



# Long-term persistent symptoms of COVID-19 infection in patients with diabetes mellitus

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## Abstract

**Objective** The study aimed to assess the long-term persistent symptoms of patients with diabetes mellitus (DM) and COVID-19 infection at 9 months after acute infection.

**Methods** This single-center cross-sectional study was conducted from May 20 to June 1, 2021.

**Results** A total of 112 patients were included in the present study. The most frequently reported persistent symptoms among DM group were fatigue ( $p=0.01$ ), shortness of breath ( $p=0.01$ ), and chest pain ( $p=0.02$ ) compared to non-DM group. Sulfonylurea use was associated with persistent cough ( $p=0.04$ ).

**Conclusion** Long-term persistent symptoms of COVID-19 infection are common among patients with DM.

**Keywords** DM · COVID-19 · Long term · Symptoms

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## Introduction

Severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) primarily involves the respiratory tract leading to flu-like symptoms and coronavirus disease-2019 (COVID-19). COVID-19 is recently recognized as a multi-organ disease often causing extra-pulmonary manifestations after the acute phase, even among those who experience mild infection [1–3].

Diabetes mellitus (DM) is major comorbidity of COVID-19 infection, and patients with DM have a high prevalence of disease severity and adverse outcome during COVID-19 infection [2]. Thus, patients with COVID-19 and DM may be particularly at risk for long-term persistent symptoms or health consequences beyond the acute phase [2].

In the literature, little is known about the long-term symptoms of COVID-19 infection in patients with DM after 9 months of the acute phase. We aimed to assess the long-term persistent symptoms of patients with DM and laboratory-confirmed SARS-CoV-2 infection at 9 months after acute infection.

## Methods

This is single-center cross-sectional study of patients with laboratory-confirmed SARS-CoV-2 infection who presented to the outpatient clinic of Al-Sader Teaching

Hospital after 9 months of acute infection from May 20 to June 1, 2021.

Patients were interviewed by a trained physician in the outpatient clinic and asked to report symptoms from a pre-defined list of symptoms, including shortness of breath interfere with routine daily activities; easy fatigue; cough; chest pain; palpitation; joint pain; and neurocognitive dysfunction which includes dizziness, headache, concentration abnormalities, memory disturbances, smell loss, and taste loss. If there was a symptom that was not mentioned in the symptom questionnaire list, patients were asked to describe it. The baseline clinical comorbidities and demographic data included age, sex, hypertension, glucose-lowering drugs or insulin, smoking, body mass index (BMI), and hospital admission and duration. DM was defined as any established diagnosis prior to acute COVID-19 infection.

### Statistical analysis

Statistical analysis was performed using SPSS ver. 23.0 (SPSS Inc., Chicago, IL, USA). Demographic, comorbidities, and long-term symptoms were expressed as mean  $\pm$  standard deviation for continuous variables or as numbers with percentages for categorical data. Continuous variables were compared using the Student *t*-test. The Chi-square test was used for comparisons of categorical data. *p* Value of  $<0.05$  was chosen for statistical significance.

### Results

A total of 112 patients with laboratory-confirmed SARS-CoV-2 at 9 months after the acute phase of COVID-19 infection were included in the present study. The patients were divided into the DM group [42 patients with age (years)  $60 \pm 10$ , 26 (62%) were males] and the non-DM group [70 patients with age (years)  $45 \pm 12$ , 48(68%) were males). The prevalence of old age, hypertension, and increased BMI was higher among the DM group than the non-DM group. Patients, characteristics are shown in Table 1.

The most frequently reported persistent symptoms among DM group compared to non-DM group were fatigue (76% vs. 53%,  $p=0.01$ ), shortness of breath (45% vs. 21%,  $p=0.01$ ), chest pain (31% vs. 13%,  $p=0.02$ ), cough (26% vs. 13%,  $p=0.07$ ), palpitation (21% vs. 13%,  $p=0.23$ ), dizziness (24% vs. 10%,  $p=0.73$ ), concentration disturbances (19% vs. 13%,  $p=0.37$ ), and memory disturbances (17% vs. 13%,  $p=0.57$ ) (Table 1).

**Table 1** Patients' characteristics

Variables	DM <i>n</i> =42	Non-DM <i>n</i> =70	<i>p</i> Value
Age (years), mean $\pm$ SD	60 $\pm$ 10	45 $\pm$ 12	<0.01
Male, <i>n</i> (%)	26 (62)	48 (68)	0.55
BMI, mean $\pm$ SD	32 $\pm$ 6	28 $\pm$ 4	<0.01
Smoking, <i>n</i> (%)	6 (14)	10 (14)	0.12
Hypertension, <i>n</i> (%)	29 (69)	18 (26)	<0.01
Hospital stay (days), mean $\pm$ SD	7 $\pm$ 1	5 $\pm$ 1	0.31
Hospital admission, <i>n</i> (%)	24 (57)	28 (40)	0.07
Persistent symptoms			
At least one symptom, <i>n</i> (%)	37 (88)	55 (79)	0.05
Fatigue, <i>n</i> (%)	32 (76)	37 (53)	0.01
Shortness of breath, <i>n</i> (%)	19 (45)	15 (21)	0.01
Chest pain, <i>n</i> (%)	13 (31)	9 (13)	0.02
Cough, <i>n</i> (%)	11 (26)	9 (13)	0.07
Joint pain, <i>n</i> (%)	10 (24)	21 (30)	0.45
Palpitation, <i>n</i> (%)	9 (21)	9 (13)	0.23
Neurocognitive dysfunction symptoms			
Dizziness, <i>n</i> (%)	10 (24)	7 (10)	0.73
Concentration abnormalities, <i>n</i> (%)	8 (19)	9 (13)	0.37
Memory disturbances, <i>n</i> (%)	7 (17)	9 (13)	0.57
Headache, <i>n</i> (%)	6 (14)	14 (20)	0.44
Smell loss, <i>n</i> (%)	2 (5)	7 (10)	0.48
Taste loss, <i>n</i> (%)	1 (2)	5 (7)	0.15

Regarding the relationship of diabetes lowering drugs and long-term post-COVID-19 infection symptoms, sulfonylurea use was associated with cough ( $p=0.04$ ) and fatigue ( $p=0.05$ ). Although not statistically significant, insulin use was associated with neurocognitive dysfunction, shortness of breath, and fatigue. On the other hand, metformin use was associated with decreased prevalence of shortness of breath, fatigue, and neurocognitive dysfunction compared to patients who did not use metformin, although the difference was not statistically significant (Table 2).

### Discussion

We found that at 9 months after the acute COVID-19 infection, 88% of patients with DM reported at least one long-term persistent symptom, especially fatigue, neurocognitive dysfunction, and shortness of breath.

Long-term persistent musculoskeletal, respiratory, and neurocognitive symptoms have been reported for other coronaviruses (SARS and MERS) in long-term follow-up studies. Persistent viremia, relapse or reinfection, immune dysfunction, deconditioning, and post-traumatic stress have

**Table 2** Diabetes lowering drugs and post-COVID-19 persistent symptoms

Symptoms	Metformin		Sulfonylurea		Insulin		p
	With n = 29	Without n = 13	With n = 14	Without n = 28	With n = 10	Without n = 32	
Shortness of breath, n (%)	11 (38)	7 (54)	7 (50)	11 (39)	6 (60)	12 (38)	0.23
Fatigue, n(%)	20 (69)	11 (85)	13 (93)	18 (64)	9 (90)	22 (69)	0.22
Cough, n (%)	8 (28)	2 (15)	6 (43)	4 (14)	1 (10)	9 (28)	0.22
Neurocognitive dysfunction*, n (%)	11 (38)	8 (62)	8 (57)	11 (39)	7 (70)	12 (38)	0.07
Chest pain, n (%)	10 (34)	3 (23)	6 (43)	7 (25)	3 (30)	10 (31)	0.89

\*Neurocognitive dysfunction which include dizziness, headache, concentration abnormalities, memory disturbances, smell, and taste loss

been suggested as potential mechanisms for long-term health consequences following acute viral infection [2, 4].

Based on recently available data, the coexistence of comorbid conditions, including older age and obesity, among patients with DM and COVID-19 infection, would predispose patients to adverse clinical outcomes and persistent symptoms [2, 3]. It has been suggested that COVID-19 infection may exhibit shared pathologies with DM and other comorbidities via immune dysfunction, chronic low-grade inflammation, high prevalence of preexisting comorbidities, and endothelial dysfunction [2].

According to available data, results related to DM lowering drugs and COVID-19 severity and prognosis have been inconsistent among clinical studies. Ethnic disparity, access to medical care, study design, number of enrolled patients, and frequency of adverse events in some studies populations may have influenced the inconsistent results of the literature [5].

The present study has several limitations. It is single-center study with a relatively small size population. This limitation did not allow us to eliminate the potential impacts of other confounders such as hypertension, older age, and obesity. Data regarding DM severity or duration before COVID-19 were not reported. Although symptoms were collected by a well-trained physician, we did not assess the severity of symptoms or perform quality of life or cognitive function assessments. There could be a possibility of selection bias as patients who attended the outpatient clinic were more likely to be more symptomatic.

Further studies are required to assess the pathogenesis and prognosis of long-term persistent symptoms following COVID-19 infection in patients with DM.

In conclusion, long-term persistent symptoms of COVID-19 infection are common among patients with DM. Fatigue, neurocognitive dysfunction, shortness of breath, and chest pain are the most common symptoms among patients with DM.

**Declarations**

**Conflict of interest** The authors declare no competing interests.

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