown" (n=321) and the "during lockdown" (n=168) study groups are presented in Table 1. As it is seen from the table 64.5% of all patients enrolled in the study are males and 35.5% are females. The mean age of the patients is 54.3 ± 13.4 (range=21 to 89) years.

Table 1. Demographic characteristics of the study groups

	Pre-lockdown n (%)	During lockdown n (%)	Total n (%)	p
Age				
<45	82 (25.5)	40 (23.8)	122 (24.9)	0.808
45-54	80 (24.9)	46 (27.4)	126 (25.8)	
55-64	83 (25.9)	47 (28.0)	130 (26.6)	
>64	76 (23.7)	35 (20.8)	111 (22.7)	
Gender				
Female	150 (46.7)	74 (44.0)	224 (35.5)	0.572
Male	171 (53.3)	94 (56.0)	265 (64.5)	
Total	321 (100)	168 (100)	489(100)	

There is no statistically significant difference between the age and gender distribution of the "pre-lockdown" and "during lockdown" groups (p=0.808 and p=0.572 respectively) and that means groups are similar in age and gender. Comparison of the biochemical parameters between pre-lockdown and during-lockdown groups are shown in Table 2. As it is seen from the table there are statistically significant differences between FPG levels and FTG levels of the groups (p=0.036 and p=0.013 respectively) while the differences between HbA1c, LDL cholesterol and creatinine levels are not significant.

In subgroup analysis, FPG and FTG median values in patients <65 years were significantly different between the groups (p = 0.045, p = 0.041 respectively) whereas the median values of these parameters for patients ≥65 years were not statistically significant (Table 3).

Subgroup analysis based on gender showed also significant difference in FPG and FTG levels for male patients (respectively, p = 0.046, p = 0.019). Whilst changes in biochemical parameters didn't reach statistical significance for females (Table 4).

Table 2. Biochemical values in pre-lockdown and during-lockdown groups

Biochemical variables	Tota		Pre-lockdown		During lockdown		p
	n	Median (IQR)	n	Median (IQR)	n	Median (IQR)	
Hemoglobin A1c (%)	489	6.7 (5.8-8.1)	321	6.7 (5.8-8.1)	168	6.5 (5.7-8.2)	0.593
Fasting Glucose Level (mg/dL)	407	123.7 (103.6-168.7)	262	121.2 (100.8-161.0)	145	131.0 (108.6-175.6)	**0.036**
LDL Cholesterol (mg/dL)	367	111.0 (88.0-131.0)	239	109.0 (88.0-130.0)	128	112.0 (89.0-134.8)	0.699
Fasting Triglyceride Level (mg/dL)	346	157.0 (113.3-224.6)	223	148.5 (103.2-209.8)	123	170.6 (122.5-245.8)	**0.013**
Creatinine (mg/dL)	381	0.8 (0.7-1.0)	250	0.8 (0.7-1.0)	131	0.8 (0.7-0.9)	0.198

Table 3. Changes in biochemical parameters between study groups stratified by age (n=489)

Biochemical variables	Age	Total		Pre-lockdown (visit 0)		During lockdown (visit 1)		p
		n	Median (IQR)	n	Median (IQR)	n	Median (IQR)	
Hemoglobin A1c (%).	<65	378	6.5 (5.6-8.1)	245	6.4 (5.7-8.1)	133	6.5 (5.6-8.2)	0.897
	≥ 65	111	7.2 (6.3-8.3)	76	7.3 (6.4-8.3)	35	7.2 (5.9-8.3)	0.232
Fasting Glucose Level (mg/dL)	<65	324	122.4 (101.1-172.7)	206	118.0 (98.7-164.2)	118	128.8 (107.8-177.2)	**0.045**
	≥ 65	83	131.6 (111.9-158.7)	56	129.4(111.2-157.4)	27	141.7 (112.2-168.5)	0.534
LDL Cholesterol (mg/dL)	<65	296	111.0 (91.3-131.0)	188	111.0(90.3-131.0)	108	112.0 (92.0-134.8)	0.920
	≥ 65	71	96.0 (74.0-133.0)	51	95.0 (74.0-120.0)	20	107.0 (73.0-134.8)	0.659
Fasting Triglyc-eride Level (mg/dL)	<65	284	163.8 (115.7-233.1)	179	155.1(102.7-227.0)	105	171.0 (129.0-258.2)	0.041
	≥ 65	62	136.3 (108.0-175.0)	44	132.1(109.4-164.5)	18	149.7 (101.3-208.2)	0.325
Creatinine	<65	300	0.8 (0.7-1.0)	194	0.8 (0.7-1.0)	106	0.8 (0.7-0.9)	0.625
	≥ 65	81	0.9 (0.7-1.2)	56	0.9 (0.7-1.2)	25	0.8 (0.6-1.0)	0.105

Table 4. Changes in biochemical parameters between study groups stratified by gender (n=489)

Biochemical variables	Gender	Total		Pre-lockdown (visit 0)		During lockdown (visit 1)		p
		n	Median (IQR)	n	Median (IQR)	n	Median (IQR)	
Hemoglobin A1c (%).	Female	224	6.2 (5.5-7.5)	150	6.3 (5.7-7.5)	74	6.2 (5.4-7.4)	0.139
	Male	265	7.1 (6.1-8.5)	171	7.1 (6.1-8.6)	94	7.0 (6.2-8.5)	0.883
Fasting Glucose Level (mg/dL)	Female	184	114.4 (97.4-148.6)	122	114.9 (96.7-146.7)	62	112.9 (99.6-150.2)	0.522
	Male	223	134.3 (109.9-182.6)	140	129.1(105.2-184.5)	83	141.4 (119.1-181.0)	**0.046**
LDL Cholesterol (mg/dL)	Female	162	109.5 (90.8-135.0)	109	107.0 (90.5-131.0)	53	114.0 (92.6-136.5)	0.475
	Male	205	110.0 (83.0-130.0)	130	110.0 (82.0-130.0)	75	108.0 (88.0-133.0)	0.909
Fasting Triglyceride Level (mg/dL)	Female	151	146.1 (96.3-194.3)	100	142.7 (96.4-183.3)	51	147.6 (89.7-211.2)	0.472
	Male	195	165.6 (121.4-245.8)	123	153.3(115.2-237.4)	72	191.1(140.9-260.4)	**0.019**
Creatinine (mg/dL)	Female	175	0.7 (0.6-0.8)	115	0.7 (0.6-0.8)	60	0.7 (0.6-0.8)	0.375
	Male	206	0.9 (0.8-1.1)	135	0.9 (0.8-1.1)	71	0.9 (0.8-1.0)	0.314

DISCUSSION

In this cross-sectional study we compared the biochemical values of a group of patients with T2DM who visited a hospital before lockdown with a group during lockdown. There were statistically significant differences of FPG and FTG levels between groups and both the FPG and FTG median values were higher in "during lockdown" group than "pre-lockdown group". No statistically significant differences were found between groups for the values of HbA1c, LDL-C and Creatinine levels.

The significant increase in FPG levels observed in our study appears to be consistent with previous meta-analysis studies which have found a significant worsening of FPG levels.[10,12] There could be several reasons for this worsening. During the pandemic lockdown period, lifestyle changes, such as diet and physical activity, may play major role among these reasons. While we could not investigate how patients' dietary habits and physical activity change, other studies have showed restriction in exercise duration and alternation of diet during the lockdown. For instance, adverse changes in dietary patterns were observed in studies in T2DM patients such as extended fried and unhealthy snacks consumption. Also, increased stress level and the fear of becoming ill during the pandemic may have provoked the eating attacks and food cravings of the patients. Generally, occasional consumption of sugary snacks may have caused temporary increases in FPG.[5,16,17] In addition, significant decreases were observed in physical activities in both individuals with and without chronic diseases, and this decrease particularly affected the people living in countries implemented lockdown policies such as Turkey.[7] It is also known that, COVID-19 pandemic related psychosocial factors, such as emotional and socio-economic instability, may have direct negative effects on glycemic control along with the negative impact on diet and physical activity.[8,12] Tanji et al. reported that glycemic control deteriorated in T2DM patients during the pandemic even in a country without a national lockdown which might correlate with increased stress level in regards of glycemic control.[18]

Although FPG values have differed significantly during lockdown, there was no significant change in HbA1c levels in our study similar to the findings of Wafa el al's meta-analysis study. The lack of significant change in HbA1c levels, despite the deterioration in FPG levels can be explained by the possibility of patients' continuity with appropriate medication methods.[12] Hence, although the possibility of an interruption in access to medications and insulin is generally mentioned, in some studies conducted from different countries including Turkey the majority of patients stated that there was no difficulty in accessing medications.[19,20] Also, as patients can spare more time for self-care and pay attention to disease control during the lockdown, this increase may not have been reflected in the HbA1c levels, which indicates long-term sugar control. Furthermore, diabetes patients were placed in high-risk group for COVID-19 infection and were warned by healthcare professionals about higher rates of mortality.[11]

However, the results of the systematic reviews by O'Mahoney et al and Eberle et al found an improvement in glycemic control in the type 1 diabetes patient, although there was short time worsening or no difference in the biochemical values of type 2 diabetes patients.[11,21] A study conducted on patients with T1DM reported an unforeseen improvement in glycemic control which may be related to an easier diabetes control perception and positive lifestyle changes.[22] A study that also determined the improvement in glycemic control parameters in T2DM patients during the pandemic lockdown period also stated that the observed increase in physical activity and possible positive lifestyle changes may cause this improvement.[14]

In our study, an increase in FTG level was found and no change in LDL level was found. Similarly, an increase in FTG was found in studies conducted in Turkey, and no change in LDL levels. This worsening may be similarly caused by changes in diet and physical activity.[15,20] When the

lipid control findings in systematic reviews are examined, the results differ from each other, both worsening and improvement in lipid parameters are reported. It is also reported that these findings are obtained from a small number of studies and this difference may be due to limited data availability.[10,12]

Subgroup analysis of our data indicated that pre-lockdown FPG and FTG levels of the patients <65 years were significantly different than the during lockdown group and no significant differences were found for the ≥65 years. Values of males also had significant differences. This finding may be concluded as result of lifestyle change since the majority of the active working group in Turkey are males between the ages of 18-65, and they may have been more affected by the lockdown due to restriction of outdoor.[23] According to a study while there was no significant change in daily eating habits of the patients aged 64 years and over, it was found that sugary foods and snacks intake have increased significantly.[16] These results may be another explanation of the change in biochemical parameters in the patients aged <65 years and males in our study. Besides, most of the women in Turkey are housewives and they spend more time at home and that may be the reason why, in our study there was no sinificant change in their biochemical levels.

In our study, more patients have admitted to our hospital during pre-lockdown period than during lockdown (n=321 and n=168 respectively). A rapid review to analyze the outpatient care utilization during the pandemic reported a major (55,5%) median decline similar to our study result.[24] This significant drop in attendance may have been due to the restrictions applied during the COVID-19. Already, some reviews have revealed the disruptions in the diagnosis, treatment and follow-up processes of chronic diseases during the pandemic period and the measures taken to eliminate them like telemedicine interventions.[25,26] Kshanti et al. also revealed that people with diabetes faced difficulties in regard of disease management for instance attending diabetes consultation, access to diabetes medication, monitoring blood glucose levels, controlling diet, and performing routine exercise.[27] As diabetes need to be followed up closely and continuously, the patients who could not access the healthcare due to COVID-19 precautions may have been affected more negatively.[25,28]

Our study has some limitations. First, this is a small-sized study conducted with data from unpaired patients admitted during study period in a private university hospital clinic therefore the findings cannot be generalized. Moreover, several important clinical parameters (e.g., duration of diabetes, medications, comorbidities, and body mass index) affecting HbA1c levels were not evaluated in the present study because of incomplete patient records. A detailed assessment of other relevant factors that might have influenced metabolic control, such as COVID-19 status, diet habits, physical activity, psychological concerns during lockdown, were also not investigated.

Regardless of these limitations, the study has produced meaningful findings. We conclude that lockdown because of COVID-19 negatively impacts metabolic control in people with T2DM. The worsening was more pronounced in the males and patients <65 years than in females and patients ≥ 65 years. A way to investigate the reasons for this result may be conducting a more detailed study focusing on risk factors for different gender and age groups. Present findings indicate that management strategies during lockdown periods should focus more on the younger population and males. One strategy of metabolic control during lockdown will be supporting diabetic patients to preserve a healthy lifestyle.

CONCLUSION

COVID-19 lockdown period negatively impacts metabolic control in people with T2DM according to our study results. Although FPG significantly increased, this increase was not found in HbA1c levels. The worsening was more pronounced in the males and patients <65 years than in females and patients ≥ 65 years possibly because of major

changes in lifestyle. A way to investigate the reasons for this result may be conducting a more detailed study focusing on risk factors for different gender and age groups. These results could be guiding in identifying patients that need closer attention to maintain metabolic control in another possible lockdown or pandemic. One strategy of metabolic control during lockdown should be supporting diabetic patients to preserve a healthy lifestyle. In addition, ensuring the continuity of primary health services in extraordinary situations such as pandemics is important in terms of chronic disease management.

Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

The study was approved by the Ethics Committee of Non-interventional Clinical Trials of Istanbul Medipol University (17/02/2022-145).

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