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Original Article

Investigation of Risk Factors for Hospitalization of COVID-19 Patients with Diabetes in Najaf, Iraq

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Abstract

Preliminary findings indicate that patients with diabetes mellitus (DM) are at additional risk of infecting with COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is associated with increased mortality in these patients. Hyperglycemia can affect inflammatory and immune responses, which leads patients to severe COVID-19 consequences. The present study investigated risk factors for hospitalized COVID-19 patients with DM in Najaf, Iraq. 127 patients with positive PCR tests were selected from Al-Hakeem Hospital and Al-Sadr Teaching Hospital. Demographic characteristics and laboratory data were collected to compare patients with and without DM. Chi-squared test followed by odds ratio calculations were used to investigate the risk factors associated with hospitalization of COVID-19 patients with or without DM in the ICU and RCU. Analysis of the relationship between risk factors indicated that age above 65 years, high BMI, hypertension, respiratory rate> 24 BPM, CVD, blood sugar> 180 mg/dl, D-dimer> 1000, ALT> 50 and AST> 40 U/L were independent risk factors for hospitalized COVID-19 patients with DM ($P \leq 0.05$). Therefore, investigating these factors may detect the risk of infection with COVID-19 in patients with DM in advance. Physicians should further consider risk factors to discover a targeted intervention to improve clinical efficacy.

Keywords: COVID-19, Diabetic Patients, Risk Factors

1. Introduction

The first human case of COVID-19 was confirmed in Wuhan, China, in December 2019 (1). The World Health Organization (WHO) declared the outbreak of a new coronavirus a Public Health Emergency of International Concern (PHEIC) in January (2). COVID-19 was more prevalent in patients with DM, associated with increased mortality, disease severity, and hospitalization. In addition, patients with DM tend to develop severe complications, including respiratory tract infections, multiple organ dysfunction syndromes, and eventual death (3). A weakened immune system is one of many factors thought to increase infection of COVID-19 in patients with DM. DM can also weaken the response of humoral immunity disorders, including T cells and neutrophils (4), leading to increased susceptibility to infections. Therefore, DM is one of the most important predisposing factors of COVID-19, which increases the severity of the condition and mortality rate.

The general appearance of COVID-19 patients with DM can help manage those at risk of being hospitalized (5). The association between uncontrolled diabetes and COVID-19 is controversial. Several studies have reported that disturbance in controlling DM occurs in patients with COVID-19 (6). Others considered uncontrolled diabetes a crucial risk factor that increases the severity of COVID-19 and mortality. Therefore, the

present study investigated risk factors for hospitalized COVID-19 patients with DM.

2. Materials and Methods

2.1. Study Design and Data Collection

Clinical data of 127 patients with positive PCR tests were collected from Al-Hakeem Hospital, and Al-Sadr Teaching Hospital from March to June 2021, among which 102 patients had DM and 25 patients had no DM.

2.2. Demographic Characteristics and Clinical Data

Demographic characteristics and clinical data, including age, gender, BMI, systolic and diastolic blood pressure, respiratory, comorbidities, CVD, cough, fever, fatigue, myalgia, duration of diabetes, and headache, were collected to compare patients with and without DM. Laboratory findings included: fasting blood sugar, HbA1c, D-dimer (µg/L), ALT, and AST (U/L).

2.3. Statistical Methods

Continuous variables are presented as Mean±SD, and categorical variables were presented as frequency (N) and percentage (%). Differences between patients with type 1 and type 2 diabetes (T1D and T2D) and patients without DM were assessed using ANOVA for continuous variables. While the Chi-squared or Fisher's exact test was used for categorical variables. Risk factors for correlation were assessed using an odds ratio with a 95% confidence interval analysis. A *P*-value of less than 0.05 was considered statistically significant. Data analysis was performed using SPSS software (version 25.0).

3. Results

Clinical data of 127 patients with positive PCR tests were collected from Al-Hakeem Hospital, and Al-Sadr Teaching Hospital from March to June 2021, among which 102 patients had DM and 25 patients had no DM. Most of the participants in the present study were COVID-19 patients with T2D (Figure 1). The mean age of patients without DM and patients with DM (T1D and T2D) were 46.16±9.46, 69.58±14.65, and 60.06±16.44 years, respectively. A significant difference (P<0.0001) was observed between the groups, indicating that the patients with DM were older than those without diabetes. Also, 43.30% of the population were women, and 56.69% were men. A significant difference (P<0.00001) in body mass index (BMI) was observed between the patients with DM and those without DM, which revealed that the group with T2D was obese. Systolic blood pressure was found to be significantly (P<0.00002) different between patients with T1D and T2D compared to those without DM. The respiratory rate of COVID-19 patients with T2D (53.85%) was 24 BPM higher. The cardiac disease has major consequences in patients with DM (61.5% and 56.76%). Cough (78.46% and 67.58%), fever (91% and 81%), fatigue (98.46% and 100%), myalgia (100% and 97.30%), and headache (100% and 100%) were the most frequent symptoms in COVID-19 patients with DM compared to COVID-19 patients without DM. While the laboratory data revealed significant differences between groups with and without DM in fasting blood sugar (P<0.00001), D-dimer (P=0.05), ALT (P=0.01), and AST (P=0.0007) (Table 1). The relationship between the two groups showed that the risk of death was 8 times more in patients with DM (RR= 8.08, 95% confidence interval (1.1614-56.3288), P=0.0348) (Table 2). The present study measured the relationship between COVID-19 patients with and without DM using an odds ratio. The higher odds ratio in hospitalized COVID-19 patients with DM was related to age over 65 years, BMI more than 25, blood pressure (systolic blood pressure >120 and diastolic blood pressure >80), respiratory rate ≥ 24 BPM, CVD, increased blood sugar, D-dimer, ALT, and AST (Table 3). The results revealed that the risk of death was 8 times more in patients with DM. Also, over 65 years (OR, 8.25; 95% CI, 1.35-50.59; P=0.03), BMI (OR, 3.12; 95% CI, 1.26-7.77; P=0.02), blood pressure (OR, 2.64 ; 95% CI , 1.08-6.45; 0.04), respiratory rate> 24 BPM (OR, 3.26; 95% CI, 1.25-8.48; P=0.01), CVD (OR, 3.53; 95% CI, 1.41-8.83; P=0:005), blood sugar > 180 mg/dl (OR, 9.48; 95% CI 3.54-25.09; P<0.0001), D-dimer > 1000 (OR, 8.64; 95% CI 1.11-66.99; P=0.01), ALT > 50 (OR, 3.11; 95% CI 1.21-8.03; P=0.02) and AST > 40 U/L (OR, 3.88; 95% CI, 1.55-9.77; P=0.003) were independent risk factors for the hospitalized COVID-19 patients with DM (Table 3).

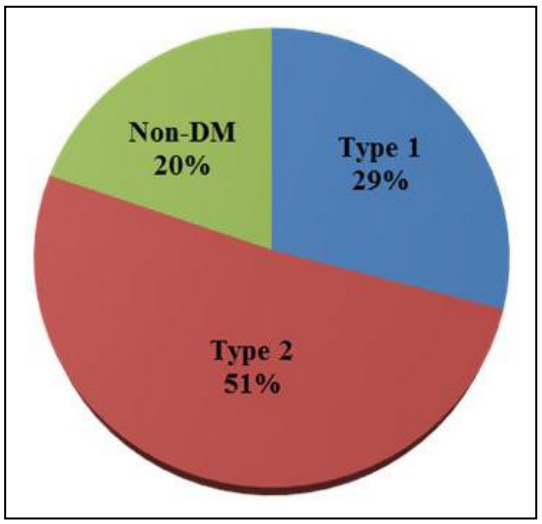

Figure 1. Prevalence of DM in COVID-19 patients in the study

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

Parameters	Total (n=127)	Non-DM (n=25)	T1D (n=37)	T2 D (n=65)	*P*-value
Demographic Characteristics					
Age (mean±SD)	60.09 ± 16.75	46.16 ± 9.46	69.58±14.65	60.06 ±16.44	< .00001
Gender (n%)					0.337
Male	72(56.69)	11 (44)	23 (62.16)	38 (58.46)	
Female	55 (43.30)	14 (56)	14 (37.84)	27 (41.54)	
Duration (years) (mean±SD)	N/A	N/A	26.73± 14.77	10.03 ± 7.33	N/A
BMI (mean±SD)	24.61 ± 3.93	22.04 ± 3.30	24.25 ± 0.60	26.20 ± 4.21	< .00001
Systolic Blood Pressure (n%)					0.00002
<120 mmHg	33 (25.98)	15 (60)	10 (27.03)	8 (12.31)	
≥120 mmHg	94 (74.02)	10 (40)	27 (72.97)	57 (87.69)	
Diastolic Blood Pressure (n%)					0.322
<80 mmHg	40 (31.50)	8 (32)	15(40.54)	17 (26.15)	
≥80 mmHg	87 (68.50)	17 (68)	22 (59.46)	48 (73.85)	
Respiratory Rate > 24 BPM (n%)	64 (50.40)	7 (28)	22 (59.46)	35 (53.85)	0.037
Comorbidities					
CVD	69 (54.33)	8 (32)	21(56.76)	40 (61.5)	0.039
Cough	95(74.80)	19 (76)	25 (67.58)	51(78.46)	0.47
Fever	112(88)	23(92)	30 (81)	59 (91)	0.278
Fatigue	126 (99.21)	25(100)	37 (100)	64 (98.46)	0.618
Myalgia	125 (98.43)	24(96)	36 (97.30)	65 (100)	0.317
Headache	126 (99.21)	24 (96)	37 (100)	65 (100)	0.127
Laboratory Findings					
Fasting Blood Sugar (mean ±SD)	262.47 ±133.47	131.08 ± 64.49	283.83 ± 121.32	312.54 ± 135.20	< .00001
HbA1c (mean ±SD)	N/A	N/A	5.12 ± 0.19	8.02 ± 0.67	N/A
D-dimer (μg/L)(n, %)					
<1000	99 (77.95)	24(96)	28 (75.68)	47 (72.31)	0.05
≥1000	28 (22.05)	1(4)	9 (24.32)	18 (27.69)	
ALT (U/L)					
>50	99 (77.95)	15 (60)	27 (72.97)	57 (87.69)	0.01
≤50	28 (22.05)	10 (40)	10 (27.03)	8 (12.31)	
AST (U/L)					
>40	79 (62.21)	9 (36)	20 (54.05)	50 (76.92)	0.0007
≤40	48 (37.79)	16 (64)	17 (45.95)	15 (23.08)	

Table 2. Possibility of death from COVID-19 in patients with diabetes

Subjects	Died	Survived	Total
DM	33	69	102
Non-DM	1	24	25
Total	34	93	127

RR,8.08; 95% confidence interval (1.1614- 56.38); *P*=0.0348

Table 3. Risk factors of hospitalization for COVID-19 patients with DM

Subjects	OR (95% CI)	*P*-value
Age (years) >65	8.25(1.35-50.59)	0.03
BMI >25	3.12(1.26-7.77)	0.02
Blood pressure (Systolic blood pressure >120 - Diastolic blood pressure > 80)	2.64 (1.08-6.45)	0.04
Respiratory rate ≥ 24 BPM	3.26 (1.25-8.48)	0.01
CVD	3.53 (1.41-8.83)	0.005
Blood Sugar (mmol/L) >180 mg/dl	9.48 (3.54-25.09)	<0.0001
D-dimer (µg/L) ≤1000 >1000	8.64 (1.11-66.99)	0.01
ALT (U/L) ≤50 >50	3.11 (1.21-8.03)	0.02
AST (U/L) ≤40 >40	3.88 (1.55-9.77)	0.003

4. Discussion

The present retrospective cohort study was conducted on 127 COVID-19 patients consisting of 102 patients with DM and 25 patients without DM to investigate the role of hospitalized COVID-19 patients. The present study's findings can be summarized as follows: (i) DM in the elderly is associated with high BMI, systolic blood pressure, D-dimer, ALT, and AST, which exposes this group of patients to be hospitalized in the ICU and RCU. Older patients with DM and respiratory rate> 24 BPM, D-dimer, ALT, and AST> 40 U/L are more likely to be admitted to ICU and RCU. The mean age of COVID-19 patients with DM was higher than those without DM. (ii) In general, patients with DM were 8 times more likely to die than those without DM. (iii) Data analysis indicated an association between the prevalence of other significant comorbidities in various studies and the present one. The present study's findings are consistent with those of other cohort studies, indicating that elderly patients are more susceptible to severe COVID-19, ICU admission, and eventual death (7). Age over 65 years should be indicated as a vital factor in hospitalizing COVID-19 patients with or without DM in ICU or RCU. These findings may be related to the impaired immune system and aging (8, 9). In particular, any dysfunction of B and T cells and markers of hyper inflammation is associated with viremia and inflammation, which leads to severe complications and death with aging (3). This means that COVID-19 patients with DM who are prone to critical events and need to be admitted to the ICU or RCU may be associated with age-related inflammatory response disorders and immunodeficiency.

Additionally, the levels of HbA1c> 7% were considered a risk factor for hospitalization in COVID-19 patients with DM. Previous studies have stated that patients with uncontrolled HbA1cl are at risk for infections, worse prognosis, and even death than those with controlled HbA1c (10). Studies have shown that high blood sugar levels are associated with worsening COVID-19 in patients with DM (11-13). Chronic hyperglycemia was believed to reduce ACE-2 expression and make cells more susceptible to the damage of SARS-CoV-2 (14). SARS-CoV-2 can directly damage β-cells and control the level of blood sugar (15). Furthermore, hyperglycemia can impair immune function, especially the innate immune system, which increases inflammatory cytokines like IL-6 (11, 16). The results indicated that increased HbA1c in

COVID-19 patients with diabetes exacerbates the disease, which leads to ICU admission; therefore, the severity of COVID-19 patients with DM is associated with glycemic control. However, the study's limitations were the lack of data on the concentration of inflammatory cytokines (MCP1, interleukin-6, IFN-γ, and IL-1β) to explore if the cytokine draft occurred in COVID-19 patients. Also, many cases failed to have an HbA1c test; therefore, their role was ignored in managing blood sugar.

Furthermore, the results of liver function tests were studied in COVID-19 patients with and without DM in the present study. Patients with DM indicated elevated levels in liver function tests compared to those in patients without DM. The higher levels of AST> 40 unit/L and ALT> 50 unit/L are associated with an increased probability of RCU and ICU admission in COVID-19 patients with DM. The results of the present study are consistent with other studies which reveal liver dysfunction in patients with severe COVID-19 (17). Some researchers believe that liver injury may be due to the direct interaction of the virus with the liver cells or synergize with the immune response (18, 19). Such findings may be suggested the importance of routine observation of liver tests in hospitalized COVID-19 patients.

D-dimer has already been used for signs of hypercoagulability. Coagulation abnormalities associated with elevated D-dimer have been found in COVID-19 patients (20). Severe hypoxia in patients with acute respiratory distress syndrome (ARDS) leads to activation of the extrinsic pathway and subsequent increase in viscosity and blood coagulation in COVID-19 infection (21).

The present study observed respiratory rate > 24 BPM in COVID-19 patients with DM. Systemic inflammation is associated with DM and lung dysfunction (22, 23). DM is a chronic, low-grade inflammatory disease (24). Severe acute respiratory syndrome coronavirus -2 cooperates with the islets and consequently intensifies the inflammatory system of DM (25). Likewise, other studies have shown that lung invasion of the SARS-CoV-2 through angiotensin-converting enzyme 2 (ACE2) leads to a risk of respiratory dysfunction and hypoxemia (26). Overall, COVID-19 patients with DM are more prone to develop deterioration of lung function, which is associated with acute conditions that lead to ICU admission. Similarly, the present study found a significant difference between breath shortness in patients with or without DM. A significant reduction in forced vital capacity and expiratory volume may produce poor outcomes in COVID-19 patients with DM in a short time (27).

The present study indicated that COVID-19 patients with DM were the majority of hospitalized patients. Also, many medical risk factors such as aging, high BMI, blood sugar > 180 mg/dl, respiratory rate > 24 BPM, HbA1c > 7%, D-dimer > 1000 (μg/L), ALT > 50, and AST > 40 U/L were investigated in hospitalized COVID-19 patients with DM. Therefore, various causes of COVID-19 should be investigated in patients with DM in the early stages to provide suitable treatment for them.

Authors' Contribution

Study concept and design: A. J. A.
Acquisition of data: S. L. I.
Analysis and interpretation of data: Z. F. M.
Drafting of the manuscript: Z. F. M.
Critical revision of the manuscript for important intellectual content: S. L. I.
Statistical analysis: S. L. I.
Administrative, technical, and material support: S. L. I. and A. J. A.

Ethics

The present study was approved by the Ethics Committee of the Faculty of Pharmacy, University of Kufa, Najaf, Iraq. Written consent was obtained from patients after fully explaining the purpose of all methods.

Conflict of Interest

The authors declare that they have no conflict of interest.

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