



# Impacts of diabetes mellitus on clinical and para-clinical parameters among COVID-19 patients

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## Abstract

**Purpose** Diabetes has several adverse effects on patients with coronavirus disease 2019 (COVID-19); however, the determinants of this effect are still poorly understood. It is tried in current study to evaluate impacts of type 2 diabetes, with and without other comorbidities, on the clinical, para-clinical, and outcome parameters among COVID-19 patients.

**Methods** A case series was applied, which involved 406 COVID-19 patients admitted in the city of Shiraz, south-central Iran, from February 20 to April 29, 2020. Demographic data, medical history, laboratory finding, chest computed tomography (CT) scan reports, and clinical outcomes of patients with and without type 2 diabetes were compared.

**Results** Results of the above-mentioned comparison showed that comorbidities such as HTN (35.5% vs. 13.7%,  $p < 0.001$ ) and CVDs (26.2% vs. 13.4%,  $P = 0.002$ ) were significantly more prevalent among the diabetic patients. Also, there was not any considerable difference between the chest CT severity parameters of both groups. After excluding all of the comorbidities except diabetes, it was found that the diabetic COVID-19 patients without other comorbidities had lower oxygen saturation level ( $P < 0.001$ ), higher AST level ( $P = 0.037$ ), higher BUN ( $P = 0.005$ ), higher WBC counts ( $P = 0.025$ ), lower lymphocyte counts ( $P = 0.029$ ), and longer ICU admission duration ( $0.72 \pm 2.83$  vs.  $1.71 \pm 4.68$ ,  $P = 0.046$ ).

**Conclusion** The diabetic COVID patients are at higher risks of hypoxemia, longer ICU stays, and more renal and hepatic dysfunction. These achievements could be useful in order to prevent the deterioration of clinical conditions among diabetic COVID-19 patients; also, they have to be considered in the management strategies.

**Keywords** COVID-19 · Comorbidity · Diabetes Mellitus · Hypoxemia

## Introduction

A novel coronavirus (nCoV) was identified in late 2019 as the cause of a cluster of pneumonia cases in Wuhan, a city in Hubei Province of China. Then, it rapidly spread and led to an epidemic throughout China followed by an increasing number of cases in other countries across the world. In February 2020, the World Health Organization (WHO) designated coronavirus disease 2019 (COVID-19), which was

caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1].

In February 19, the first official report of the cases with COVID-19 in the city of Qom, Iran, was correspondingly released. COVID-19 outbreak has infected at least 32 million people in the world since September 25, 2020 [2]. According to the WHO statistics, more than 435,000 cases and 25,000 deaths have been reported in Iran so far. Based on a report represented by Shiraz University of Medical Sciences, Shiraz, Iran, COVID-19 cases in Fars Province have surpassed 50,000 people since September 20, 2020; moreover, the mortality rate has crossed 940 patients [2, 3].

According to the findings, the symptomatic infections range from mild to critical and most of the infections are not severe [4–6]. Pneumonia seems to be the most frequent serious symptom, which is primarily characterized by fever, cough, dyspnea, and bilateral infiltrates on the chest imaging tests [7–9].

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Also, the upper respiratory tract infection symptoms, myalgia, diarrhea, and loss of smell or taste are prevalent [10, 11].

The acute respiratory distress syndrome (ARDS), which could be manifested shortly after the dyspnea, is considered as the main complication in patients with the severe type of the disease. Furthermore, other side effects are arrhythmias, acute cardiac injury, thromboembolic complications, and shock [7, 9, 12–14].

There are various mortality rates, comorbidities, and other difficult conditions associated with the severe cases of the disease. The severe condition can occur in healthy individuals of any age; however, it is predominantly observed in older adults or those with underlying medical comorbidities such as cardiovascular diseases (CVDs), diabetes mellitus (DM), hypertension (HTN), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), various types of cancer, obesity, and smoking [10, 15–20].

DM and poor glycemic control are considered as the major risk factors for infections, especially influenza and pneumonia [21]. In addition, studies on patients with DM showed that viral respiratory infections may cause a more severe type of the disease compared with non-diabetic cases [22]. Indeed, DM has been widely investigated in previous epidemics and pandemics such as influenza A virus subtype H1N1 (A/H1N1), SARS, and Middle East respiratory syndrome-related coronavirus (MER-SCoV). It has been further identified as an important risk factor for mortality and morbidity [23–25]. There are data regarding the association between DM and COVID-19, which indicated that DM has to be considered as a major risk factor for rapid progression and poor prognosis of COVID-19 [22, 26]. Also, they demonstrate a significant association between DM status and higher mortality rate in diabetic patients with COVID-19 [17]. The importance of investigating the relationship between diabetes and glycemic control in COVID-19 patients could be reflected through reports on better clinical outcomes among COVID-19 patients with type 2 diabetes who showed better blood glucose control [27]. Therefore, evaluating the role of diabetes in COVID-19 patients, the possible pathophysiological mechanisms, and its management are still being carried out; however, there are not any appropriate conclusions based on current evidence [28, 29].

Current study was carried out on a population of COVID-19 patients in order to assess impacts of type 2 diabetes, with and without other comorbidities, on the clinical, para-clinical, and outcome parameters among COVID-19 patients.

## Materials and methods

### Design and settings

In current cross sectional study, it was tried to evaluate 406 adult COVID-19 patients who were more than 18 years of age and admitted to two hospitals for COVID-19, which

were affiliated to Shiraz University of Medical Sciences, from February 20 to April 29, 2020. The exclusion criteria were denial or withdrawal of informed consent, pregnancy, and being under 18 years of age. Furthermore, COVID-19 management protocols among adult hospitalized patients were on the basis of the interim guidance, which was issued by Centers for Disease Control and Prevention and World Health Organization guidelines [1, 30].

### Data collection

COVID-19 was diagnosed in the above-mentioned patients through the positive reverse-transcription polymerase chain reaction (RT-PCR) of the upper respiratory tract, or by an expert team that noticed the clinical symptoms and high-resolution computed tomography (HRCT) scan reports. These individuals were selected using the convenience sampling method. Specific questionnaires were distributed between all of the investigated COVID-19 patients, which contained the demographic data, exposure history, and the disease symptoms at the presentation time. In addition, the presence of comorbidities that were defined as the positive medical history of type 2 diabetes, hypertension, cardiovascular diseases, chronic kidney disease, hypothyroidism, malignancy, and respiratory failure was included in the questionnaire. The complete medication history was also self-reported.

All of the COVID-19 patients were classified into four distinct groups. First, they were divided into two groups of diabetic and non-diabetic COVID-19 patients and then, patients with comorbidities other than diabetes were excluded. The remaining patients were divided into two groups of diabetic and non-diabetic COVID-19 patients without other comorbidities. It is noteworthy that diabetes diagnosis was confirmed with regard to receiving insulin or oral hypoglycemic agents and ADA criteria [28].

### Laboratory measures

Throat-swab specimens achieved from the upper respiratory tract of the patients upon their admission were stored in a viral-transport medium (VTM). Total ribonucleic acid (RNA) was further extracted using QIAamp™ viral RNA mini kit from Qiagen™ according to the instructions of the manufacturer. With E-gene and Rdrp-gene probe/primer and superscript™ III platinum, the one-step qRT-PCR kit of Invitrogen company mixtures was prepared. The mixtures were transferred to Roche Light cycler™ 96 and applied Biosystem ABI step one plus™ real time thermal cyclers with positive control and no template control (NTC), as well as an internal control. After 45 cycles and observing the produced graphs, the rises after the noise and before cycle 32 were considered as positive for COVID-19 [31, 32]. Blood samples were collected for differential cell blood count in tubes

with EDTA and immediately became processed using an automated hematology analyzer called SYSMEX XN-1000.

BUN (Blood Urea Nitrogen), creatinine, Sodium (Na), Potassium (K), Blood Sugar (BS), and Liver function tests (ALT, AST and Alkaline phosphatase), CRP (C-reactive protein), D-dimer, Troponin, CPK, and LDH were measured for each patient. Troponin I was measured by Chemiluminescence Microparticle Immune-Assay (CMIA) (Cobas c601), while other chemical assessment were measured by Roche Cobas c501 chemistry analyzer (RocheDiagnostics).

### Imaging evaluation

Non-contrast CT scan was conducted in a supine position during the full inspiration. Scanning was performed from thoracic inlet to the upper abdomen. The CT scans were performed on a scanner (GE Medical Systems, Milwaukee, WI, and USA) 120Kvp with the thickness of 1.25-2 mm and 1.25 mm interval. The CT images were reviewed by cardiothoracic radiologist. To further assess the abnormalities in CT images, the following parameters were analyzed:

Ground-glass opacity, local patchy shadowing, bilateral patchy shadowing, and interstitial abnormalities.

### Study outcomes

The hospital course and clinical outcomes during the period of admission to discharge or death were followed for each patient. All of the comorbidities such as CKD, CVDs, or respiratory failure were additionally recorded.

### Ethical considerations

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (No.IR.SUMS.REC.1399.076), Shiraz, Iran. Written informed consent was achieved from each patient.

### Statistical analysis

The qualitative and quantitative data were respectively described by frequency (percentage) and mean  $\pm$  standard

**Table 1** The demographic data, comorbidities, signs and symptoms, imaging results, and admission duration among diabetic and non-diabetic COVID patients

Variables		Non-diabetic COVID-19 patients (N=299)	Diabetic COVID-19 patients (N=107)	P-value
Age (years old)	< 30	37 (12.4)	2 (1.9)	<0.001
	30–49	122 (40.9)	10 (9.5)	
	50–64	62 (20.8)	41 (39.0)	
	> 65	77(25.8)	52 (49.5)	
Gender	Male	178 (59.5)	63 (58.9)	0.906
	Female	121 (40.5)	44 (41.1)	
Comorbidities	HTN	41 (13.7)	38 (35.5)	<0.001
	CVDs	40 (13.4)	28 (26.2)	0.002
	Respiratory failure	18 (6.0)	11 (10.3)	0.142
	Hypothyroidism	19 (6.4)	11 (10.3)	0.183
	CKD	14 (4.7)	11 (10.3)	0.390
	Malignancy	5 (1.7)	4 (3.7)	0.251
	Signs and symptoms	Fever	90 (30.1)	27 (25.2)
	dyspnea	191 (63.9)	68 (63.3)	0.952
	Cough	168 (56.2)	65 (60.7)	0.413
	Diarrhea	11 (3.7)	2 (1.9)	0.361
	Vomiting	28 (9.4)	5 (4.7)	0.127
	O2 saturation	91.71 $\pm$ 6.88	88.01 $\pm$ 12.96	0.001
CT scan results	Ground-glass opacity (GGO)	101 (77.7)	29 (22.3)	0.866
	Local patchy shadowing	10 (71.4)	4 (28.6)	
	Bilateral patchy shadowing	42 (73.7)	15 (26.3)	
	Interstitial abnormalities	1 (50.0)	1 (50.0)	
Status	Alive	270 (93.8)	86 (88.7)	0.100
	Dead	18 (6.3)	11 (11.3)	
Hospital stay	Ward stay	5.75 $\pm$ 4.60	6.66 $\pm$ 4.95	0.121
	ICU stay	1.00 $\pm$ 3.68	1.71 $\pm$ 4.69	

deviation (SD). Differences between two groups were analyzed using the  $\chi^2$  test or Fischer exact test for categorical variables; moreover, the Student *t* test or Mann–Whitney *U* test were applied for the continuous variables. After the exclusion of patients with comorbidities except diabetes, similar analyses were carried out in order to achieve the laboratory test results and status of the diabetic patients. These findings were then become compared with non-diabetic COVID patients without other comorbidities. To make a comparison between the hospital mortality of diabetic and non-diabetic groups through the log rank test, Kaplan–Meier curves were plotted. All statistical analyses were performed using the SPSS Statistics software (version 19) for windows. Also, a  $<0.05$  *p*-value was considered to statistically be significant.

## Results

There were 241 (59.4%) male cases among all of the 406 COVID-19 patients. As it could be seen in Table 1, the prevalence of preexisting type 2 DM, HTN, and CVDs, were respectively 26.4% (107 cases), 19.5% (79 cases), and 16.7% (68 cases). Furthermore, DM prevalence was found to be 49.5% among the cases aged more than 65 ( $p < 0.001$ ), which was the highest ratio. Results showed that the comorbidities of HTN (35.5% vs. 13.7%,  $p < 0.001$ ) and CVDs (26.2% vs. 13.4%,  $P = 0.002$ ) were significantly more prevalent among diabetic COVID-19 cases compared to non-diabetic ones (Table 1).

## Signs and symptoms

Table 1 represents the demographic data, and signs and symptoms on the presentation. The most common symptoms were dyspnea (63.8%), dry cough (57.4%), and fever (28.8%). Diabetic cases had lower oxygen (O<sub>2</sub>) saturation than non-diabetic ones on the admission day ( $P = 0.001$ ). Other signs and symptoms at the presentation time were not statistically different between diabetics and non-diabetics. In addition, we did not find any significant difference in CT findings of the mentioned groups.

The mean durations of hospital stay were respectively found to be  $7.64 \pm 4.53$  and  $6.06 \pm 4.53$  days for diabetic and non-diabetic cases ( $P = 0.006$ ). Correspondingly, the mean durations of ICU admission were  $1.71 \pm 4.69$  and  $1.00 \pm 3.68$  days for the diabetic and non-diabetic cases ( $P = 0.160$ ), respectively. Although the in-hospital death rate was higher in patients with pre-existing DM compared to the non-diabetic individuals (11.3% vs. 6.3%), this difference was not statistically significant ( $P = 0.100$ ).

## Laboratory measurements

Table 2 represents the biochemical findings among diabetic and non-diabetic patients. Results of comparing the laboratory test results for patients on the admission day showed that serum sodium (Na) level was lower among the diabetic cases ( $P = 0.003$ ).

Considering the diabetic group, the lymphocyte count was lower and levels of PMN, CRP, LDH, AST, ALT, and

**Table 2** Laboratory test results for diabetic and non-diabetic patients with COVID-19

	Mean $\pm$ SD		<i>P</i> -value
	Non-diabetic COVID-19 patients	Diabetic COVID-19 patients	
WBC	6.91 $\pm$ 3.21	7.22 $\pm$ 3.20	0.414
Hb	13.16 $\pm$ 2.26	14.12 $\pm$ 12.33	0.283
Platelet	233.45 $\pm$ 103.41	210.11 $\pm$ 87.12	0.062
PMN	67.71 $\pm$ 18.83	70.93 $\pm$ 14.46	0.195
Lymphocyte	21.71 $\pm$ 11.23	19.27 $\pm$ 12.31	0.120
CRP	32.33 $\pm$ 35.39	40.08 $\pm$ 33.92	0.125
Blood urea nitrogen (BUN)	16.83 $\pm$ 16.69	19.37 $\pm$ 13.46	0.200
Creatinine	1.39 $\pm$ 1.70	1.61 $\pm$ 1.39	0.239
Na	138.46 $\pm$ 4.52	136.74 $\pm$ 4.48	0.003
Potassium (K)	4.68 $\pm$ 8.27	4.15 $\pm$ 0.75	0.564
LDH	605.19 $\pm$ 545.89	984.4 $\pm$ 2170.28	0.252
ALT	47.91 $\pm$ 59.40	94.73 $\pm$ 464.06	0.192
AST	43.06 $\pm$ 50.01	52.34 $\pm$ 64.75	0.234
Alkaline phosphatase (ALP)	230.34 $\pm$ 104.78	234.14 $\pm$ 138.59	0.829
D-dimer	2018.15 $\pm$ 2662.72	1367.92 $\pm$ 1979.79	0.444
Troponin	7.9 $\pm$ 35.9	0.06 $\pm$ 0.25	0.389
Creatine phosphokinase (CPK)	212.12 $\pm$ 272.73	183.82 $\pm$ 151.52	0.565

creatinine were higher. However, these differences were not statistically significant.

For further evaluation, patients with comorbidities other than DM were excluded in order to avoid their possible impacts on the results. The demographic data, laboratory measures, and outcomes among diabetic and non-diabetic COVID-19 patients without other comorbidities were provided in Table 3.

At the admission time, diabetic cases had lower oxygen saturation than non-diabetics ( $p < 0.001$ ). Laboratory results established that as it was expected, the blood glucose level was much higher in the diabetic group compared with cases without comorbidities ( $p < 0.001$ ). Also, the increased AST ( $P = 0.037$ ) and decreased kidney function ( $P = 0.005$ ) were found to be more frequent in the diabetic

patients than non-diabetics in the cases without other comorbidities. Furthermore, DM patients had reduced lymphocyte count ( $P = 0.029$ ) and increased WBC count ( $P = 0.025$ ) significantly.

The clinical outcomes achieved from current study demonstrated in the Kaplan–Meier survival curve (Fig. 1), did not show any significant difference in overall survival time between diabetic and non-diabetic patients.

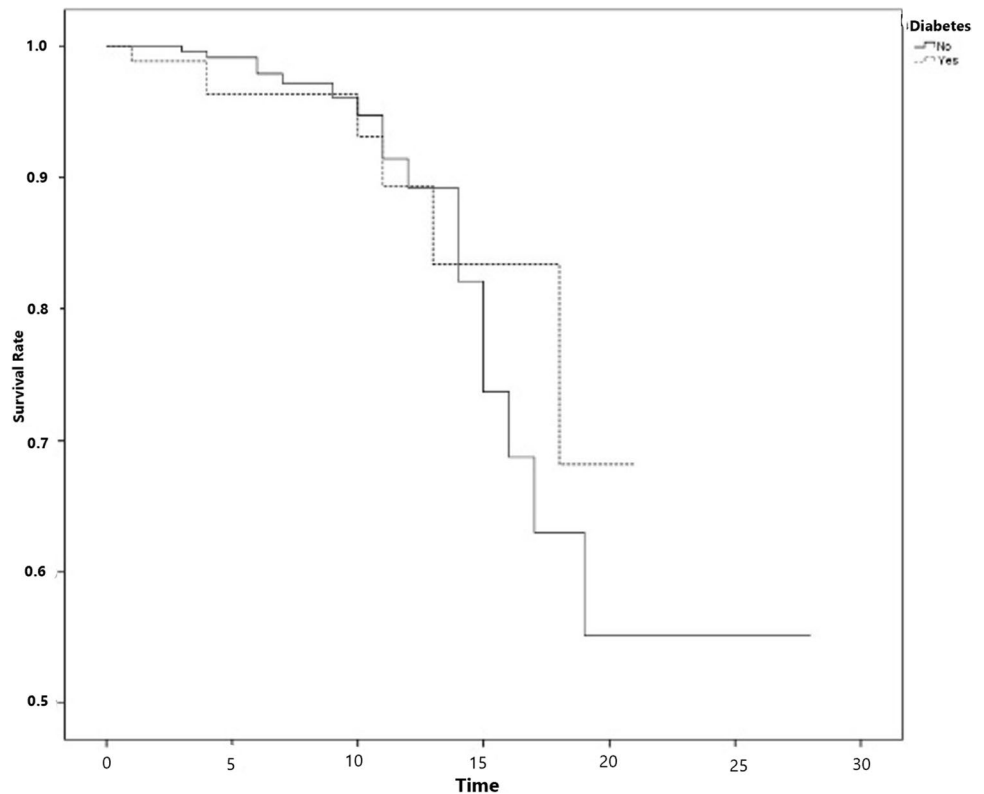
## Discussion

It has been acknowledged that DM with its high prevalence is an important comorbidity in patients with COVID-19. Compared to non-diabetic patients, DM cases are more

**Table 3** A comparison of demographic data, laboratory test results, and general status between diabetic COVID-19 cases and non-diabetic ones without other comorbidities

Variables		Non diabetic COVID-19 patients without other comorbidities (N=204)	Diabetic COVID-19 patients without other comorbidities (N= 105)	P-value
Age (years old)	< 30	33(16.2)	2 (1.9)	<0.001
	30–49	94(46.1)	10 (9.5)	
	50–64	44(21.6)	41 (39.0)	
	> 65	33(16.2)	52 (49.5)	
Gender	Male	132 (64.4)	63 (58.9)	0.340
	Female	73 (35.6)	44 (41.1)	
Laboratory findings	Fasting blood sugar (FBS)	113.12 ± 34.04	167.37 ± 59.12	<0.001
	WBC	6.47 ± 3.11	7.34 ± 3.30	0.025
	Hb	13.4 ± 2.03	13.99 ± 11.93	0.552
	Platelet	232.52 ± 96.11	217.28 ± 108.93	0.224
	PMN	67.24 ± 20.94	70.98 ± 14.21	0.175
	Lymphocyte	22.73 ± 11.78	19.00 ± 11.83	0.029
	CRP	33.33 ± 39.37	40.66 ± 33.40	0.187
	BUN	13.45 ± 8.75	19.11 ± 13.15	<0.001
	Creatinine	1.2 ± 1.02	1.60 ± 1.34	0.005
	Na	138.46 ± 4.03	136.88 ± 4.27	0.003
	K	4.76 ± 9.79	4.13 ± 0.75	0.546
	LDH	537.5 ± 377.59	966.56 ± 2065.12	0.094
	ALT	45.14 ± 40.95	90.11 ± 438.47	0.304
	AST	38.03 ± 24.69	53.25 ± 68.35	0.037
	ALP	221.4 ± 92.27	234.14 ± 138.59	0.200
	D-dimer	2169 ± 2396.87	1383.85 ± 1896.37	0.351
	Troponin	1.74 ± 8.57	0.063 ± 0.25	0.440
	CPK	164.35 ± 153.73	187.66 ± 153.72	0.466
	O <sub>2</sub> saturation	92.40 ± 60.07	88.01 ± 12.96	<0.001
	Status	Alive	189 (94.0)	85 (88.5)
Dead		12 (6.0)	11 (11.5)	
Hospital stay	Ward stay	6.09 ± 4.78	6.66 ± 4.95	0.352
	ICU stay	0.72 ± 2.83	1.71 ± 4.69	

**Fig. 1** Kaplan–Meier survival curve of the patients with and without diabetes



vulnerable to the infection and development of poor prognosis [33].

The United States Centers for Disease Control and Prevention (CDC) created a list of certain comorbidities associated with severe COVID-19. Among these comorbidities, DM was introduced as an established risk factor for the progression of the disease [25, 27, 34]. Also, CDC declared increased mortality in DM cases (2.3% overall and 7.3% patients with DM) [15]. The main findings of this study were in line with this statement. In this report, the diabetic patients were presented with advanced age, lower oxygen saturation, and signs of greater liver and kidney dysfunction.

In addition, type 2 DM was associated with the activation of the renin-angiotensin system in different tissues that may contribute to higher adverse risks in diabetic COVID-19 patients [35]. By binding to angiotensin-converting enzyme 2 (ACE2), the virus would enter into the cells and reduce the expression of ACE2 [36]. Therefore, the wide distribution of ACE2 level in the lungs, vascular endothelium, heart, kidney, and intestines could partially explain the underlying mechanism of multi-organ failure, especially myocardial, kidney, and liver injury in COVID-19 patients [26, 34].

Results showed that there was a bidirectional relationship between COVID-19 and DM [37]. DM was associated with an increased risk of severe COVID-19; also, COVID-19 could influence the pathophysiology of DM with transient

insulin resistance and worsening of blood glucose control [23, 38]. This could be due to the cytokine storm, direct virus-mediated beta-cell damage, and special medications prescribed in the treatment course of viral infections such as anti-viral drugs or corticosteroids [34, 39].

Poor glycemic control was generally specified in various studies as a factor that influences the poor recovery of hospitalized patients [27, 40, 41]. This process was explained by a wide variety of immune response alterations associated with hyperglycemia. It was also specified that even transient stress hyperglycemia could cause innate immune response dysfunctions such as impairments in polymorphonuclear and monocytic cell chemotaxis and phagocytosis, complement function, and cytokine dysregulation [27, 41]. Accordingly, the investigated diabetic individuals with higher blood glucose level at the admission time had complications including lower oxygen saturation and lymphocyte count, abnormal liver enzyme levels and signs of renal function impairment.

Besides, The idiosyncratic effect of COVID-19 on the respiratory control system was also proposed in studies [42]. Patients with coronavirus disease (COVID-19) are described as exhibiting oxygen levels incompatible with life without dyspnea. The hypoxic ventilator response was diminished by more than 50% in diabetic patients. The diabetic cases had a 1.8-fold reduced ability to perceive respiratory sensations



[43]. This is in line with this study that the patients with diabetes had lower oxygen (O<sub>2</sub>) saturation despite similar level of dyspnea and chest CT severity parameters at presentation in comparison with non-diabetic patients.

There are still some controversies regarding the effect of DM on mortality rate in COVID-19 patients; however, the bulk of studies have reported this association [26, 27, 44, 45]. It was found in current study that although the in-hospital death rate was higher in patients with pre-existing DM compared to non-diabetic cases, the difference was not statistically significant. It seemed that respiratory failures such as the lung volumes, pulmonary diffusing capacity, bronchomotor tone, and bronchial neuroadrenergic innervation led to the increase of mortality among diabetic COVID-19 patients [46]. The clinical outcomes achieved from current study analyzed by Kaplan–Meier survival curve, did not show any significant difference in overall survival time between diabetic and non-diabetic patients. Some other investigations revealed that the mortality rate was higher among DM patients [47, 48].

## Conclusion

Comparing the health conditions of diabetic and non-diabetic COVID-19 patients, it was found that the first group was at a higher risk of complications. The unusual clinical picture of the respiratory distress-caused hypoxia and chest CT finding in of DM cases emphasized the importance of identifying the subtle clinical signs that were often missed for these patients. More investigations are required in order to achieve a better understanding of the pathophysiological and molecular mechanisms of this clinical entity, to prevent the complications and mortality among diabetic COVID-19 patients.

## Limitations

Current study was faced with some limitations. Data was achieved from admitted diabetic patients with COVID-19, and the ones in the outpatient settings were not included. In addition, the glycemic data of pre-hospital status of these individuals was not accessible, which could be significantly associated with numerous clinical parameters. Therefore, several large-scale prospective cohort studies are required to understand the importance and association of glycemic control in COVID-19 progression.

**Abbreviations** ACE2: Angiotensin-Converting Enzyme 2; ALT: Alanine Aminotransferase; ARDS: Acute Respiratory Distress Syndrome; AST: Aspartate Aminotransferase; BUN: Blood Urea Nitrogen; CDC: Centers for Disease Control and Prevention; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary

Disease; COVID-19: Coronavirus Disease 2019; CRP: C-Reactive Protein; CT: Computed Tomography; CVDs: Cardiovascular Diseases; DM: Diabetes Mellitus; Hb: Hemoglobin; A/H1N1: Influenza A virus subtype H1N1; HRCT: High-Resolution Computed Tomography; HTN: Hypertension; ICU: Intensive Care Unit; LDH: Lactate Dehydrogenase; MERS-CoV: Middle East Respiratory Syndrome-related Coronavirus; NTC: No Template Control; PMN: Polymorphonuclear; RNA: Ribonucleic Acid; RT-PCR: Reverse-Transcription Polymerase Chain Reaction; SARS: Severe Acute Respiratory Syndrome; VTM: Viral-Transport Medium; WBC: White Blood Cell; WHO: World Health Organization

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**Data availability** The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate** This study was approved by the ethics committee of Shiraz University of Medical Sciences.

**Consent to publish** Not applicable.

**Competing interests** The authors declare that they have no competing interests.

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