Epidemiological characteristics and outcomes of COVID-19 in diabetic versus non-diabetic patients

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Abstract

Objectives and background People with diabetes (PWD) are one of the high-risk groups for coronavirus disease 2019 (COVID-19) infection, increasing the disease mortality. This study was aimed to compare the epidemiological characteristics and outcomes of COVID-19 in diabetic versus non-diabetic individuals.
Methods In this retrospective observational study, the epidemiological characteristics of the two groups of diabetic (n=1365) and non-diabetic (n=15,026) subjects with definite diagnosis of COVID-19 in the southwestern region of Iran were compared. All clinical signs and comorbidities of the patients were evaluated. Chi-square test was used to examine the differences in qualitative variables between diabetic and non-diabetic groups.
Results Of 16,391 enrolled subjects, 8.3% had diabetes, and 28.3% of COVID-19-related deaths occurred in diabetics. Also, the mortality rate among diabetics was reported as 14.3%. The average age of diabetic patients and non-diabetic patients was 59 and 37 years, respectively. The odds of fever, cough, shortness of breath, headache, and underlying diseases, such as hypertension, cardiovascular disease, chronic lung disease, immune deficiency, and hyperlipidemia, were significantly higher in diabetic patients than in non-diabetics.
Conclusion Diabetes is associated with increased mortality rate in patients with COVID-19 and is considered as a major risk factor for COVID-19 infection, posing a major public health challenge for health policymakers in managing and controlling the disease. Therefore, development of prevention and treatment strategies aimed at reducing COVID-19 morbidity and mortality in diabetes patients is of significant importance.

Keywords COVID-19 · Diabetes · Mortality

Introduction

Diabetes is the fifth leading cause of death throughout the world (approximately 3 million deaths per year), which is mainly caused by defects in either insulin secretion or action. The prevalence of diabetes has dramatically increased over the past two decades and is projected to increase from 285 million in 2010 to 438 million in 2030 [1]. Also, according to the

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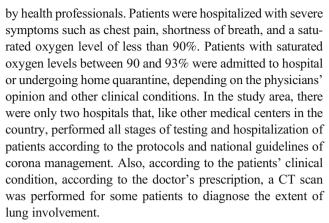
World Health Organization, the prevalence of diabetes in Iran will increase from 3 million in 2010 to 6 million in 2030 [2]. People with diabetes (PWD) are one of the high-risk groups for Coronavirus Disease 2019 (COVID-19) due to their weakened immune system [3] .

According to the World Health Organization, COVID-19 highlighted on December 30, 2019 in Wuhan, China, and quickly infected many Chinese people [4]. On January 30, 2020, WHO identified corona as a global public health concern [5]. The family of coronaviruses is the cause of a variety of well-known diseases occurring in humans, ranging from common cold to Middle Respiratory Syndrome (MERS) and Acute Severe Respiratory Syndrome (SARS), and currently COVID-19 as a new problematic member of this family [6, 7]. Symptoms of the virus range from mild to severe, including fever, cough, and difficulty breathing [8]. PWD are at higher risk of infection, especially flu and pneumonia, and with proper blood sugar control, the risk can be reduced among these individuals. In fact, it was observed that diabetes was a leading cause of death in patients with the 2009 pandemic influenza (H1N1), SARS, coronavirus, and MERS [9]. In a study conducted in Wuhan on 140 patients with COVID-19, diabetes was not a risk factor for severe COVID-19 [10]. However, another study on 150 patients (68 deaths and 82 recovered patients) in Wuhan showed diabetes as an important predictor of COVID-19 [11]. Analysis of 11 studies on patients with COVID-19 showed that hyperglycemia and diabetes were not predictors of severe COVID-19 [12]. However, among 72,314 reported cases of COVID-19 by the China Centers for Disease Control and Prevention, mortality in PWD showed an increasing trend (2.3% and 7.3% of PWD in general) [13].

Due to the fact that limited information about the complications of COVID-19 in PWD is unknown, the present study was carried out to answer the question whether COVID-19 is more severe in PWD with higher mortality rate. This study was aimed to investigate and compare the epidemiological characteristics and outcomes of COVID-19 in patients with diabetes mellitus and non-diabetic patients.

Methods

This retrospective observational study was performed on 16,391 patients with COVID-19 who were under care in the southwestern region of Iran (Khuzestan province) from March to September 2020. The total population of this region was estimated 627,970 based on the annual growth, using the databases of province health centers and the national census of 2020. Confirmation of definite COVID-19 cases by RT-PCR was performed using nasal and throat swab samples. Patients with normal vital signs (pulse, respiration rate, and blood pressure) with saturated oxygen levels above 93% and mild symptoms were sent to home quarantine and monitored daily

by health professionals. Patients were hospitalized with severe symptoms such as chest pain, shortness of breath, and a saturated oxygen level of less than 90%. Patients with saturated oxygen levels between 90 and 93% were admitted to hospital or undergoing home quarantine, depending on the physicians' opinion and other clinical conditions. In the study area, there were only two hospitals that, like other medical centers in the country, performed all stages of testing and hospitalization of patients according to the protocols and national guidelines of corona management. Also, according to the patients' clinical condition, according to the doctor's prescription, a CT scan was performed for some patients to diagnose the extent of lung involvement.

All clinical and demographic information of patients, as well as the results of daily follow-up and the final outcome of each patient, were recorded by health experts. Duplicate samples have been identified and removed based on the national code of participants. Subjects were divided into two groups: diabetic group (n=1365) and non-diabetic group (15,026). First, demographic characteristics, symptoms, and other comorbid diseases were compared between diabetic and non-diabetic groups; then, the role of comorbid diseases in mortality and survival of all study subjects was compared. Finally, diabetic and non-diabetic patients were compared in terms of clinical symptoms and comorbid diseases. Variables used in this study include age, gender, final outcome (e.g., death and survival), symptoms (e.g., negative stenosis, fever, cough, lack of smell, lack of taste, fatigue, muscle pain, diarrhea, sore throat, and headache), and comorbidities, such as hypertension, diabetes, cardiovascular disease, kidney disease, liver disease, immune deficiency, high blood fats, and chronic lung disease.

Statistical analyses

Descriptive quantitative data were expressed as mean and median, and qualitative data were expressed as percentage and frequency. The distribution of continuous variables was performed using Kolmogorov-Smirnov test. Mann-Whitney test was also used to analyze abnormal data analysis. Chi-square test and Fisher's exact test were used to evaluate the differences between qualitative variables in the mortality of two study groups. Data analysis was performed using SPSS version 19.0. The significance level was set as 0.05.

Results

During the study period, a total of 16,391 cases of COVID-19 occurred in the cities affiliated to Abadan University of Medical Sciences. The average age of the patients was 38 years, with an interquartile range of 30–51 years. A total of 54.55% of the patients were male, and 62.60% (n=10,256)

had a history of contact with definite or suspected cases of COVID-19. Also, 4.21% of the patients (*n*=691) died, of whom 28.36% (*n*=196) had diabetes (Table 1). The most common symptoms displayed by subjects were fever (68.70%), cough (67.80%), and shortness of breath (49.30%). The most common comorbidities in all patients were hypertension (5.50%), cardiovascular disease (5%), chronic lung disease (1.90%), and chronic liver disease (1.70%) (Table 1).

Of all participants, 1365 (8.32%) were diabetic and 15,026 (91.68%) were non-diabetic. Also, 55.50% of diabetic patients were female, and 755 (55.30%) had a history of contact with definite or suspected cases of COVID-19. Compared with non-diabetic patients, diabetic patients were older, with an average age of 59 years (IQR: 49–67) vs. 37 years (IQR 29–49), and risk of comorbidities was higher in diabetic patients than in non-diabetic individuals, including hypertension as 418 (30.60%) vs. 478 (3.20%), heart disease as 266 (19.50%) vs. 549 (3.70%), chronic kidney disease as 72 (5.30%) vs. 213 (1.40%), chronic lung disease as 56

(4.10%) vs. 258 (1.70%), chronic liver disease as 13 (1%) vs. 27 (0.20%), immunodeficiency as 24 (1.80%) vs. 63 (0.40%), and hyperlipidemia as 18 (1.30%) vs. 34 (0.20%).

Fever, cough, and shortness of breath were significantly higher in diabetic patients compared with non-diabetic patients, and sore throat, chest pain, and reduced sense of taste and smell were significantly higher in non-diabetic patients than in diabetic patients. Diabetic patients had higher mortality (14.40% in diabetic patients vs. 3.30% in non-diabetic). The history of contact with definite or suspected cases of COVID-19 was higher in non-diabetic subjects (63.20% vs. 55.30%) (Table 1).

In addition, 15,700 patients (95.78%) survived from COVID-19. Compared with COVID-19 survivors, non-survivors were significantly older (median age of 66 years (IQR 55–76) versus 38 years (IQR 30–50)). Chronic diseases were significantly higher in non-survivors, including diabetes as 196 (28.40%) patients vs. 1169 (7.44%), hypertension as 143 (20.70%) vs. 753 (4.79%), heart disease as 142 (20.50%)

Table 1 The characteristics of patients with COVID-19 with or without diabetes

Variable	Total (*n*=16,391) Number (%)	Diabetes (*n*=1365) Number (%)	Non-diabetes (*n*=15,026) Number (%)	*p* value
Age, median (IQR)	38 (30–51)	59 (49–67)	37 (29–49)	<0.001
Gender				
Male	8940 (54.55)	607 (44.50)	8333 (55.50)	<0.001
Female	7446 (45.45)	758 (55.50)	6688 (44.50)	
Symptoms				
Fever	11258 (68.70)	1075 (78.80)	10183 (67.80)	<0.001
Cough	11106 (67.80)	1035 (75.80)	10071 (67.00)	<0.001
Dyspnea	8086 (49.30)	910 (66.70)	7176 (47.80)	<0.001
Muscular pain	1520 (9.30)	124 (9.10)	1396 (9.30)	0.801
Diarrhea	351 (2.10)	26 (1.90)	325 (2.20)	0.528
Nausea	436 (2.70)	39 (2.90)	397 (2.60)	0.636
Sore throat	1239 (7.60)	79 (5.80)	1160 (7.70)	0.010
Anorexia	78 (0.50)	6 (0.40)	72 (0.50)	0.839
Headache	618 (3.80)	57 (4.20)	561 (3.70)	0.270
Fatigue	54 (0.30)	3 (0.20)	51 (0.30)	0.460
Chest pain	121 (0.70)	4 (0.30)	117 (0.80)	0.045
Decreased sense of smell	378 (2.30)	10 (0.70)	368 (2.40)	<0.001
Decreased sense of taste	85 (0.50)	1 (0.10)	84 (0.60)	0.017
Comorbidities				
Hypertension	896 (5.50)	418 (30.60)	478 (3.20)	<0.001
Cardiovascular disease	815 (5.00)	266 (19.50)	549 (3.70)	<0.001
Immunodeficiency	87 (0.50)	24 (1.80)	63 (0.40)	<0.001
Chronic kidney disease	285 (1.70)	72 (5.30)	213 (1.40)	<0.001
Chronic pulmonary disease	314 (1.90)	56 (4.10)	258 (1.70)	<0.001
Chronic liver disease	40 (0.20)	13 (1.00)	27 (0.20)	<0.001
Hyperlipidemia	52 (0.30)	18 (1.30)	34 (0.20)	<0.001
Exposure to disease	10256 (62.60)	755 (55.30)	9501 (63.20)	<0.001
Mortality	691 (4.20)	196 (14.40)	495 (3.30)	<0.001

vs. 673 (4.28%), immunodeficiency as 14 (2.20%) vs. 72 (0.45%), chronic kidney disease as 43 (6.20%) vs. 242 (1.54%), and chronic lung disease as 31 (4.50%) vs. 283 (1.80%) (Table 2).

Of 1365 diabetic patients with COVID-19, COVID-19 non-survivors were considerably older than survivors (median age of 66 years (IQR 57–73) vs. 57 years (IQR 48–66)). The risk of heart disease was higher in non-survivors (56 patients (28.57%) vs. 193 patients (16.50%)). Gender, other comorbidities, and disease symptoms showed no significant difference with survived diabetic patients and non-survived patients (Table 3).

Discussion

This was a retrospective observational study, performed on 16,391 patients with COVID-19 in southwestern Iran. This study compared clinical features and mortality between people with type 2 diabetes and non-diabetic patients. Since the onset of COVID-19 pandemic, the disease has become widespread throughout the world, affecting a large number of people. The most vulnerable groups against COVID-19 are those with comorbid diseases, including diabetes. Various epidemiological evidences have shown that PWD are at higher risk for infectious diseases, such as measles and mumps [14]. Also, according to the results of previous studies, diabetes is one of the most common comorbidities associated with COVID-19. In our study, 8.3% of COVID-19 patients had type 2 diabetes. Other studies showed various percentages of COVID-19 patients with type 2 diabetes, as 20% [15], 52% [16], 24.9% [17], 14.5% [18], and 21.8% [19]. However, a number of studies have shown that the severity and complications of COVID-19 disease and the need for ICU stay were higher in

diabetic patients than in non-diabetic individuals [9, 14, 15, 17, 20–22].

According to the results of our study, the median age of COVID-19 patients who had diabetes was higher than COVID-19 patients without diabetes (59 vs. 37), which was consistent with the results of many previous studies [17, 19, 23]. Since diabetes is a chronic disease and chronic diseases are more common at older age, which explains higher average age of COVID-19 patients with diabetes.

The results of our study showed that symptoms of COVID-19, including fever, shortness of breath, and cough, were mostly reported in diabetic patients than in non-diabetic patients, while chest pain, sore throat, and decreased sense of smell and taste were more common in non-diabetic COVID-19 patients. In a study conducted in China, fever, dry cough, and fatigue were the most common symptoms in diabetic COVID-19 patients [23], and another study showed cough and fever as the most common symptoms in these patients [24]. A systematic review study indicated that no significant differences in signs and symptoms of these differences may be due to variation in selected sample sizes in various studies, study population, and type of collected data [18]. As such, some studies have examined only patients with severe form of COVID-19, while others have examined patients with various severity of the disease. Undoubtedly, patients with different severities of the disease display different symptoms.

According to the results of our study, COVID-19-related mortality was higher in PWD than in non-diabetic individuals (14.4% vs. 3.3%). Also, a study performed on 46 cases of COVID-19 in Wuhan, China, showed that 42% of COVID-19 deaths occurred among PWD. However, small sample size of this study should be considered in assessing the validity of the results. In another study on 72,312 people in China, mortality rate was higher in diabetic patients compared with non-

Table 2 The baseline characteristics of survivors and non-survivors infected with COVID-19

Variable	Total (n=16,391) Number (%)	Survivors (n=15,700) Number (%)	Non-survivors (n=691) Number (%)	p value
Age, median (IQR)	38 (30–51)	38 (30–50)	66 (55–76)	<0.001
Gender				
Male	8940 (54.55)	8424 (54.70)	378 (54.70)	0.986
Female	7446 (45.45)	6966 (45.30)	313 (45.30)	
Comorbidities				
Diabetes mellitus	1365 (8.30)	1169 (7.44)	196 (28.40)	<0.001
Hypertension	896 (5.50)	753 (4.79)	143 (20.70)	<0.001
Cardiovascular disease	815 (5.00)	673 (4.28)	142 (20.50)	<0.001
Immunodeficiency	87 (0.50)	72 (0.45)	15 (2.20)	<0.001
Chronic kidney disease	285 (1.70)	242 (1.54)	43 (6.20)	<0.001
Chronic pulmonary disease	314 (1.90)	283 (1.80)	31 (4.50)	<0.001
Chronic liver disease	40 (0.20)	38 (0.20)	2 (0.30)	0.797
Hyperlipidemia	52 (0.30)	51 (0.32)	1 (0.10)	0.449

Table 3 The baseline characteristics of survivors and non-survivors in patients with COVID-19 with diabetes

Variable	Total (n=1365) Number (%)	Survivors (n=1169) Number (%)	Non-survivors (n=196) Number (%)	p value
Age, median (IQR)	59 (49–67)	57 (48–66)	66 (57–73)	<0.001
Gender				
Male	607 (44.50)	488 (44.30)	98 (50.00)	0.141
Female	758 (55.50)	613 (55.70)	98 (50.00)	
Symptoms				
Fever	1075 (78.80)	874 (79.40)	162 (82.70)	0.293
Cough	1035 (75.80)	861 (78.20)	156 (79.60)	0.663
Dyspnea	902 (66.08)	755 (68.60)	147 (75.00)	0.072
Muscular pain	106 (7.76)	93 (7.95)	13 (6.63)	0.393
Diarrhea	23 (1.68)	22 (1.88)	1 (0.51)	0.146
Nausea	29 (2.12)	25 (2.13)	4 (2.04)	0.841
Sore throat	68 (4.98)	63 (5.38)	5 (2.55)	0.066
Comorbidities				
Hypertension	391 (28.64)	324 (27.71)	67 (34.18)	0.181
Cardiovascular disease	249 (18.24)	193 (16.50)	56 (28.57)	<0.001
Immunodeficiency	20 (1.46)	17 (1.45)	3 (1.53)	0.989
Chronic kidney disease	71 (5.20)	57 (4.87)	14 (7.14)	0.265
Chronic pulmonary disease	53 (3.88)	45 (3.84)	8 (4.08)	0.997
Chronic liver disease	13 (0.95)	12 (1.02)	1 (0.51)	0.453
Exposure to disease	690 (50.54)	599 (51.24)	91 (46.42)	0.039D

diabetic individuals [9]. The results of our study were supported by previous studies [17–19, 25] (17-40-42-12). The higher rate of mortality in diabetic patients can be due to their weakened immune system [26], poor lung function, and reduced lung capacity along with their common respiratory problems [18]. Furthermore, COVID-19 can affect diabetes pathogenicity as well as blood sugar control [20], all of which together can lead to increased mortality rate among these people. However, further research is needed to find out if COVID-19-related mortality was actually caused by diabetes or other factors, as most of these people are elderly and may have at the same time some other chronic diseases, including hypertension and cardiovascular disease, which makes it a little difficult for us to identify the main cause of death due to COVID-19. According to the findings of this study, the incidence of hypertension and heart disease was higher in PWD who died from COVID-19 than in non-diabetics. Other studies have shown that the mortality rate of COVID-19 was significantly higher in diabetic patients with heart disease as a comorbidity compared with non-diabetic patients.

Conclusion

The findings of this study suggest that diabetes increased mortality rate in patients with COVID-19 and is a major threat to these patients. Since COVID-19 is an unknown emerging disease, disease management has posed a huge challenge to health policymakers around the world. As a result, there is a need to develop prevention and treatment strategies for high-risk people, especially those with diabetes to reduce morbidity and mortality. It is also recommended that diabetic patients should take preventive measures, such as home quarantine, avoid unnecessary visits to medical centers, control blood glucose level, and follow the prevention guidelines developed by WHO experts for diabetics.

Strengths and weaknesses

Although, in our study, laboratory results and comprehensive information from patients were not available for further analysis, our study is one of the first studies in Iran, which examined clinical features of diabetic patients with COVID-19 and also, unlike many other similar studies, our study had a large sample size and also examined all cases of the disease, while many studies have been performed on only severe form of COVID-19.

We predict that we may have a diagnostic bias in our study. Because some people with asymptomatic or mild symptoms did not come to perform the test or the result of some tests was falsely negative, of course, our high sample size solves this problem

Declarations

Consent for publication   Not applicable.

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

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