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Clinical Manifestations and Outcomes of COVID-19 in Diabetes Mellitus People, Yazd, Iran-2021

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Abstract

Objective: Diabetes mellitus is reported to be the third most prevalent comorbidity with COVID-19, after cardio-cerebrovascular disease and hypertension. Furthermore, diabetes increases the likelihood of admission to the hospital and intensive care unit and death from COVID-19. The aim of the present study was to compare the clinical manifestations and outcomes of COVID-19 in diabetic versus non-diabetic inpatients.
Materials and Methods: The medical records of 6525 patients with definitive diagnosis of COVID-19 were obtained from the reference COVID-19 diagnosis laboratory from January to July 2021 in Yazd, Iran. Patients were investigated for data on onset, clinical history, and fatality rate. COVID-19-related death was defined as positive RT-PCR in at least one of three nasal samples. Data were analysed using SPSS 24.
Results: Among inpatients, 21.2% were diabetic. The mean ages of diabetic and non-diabetic patients were 64.45 (±13.87) and 52.98 (±20.36) years, respectively. Diabetics were more likely to be admitted to the intensive care unit (6.8% vs. 5%, P= 0.02) and the fatality rate was higher among them than non-diabetics (22.6% vs. 12%, P< 0.001). In diabetics, the mean age of non-survivors was lower than that of survivors (62.57 vs. 70.48, P= 0.0001) and the frequency of death was higher among men than women (53% vs. 47.5%, P= 0.045). Generally, diabetes has the strongest association with COVID-19 death (P= 0.0001).
Conclusion: Diabetic patients experience more adverse outcomes because of COVID-19. These findings indicate the need for special attention in relation to prevention treatment against COVID-19 in patients with diabetes.

Keywords: COVID-19, Diabetes, Inpatients, Outcomes

QR Code:

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Introduction

In late December 2019, a respiratory infection was reported in Wuhan, China, which was temporarily named 2019 Novel Coronavirus (2019-nCoV) after etiological studies(1). The new coronavirus infection quickly spread around the world, and on March 11, 2020, it was declared a pandemic by the World Health Organization (2). At the time of writing this article (February 28, 2022), according to the WHO report, there have been 440,807,756 confirmed cases of COVID-19, including 5,978,096 deaths, of which 7073747 cases and 137439 deaths were related to Iran (3). The consequences of this infection in different people are categorized from mild respiratory illness to severe conditions such as acute respiratory distress syndrome and septic shock, which has even resulted in death (4,5).

Diabetes is another epidemic that has plagued the world for many years, and according to reports, 463 million people aged 20 to 79 years were affected by this disease in 2019 (6).

After cardiovascular diseases and high blood pressure, diabetes is the third comorbidity with COVID-19 (7,8). Diabetic patients with COVID-19 are more likely to be hospitalized, have more severe pneumonia, and have even higher mortality rates, especially for those with poor glycaemic control than those without any co-morbidity (9-11).

People with diabetes are more at risk for COVID-19 because their immune system, especially those with poor glycaemic control, is at risk, and this deficiency makes them vulnerable to various infections, including COVID-19 (12). In addition, diabetics usually have chronic inflammation in which COVID-19 through an imbalance in angiotensin-converting enzyme 2 (ACE2) activation pathways causes an extra inflammatory response. ACE2 imbalance leads to acute β-cell dysfunction and makes these patients prone to worsened COVID-19 complications (13,14).

Several studies in China estimated the prevalence of diabetes among COVID-19 patients to be between 8% and 25% (15,16). According to a national report in China, 8.2% of 1,590 hospitalized COVID-19 patients with a mean age of 48.9 years suffered from diabetes (17). Similar results have been reported in other countries, and diabetes is mentioned as the second major comorbidity after hypertension (18, 19). In addition, people with diabetes have a significantly higher risk of developing a severe form of COVID-19, hospitalization in the ICU and death than non-diabetic people (20,21).

The alarming increase in cases of COVID-19 in Iran, as well as the high prevalence of diabetes in Yazd province, prompted researchers to investigate the comorbidity and mortality of COVID-19 and diabetes among people in Yazd.

Material and methods

After receiving the ethical code from the ethics committee of Yazd University of Medical Sciences, the medical records of 6525 patients with a definitive diagnosis of COVID-19 were obtained from the COVID-19 reference laboratory from January 2021 to July 2021 (6 months). The criterion for definitive COVID-19 diagnosis was a positive result of the reverse transcriptase polymerase chain reaction (RT-PCR) test. Patients were investigated for data about age, sex, signs and symptoms, clinical history (cardiovascular, respiratory and chronic kidney disease and, malignancy), radiological findings, admission to the ICU, mechanical ventilation treatment, and death. COVID-19-related death was defined as positive RT-PCR in at least one of three nasal samples. Note that all tests were performed in a COVID-19 reference laboratory. Data were analysed using SPSS 24. To compare quantitative and qualitative variables between diabetic and non-diabetic groups, independent sample T-test and chi-square tests were used, respectively. Finally, to

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determine the predictive effect of diabetes on death among patients with COVID-19, logistic regression was done.

Ethical considerations

This project was approved by ethics committee of Shahid Sadoughi University of Medical Sciences, Yazd. (No: IR.SSU.REC. 1399.062)

Results

A total of 6525 patients hospitalized due to COVID-19 participated in this study, 21.2% suffered from diabetes. The mean age of diabetic and non-diabetic patients was 64.45 (±13.87) and 52.98 (±20.36) years, respectively. The mean duration of hospital stay was 8.8 days in patients with diabetes and 6.7 days in non-diabetic individuals. The most common symptoms in both groups were fever, cough, and dyspnea. The demographic and clinical characteristics of patients are shown in Table 1.

Compared with non-diabetic patients, diabetic patients reported more cardiovascular (42.9% vs. 11.1%, $P< 0.001$), kidney (5.4% vs. 1.2%, $P< 0.001$), respiratory (1.4% vs. 0.7, $P= 0.013$), and malignant diseases (1.3% vs. 0.8, $P= 0.045$). Admission to the intensive care unit was higher among diabetics than non-diabetics (6.8% vs. 5%, $P= 0.02$). Moreover, the fatality rate was higher among diabetic patients (22.6% vs. 12%, $P< 0.001$).

The baseline characteristics of survivors and non-survivors of diabetic patients with COVID-19 are summarized in Table 2. The mean age of non-survivors was lower than that of survivors (62.57 vs. 70.48, $P= 0.0001$). Meanwhile, the death frequency was higher among men than among women (53% vs. 47%, $P= 0.045$). In relation to the signs and symptoms, the deceased showed more symptoms of dyspnea (52.4% vs. 45.1%, $P= 0.012$). Compared with the survivors, a higher percentage of non-survivors were admitted to

Table 1. Demographic and clinical characteristics of COVID-19 patients with and without diabetes

Variables	Diabetics N=1388	Non-Diabetics N=5137	*P*-value
Age, years (mean± SD)	64.45 (±13.87)	52.98 (±20.36)	0.0001*
Duration of hospital stay, days (mean± SD)	8.8 (±0.22)	6.7 (±0.09)	0.001*
Gender			
Male	667 (48.8%)	2775 (54%)	0.0001**
Female	711 (51.2%)	2362 (46%)	
Sign and Symptoms			
Headache	170 (12.2%)	632 (12.3%)	0.499**
Fever	460 (49.6%)	1670 (58%)	0.0001**
Chills	51 (3.7%)	257 (5%)	0.023**
Aches and pains	577 (41.6%)	2389 (46.5%)	0.001**
Loss of taste or smell	1 (0.1%)	12 (0.2%)	0.201**
Cough	776 (55.9%)	2899 (56.4%)	0.374**
Diarrhea	120 (8.6%)	443 (8.6%)	0.5**
Dyspnea	651 (46.9%)	1944 (37.8%)	0.0001**
Comorbidities			
Cardiovascular disease	595 (42.9%)	568 (11.1%)	0.0001**
Respiratory disease	19 (1.4%)	35 (0.7%)	0.013**
Chronic kidney disease	75 (5.4%)	63 (1.2%)	0.0001**
Malignancy	18 (1.3%)	39 (0.8%)	0.045**
Admission to ICU			
Yes	95 (6.8)	257 (5)	0.02**
Mechanical ventilation treatment			
Yes	68 (5.6%)	212 (5.1%)	0.265**
Outcome			
Alive	1058 (76.2%)	4424 (86.1%)	<0.001**
Death	314 (22.6%)	618 (12%)	

*Independent sample T-test
**chi-square

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the intensive care unit (19.7% vs. 3.4%, *P*< 0.0001) and used ventilators (10.6% vs. 3.1%, *P*< 0.0001).

Table 3 shows the predictors of death among COVID-19 inpatients. Among the risk factors, diabetes has the strongest association with COVID-19 death (OR= 2.14, *P*= 0.0001).

Discussion

The aim of this study was to evaluate the clinical manifestations and outcomes of COVID-19 in diabetic versus non-diabetic inpatients. This research generally showed that patients with diabetes were older than non-diabetic inpatients, were hospitalized longer, had a higher risk of being admitted to the intensive care unit, and required mechanical ventilation. Meanwhile, a higher fatality rate was reported in this group. According to previous studies and the report of the Centres for Disease Control, people with diabetes have a significantly higher risk of ICU admission than non-diabetic individuals (OR= 2.79) (22-24). In addition, the combined endpoint (i.e., the need for intensive care and mechanical ventilation and even death) was significantly higher among diabetic than non-diabetic patients (22.2% vs. 4.8%). These results can be attributed to poor respiratory function in patients with diabetes. In fact, the complex alveolar– capillary network of the lungs can be targeted by microvascular damage caused by type 2 diabetes. Furthermore, insulin resistance and altered glucose homeostasis lead to alveolar-capillary microangiopathy and interstitial fibrosis, which ultimately leads to

Table 2. The characteristics of survivors and non-survivors diabetic patients with COVID-19

Variables	Survivors (N=1074)	Non-survivors (N=314)	*P*-value
Age, years (mean± SD)	70.48 (±0.71)	62.57(±0.41)	0.0001
Duration of hospital stay, days (mean± SD)	11.41 (±0.58)	8.22 (±0.23)	0.001
Gender			
Male	502 (47.5%)	175 (53%)	0.045
Female	555 (52.5%)	155 (47%)	
Sign and Symptoms			
Headache	143 (13.5%)	27 (8.2%)	0.005
Fever	360 (50.3%)	112 (51.6%)	0.402
Aches and pains	459 (43.4%)	117 (35.5%)	0.006
Cough	603 (57%)	173 (52.4%)	0.374
Diarrhea	98 (9.3%)	22 (6.7%)	0.085
Dyspnea	477 (45.1%)	173 (52.4%)	0.012
Comorbidities			
Cardiovascular disease	449 (42.5%)	145 (43.9%)	0.079
Chronic kidney disease	43 (4.1%)	32 (9.7%)	0.0001
Malignancy	13 (1.2%)	5 (1.5%)	0.433
Admission to ICU			
Yes	33 (3.4%)	62 (19.7%)	0.0001
Mechanical ventilation treatment			
Yes	33 (3.1%)	35 (10.6%)	0.0001

Table 3. Multivariable analysis of independent risk factors associated with in-hospital death

Variables	*P*-value	OR (95% CI)
Age, years	0.0001	0.95
Sex, (male vs. female)	0.033	0.8
Cardiovascular disease (yes vs. no)	0.0001	1.649
Diabetes (yes vs. no)	0.0001	2.14
Chronic kidney disease (yes vs. no)	0.0001	1.114
Respiratory symptoms (yes vs. no)	0.032	1.106
Gastrointestinal symptoms (yes vs. no)	0.014	1.43
Fever (yes vs. no)	0.049	1.23
Headache (yes vs. no)	0.0001	1.98

Logistic regression

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poorer lung function among these patients compared with non-diabetic patients (24-26).

All comorbidities investigated in this study (cardiovascular, kidney and respiratory diseases) were higher in diabetic patients than in non-diabetic patients. Previous studies also confirmed the results of this study (27-29). The rate of comorbidities among patients with diabetes may be attributed to the incidence of micro- and macrovascular complications due to diabetes (30). However, studies that have exclusively examined the effect of diabetes on the severity of COVID-19 have not reported the same results, but in Petrilli's study, the results showed that diabetes and its associated diseases are independent predictors of hospital admission (31).

In our study, the number of deaths among patients with diabetes was higher than non-diabetic individuals (22.6% vs. 12%). Along with the present study, numerous studies have shown that the fatality rate in hospitalized diabetic patients with COVID-19 was significantly higher than non-diabetic patients (27,32,33). In explaining this part, it should be noted that because diabetic patients are twice as likely as others to have a severe infection, not only have more adverse outcomes, including ARDS, and need to be admitted to the ICU and use invasive ventilation but also show less resistance to the mentioned situations and therefore surrender to death sooner (21).

In the present study mean age of patients with diabetes who died of COVID-19 was significantly lower than that of those who survived. Although in most studies, increasing age has been considered as a risk factor for increased risk of death in COVID-19 disease, it should be noted that the patients in this part of our study were diabetic, and based on previous studies, young people are more likely to be affected by the negative effects of diabetes when they are infected. Therefore, younger diabetics are more likely to die of COVID-19 (34).

The fatality rate was higher among men with diabetes than among women. This association has been confirmed several times in previous studies (35). There are some reasons for the severity of the disease in men compared with women. Since life expectancy is naturally higher in women than in men, the higher incidence of mortality among men can be attributed to this feature (36).

In addition, the X chromosome and sex hormones in women play an important role in innate and adaptive immunity. In this regard, many studies have indicated the presence of higher levels of ACE2 (as a receptor for the virus) in men than in women, which may explain why women are less sensitive than men to viral infections (37,38).

In terms of clinical symptoms, patients with diabetes reported less fever and more dyspnea than non-diabetic individuals. Similar results were found among Chinese patients in whom the incidence of fever was lower (59.5% vs. 83.2%) and the incidence of dyspnea was higher (86% vs. 81%.) among diabetic patients compared with non-diabetic patients. In general, patients with diabetes have a higher risk of developing respiratory infections because of immune deficiencies, especially innate immunity (39,40). Even transient hyperglycemia may temporarily affect innate immune responses to infection and predispose them to a variety of infections (12).

Our findings indicated that diabetes was the most important predictor of mortality among patients with COVID-19 (OR= 2.14). In previous studies conducted in China and Italy, diabetes mellitus was considered as a strong predictor of death outcome among people with COVID-19 infection (36,41). Moreover the ratio of fatality in patients with diabetes in several studies has been reported to be between 1.90 - 2.2 (21,27).

Despite the strengths of this study, there were some limitations. The first limitation was that the patients' laboratory parameters were not examined, and the second limitation was that in diabetic patients, the association between their glycaemic control status before hospitalization and the outcome of death was not analysed.

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Conclusions

The findings showed that patients with diabetes experience more adverse outcomes, including dyspnea, the need to be admitted to the intensive care unit and the use of mechanical ventilation, and ultimately death compared with non-diabetic patients during COVID-19 infection. These implications indicate the need for special attention in relation to preventive behaviours COVID-19 or therapeutic interventions when the infection occurs in patients with diabetes.

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Conflict of Interest

No potential conflict of interest was reported by the authors.

Authors' contributions

All authors have accepted responsibility for the entire content of this manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved and approved the version to be published.

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