World Journal of

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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

  WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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Case Control Study

Risk and predictors of severity and mortality in patients with type 2 diabetes and COVID-19 in Dubai

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Abstract

BACKGROUND

Globally, patients with diabetes suffer from increased disease severity and mortality due to coronavirus disease 2019 (COVID-19). Old age, high body mass index (BMI), comorbidities, and complications of diabetes are recognized as major risk factors for infection severity and mortality.

AIM

To investigate the risk and predictors of higher severity and mortality among in-hospital patients with COVID-19 and type 2 diabetes (T2D) during the first wave of the pandemic in Dubai (March–September 2020).

METHODS
In this cross-sectional nested case-control study, a total of 1083 patients with COVID-19 were recruited. This study included 890 men and 193 women. Of these, 427 had T2D and 656 were non-diabetic. The clinical, radiographic, and laboratory data of the patients with and without T2D were compared. Independent predictors of mortality in COVID-19 non-survivors were identified in patients with and without T2D.

RESULTS
T2D patients with COVID-19 were older and had higher BMI than those without T2D. They had higher rates of comorbidities such as hypertension, ischemic heart disease, heart failure, and more life-threatening complications. All laboratory parameters of disease severity were significantly higher than in those without T2D. Therefore, these patients had a longer hospital stay and a significantly higher mortality rate. They died from COVID-19 at a rate three times higher than patients without. Most laboratory and radiographic severity indices in non-survivors were high in patients with and without T2D. In the univariate analysis of the predictors of mortality among all COVID-19 non-survivors, significant associations were identified with old age, increased white blood cell count, lymphopenia, and elevated serum troponin levels. In multivariate analysis, only lymphopenia was identified as an independent predictor of mortality among T2D non-survivors.

CONCLUSION
Patients with COVID-19 and T2D were older with higher BMI, more comorbidities, higher disease severity indices, more severe proinflammatory state with cardiac involvement, and died from COVID-19 at three times the rate of patients without T2D. The identified mortality predictors will help healthcare workers prioritize the management of patients with COVID-19.

Key Words: Type 2 diabetes; COVID-19; Risk factors; Mortality; United Arab Emirates

Core Tip: Globally, patients with diabetes suffer from increased disease severity and mortality due to coronavirus disease 2019 (COVID-19). Old age, high body mass index (BMI), comorbidities, and complications of diabetes were recognized as major risk factors for infection severity and mortality. To identify the independent predictors of mortality in patients with type 2 diabetes (T2D) in Dubai, United Arab Emirates, we performed a cross-sectional nested case-control study during the first wave of the pandemic. It seems that the mortality of patients with T2D is driven by a significantly higher pro-inflammatory response to COVID-19 as evidenced by higher C-reactive protein, white blood cell, and lymphopenia. Mortality also seems to be synergistic with the comorbidities and complications of T2D in patients with COVID-19. The identified mortality predictors will help healthcare workers prioritize the management of patients with COVID-19.

INTRODUCTION

It has been established that older age, higher body mass index (BMI), and comorbidities such as diabetes mellitus, hypertension, cardiovascular disease (CVD), and chronic kidney disease (CKD) are the major risk factors for severity and mortality of coronavirus disease 2019 (COVID-19) infection in patients in China[1,2], United Kingdom[3,4], United States [5-7], Sweden[8] and many other countries[9,10]. Evidence of higher severity and mortality of COVID-19 in patients with diabetes has been reported in many of the aforementioned studies and confirmed by others[11-14]. Systematic reviews [15] and meta-analyses[16-20] have established that the severity of COVID-19 in patients with diabetes is observed across all ethnicities. Similar observations were recorded in the United Arab Emirates during the first and subsequent waves of the pandemic[21-26].

The aim of this retrospective study was to determine the risk and predictors that drove the higher severity among in-hospital patients with COVID-19 and type 2 diabetes (T2D) and to describe the relationship between diabetes and all-cause mortality during the first wave of the pandemic in Dubai, United Arab Emirates.

MATERIALS AND METHODS

Study design
During the early phase of the COVID-19 pandemic, Dubai Hospital, where the study was conducted, was among the three main centers designated for the isolation and admission of all patients with COVID-19 in the Emirate of Dubai. Dubai Hospital is a specialized hospital equipped with 625 beds and incorporates 26 surgical and medical departments, including the intensive care unit (ICU), cardiology, oncology, nephrology, and endocrinology. During the first wave of the COVID-19 pandemic, most hospital wards were converted into isolation units. In this cross-sectional nested case-control study, 1083 patients with COVID-19 admitted to Dubai Hospital between March 21st and September 30th, 2020, were recruited.

Patients
All patients positive for COVID-19 were admitted to hospital. Patients were tested using reverse transcription-polymerase chain reaction (RT-PCR) using a nasopharyngeal swab for respiratory tract infection to test for COVID-19. A total of 1083 patients were randomly recruited for the study. This study included 890 men and 193 women. Of these patients, 427 had T2D and 656 did not.

Patients with type 1 diabetes were excluded. This was based on their previous medical history collected from the SALAMA Electronic Health Records (EHR) and confirmed upon admission. The following clinical data were obtained from the EHR: Age (13–87 years), sex (men/women), nationality (emirates/expatriates), and comorbidities [hypertension, ischemic stroke, cardiomyopathy, heart failure, chronic obstructive pulmonary disease, asthma, and diabetic ketoacidosis]. The following presenting symptoms were recorded at admission: Fever, cough, shortness of breath, sore throat, chest pain, myalgia, headache, chills, fatigue, malaise, loss of appetite, runny nose, abdominal pain, loss of taste, loss of smell, vomiting, diarrhea, dizziness, confusion, skin rash, and arthralgia. Noninvasive ventilation, intubation, and admission to the ICU were also recorded.

Clinical parameters
The mean ages of the patients were 51 and 39 years for those with and without T2D, respectively. Demographic features and the presence of co-morbidities, such as a prior diagnosis of cardiac disease, hypertension, diabetes, or respiratory disease, and any medication used were recorded. Patients were further categorized as asymptomatic, mild, moderate, severe, or critical according to the National Institutes of Health categorization of COVID-19 severity[26], as follows:

Asymptomatic: Patients have no symptoms but have tested positive for COVID-19.

Mild: Patients have symptoms and signs such as fever, cough, sore throat, malaise, headache, or muscle pain, but no shortness of breath, dyspnea, or abnormal chest radiography.

Moderate: Patients had clinical or imaging findings suggestive of lower respiratory disease but maintained an oxygen saturation of > 93% on room air.

Severe: The respiratory rate (RR) of the patients was above 30/min, oxygen saturation was ≤ 93%, PaO2/FiO2 was < 300, and/or pneumonic infiltrates involving > 50% of the lungs were observed.

Critical: Patients suffer respiratory failure, septic shock, and/or multiple organ dysfunction.
The vital signs recorded at the time of admission included blood pressure, heart rate, RR, SpO_2, and temperature.

Data collection
Data were collected from all patients with and without T2D from the Dubai Hospital SALAMA Electronic Medical Record System. The information collected was categorized into demographic data, medical and glycemic histories, physical examination results, comorbidities, laboratory investigation results, chest radiographs, complications, and treatment protocols. The collected data were entered into an SPSS data collection sheet explicitly designed for this study. All patient data were de-identified throughout the collection, categorization, and creation of the database. The reporting of this study conformed to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines[27].

Laboratory and imaging data:
Laboratory measurements recorded for patients with COVID-19 included complete blood count, ferritin, absolute lymphocyte count, lactate dehydrogenase, procalcitonin, C-reactive protein (CRP), creatine phosphokinase, D-dimer, pro-BNP, serum creatinine, fasting blood glucose, and Hb_{A1C}.

Chest X-ray scoring: A chest radiograph severity scoring system was used to determine the severity of the pneumonia. The images were also classified as exhibiting ground-glass opacities, reticular patterns, or consolidations and as normal, mild, moderate, or severe.

Treatment protocol
The management and Treatment of COVID-19 followed the United Arab Emirates Guidelines[28]. which are based on the National Institutes of Health (NIH) guidelines (NIH, 2021)[29]. After a thorough assessment of clinical severity, all patients with COVID-19 were treated (March–September 2020) with a standard combination of hydroxychloroquine

sulfate and Kaletra antiviral (lopinavir/ritonavir). Therefore, there were no differences in drug management between patients with and without T2D. Patients were considered cured after two consecutive negative (determined through RT-PCR) nasopharyngeal swabs following clinical recovery.

Statistical analysis

Data were analyzed using SPSS for Windows version 28.0 (SPSS Inc., Chicago, IL, United States). Categorical variables are described as percentages. Continuous variables were described using a measure of tendency and dispersion. Continuous data were tested for normality using the Kolmogorov-Smirnov test. The Mann-Whitney U test and *t*-test were used when appropriate to compare the means between continuous variables. Categorical variables were cross-tabulated to examine the independence between variables, the χ^2 test or Fisher's exact test was used as appropriate.

Kaplan-Meier estimates were used to examine the effect of T2D on survival. The estimate was based on the serial time to death of patients with T2D and controls. The results of the computed model are visualized in a survival plot (Figure 1). In addition to the Kaplan-Meier analysis, univariate and multivariate analyses containing all the variables that differed statistically between survivors and non-survivors were performed to identify the independent predictors of mortality among patients with COVID-19 and T2D. Statistical significance was set at $P < 0.05$.

RESULTS

Demographic characteristics

A total of 1083 patients (890 men and 193 women) diagnosed with COVID-19 were enrolled in this study. Among the men, 378 (42%) had T2D, whereas among the women, only 49 (25%) had T2D. The mean age of patients with T2D is 51.4 (± 11.2), whereas for patients without T2D is 39.4 (± 13.5) ($P < 0.001$). There was also a significant difference in BMI between patients with T2D [28.80 (± 5.47)] compared to patients without T2D [27.20 (± 4.94)] ($P < 0.001$).

The demographic characteristics and comorbidities of patients with T2D and patients without are shown in Table 1. Patients with T2D and COVID-19 had higher rates of comorbidities, such as hypertension, ischemic heart disease, and heart failure compared to patients with COVID-19 without T2D.

Presenting symptoms and signs

Only dyspnea, cough, sore throat, and headache were significantly more frequent in patients with T2D (Table 1).

Laboratory measurements

All 18 Laboratory measurements indicative of disease severity were significantly higher among patients with T2D (Table 1).

Radiographic and severity indices of chest infection

Chest radiographs of patients with COVID-19 and T2D exhibited significantly more lung consolidation, ground-glass appearance, and severity than patients without (Table 1). Consequently, COVID-19 patients with T2D had significantly lower SpO$_2$ saturation and required more noninvasive assisted ventilation as well as frequent mechanical ventilation. They also had more life-threatening complications, such as diabetic ketoacidosis and acute kidney failure. Therefore, these patients had longer hospital stays and significantly higher mortality rates.

Treatment protocols

All patients with COVID-19 were treated (March-September 2020) with a standard combination of hydroxychloroquine sulfate and Kaletra antiviral medication (lopinavir/ritonavir). Therefore, there were no differences in drug management between patients with and without T2D.

The frequency and/or absolute values of independent predictors of mortality between survivors and non-survivors of COVID-19, with and without T2D

In general, patients with COVID-19 with T2D were 12 years older than those without T2D (Table 1). In addition, non-survivors were older than survivors in both groups (Table 2). On admission, there were no significant differences in the symptoms between the two groups.

Most laboratory indicators of disease severity were equally high among the COVID-19 non-survivors in each group (Table 2). The association of radiographic and severity indices of chest infection with mortality in patients with COVID-19 was also equally high among the patients in each group. Therefore, most risk factors for severity and predictors of mortality in T2D non-survivors and controls were similar, with few exceptions (Table 2).

The relationship between glycemic control and mortality

The relationship between random blood glucose, fasting blood glucose and blood Hb$_{A1C}$, and mortality among patients with COVID-19 and T2D was tested using the Mann-Whitney U test and found to be statistically insignificant.

Predictors of mortality among non-survivors of COVID-19 with T2D

Predictors of mortality were determined in non-survivors of COVID-19 with and without T2D, using univariate analysis.

Table 1 Demographic characteristics, comorbidities, symptoms, signs, laboratory measurements, radiographic and severity indices of chest infection, and disease outcome observed in coronavirus disease 2019 patients with and without type 2 diabetes; in Dubai

Characteristics	T2D (*n* = 427)	Without T2D (*n* = 656)	*P* value[a]
A: Demographics and comorbidities [*n* (%)]			
Gender	No (%)		
Male	378 (42.5)	512 (57.5)	
Female	49 (25.4)	144 (74.6)	< 0.001
Nationality			
United Arab Emirates	23 (59)	16 (41)	
Expatriate	404 (38.7)	640 (61.3)	0.009
Hypertension	165/427 (38.6)	88/656 (13.4)	< 0.001
Ischemic heart disease	21/427 (4.9)	3/656 (0.5)	< 0.001
Cardiomyopathy	2/427 (0.5)	0/656	0.155
Heart failure	13/427 (3)	4/656 (0.6)	0.002
COPD	2/427 (0.5)	1/656 (0.2)	0.344
Asthma	10/427 (2.3)	18/656 (2.7)	0.421
B: Symptoms and signs [*n* (%)]			
Fever	358 (85.9)	528 (82.8)	0.105
Cough	303 (72.7)	388 (60.8)	< 0.001
Sore throat	52 (12.5)	150 (23.5)	< 0.001
Running nose/rhinorrhoea	17 (4.1)	40 (6.3)	0.079
Shortness of breath (dyspnoea)	276 (66.2)	250 (39.2)	< 0.001
Chest pain	22 (5.3)	29 (4.5)	0.344
Chills	13 (3.1)	35 (5.5)	0.047
Headache	24 (5.8)	74 (11.6)	< 0.001
Fatigue	92 (22.1)	116 (18.2)	0.071
Malaise	8 (1.9)	15 (2.4)	0.405
Nausea	11 (2.6)	17 (2.6)	0.572
Loss of appetite/anorexia	19 (4.6)	22 (3.4)	0.226
Loss of taste	1 (0.2)	6 (0.9)	0.164
Anosmia/loss of smell	1 (0.2)	6 (0.9)	0.164
Abdominal pain	12 (2.9)	46 (7.2)	0.001
Vomiting	39 (9.4)	47 (7.4)	0.150
Diarrhoea	26 (6.2)	34 (5.3)	0.312
Myalgia	123 (29.5)	180 (28.2)	0.351
Arthralgia/joint pain	1 (0.2)	2 (0.2)	0.635
Dizziness	10 (2.4)	21 (3.3)	0.259
Confusion	4 (1.0)	2 (0.3)	0.216
Skin rash	1 (0.2)	1 (0.2)	0.635
C: Laboratory measurements [mean (± SD)]			
Haemoglobin (g/dL)	12.42 (2.07)	13.45 (1.84)	< 0.001
MCV (fL)	85.66 (37.79)	84.54 (7.74)	0.01
WBC (10^9/L)	9.62 (7.87)	8.31 (7.25)	< 0.001

Lymphocyte (%)	14.57 (8.52)	18.46 (10.08)	< 0.001
Absolute lymphocyte count	1.05 (0.82)	1.26 (0.78)	< 0.001
Random blood glucose (mg/dL)	222.53 (114.59)	119.16 (42.75)	< 0.001
Fasting blood glucose POCT (mg/dL)	192.06 (88.88)	126.77 (48.38)	< 0.001
Hb_{A1C} (%)	9.26 (2.44)	5.74 (0.47)	< 0.001
CRP (mg/L)	86.38 (88.05)	50.23 (64.68)	< 0.001
Troponin (ng/mL)	180.10 (917.58)	18.29 (64.11)	< 0.001
D-Dimer (mcg/mL)	4.14 (6.43)	2.46 (5.04)	< 0.001
Pro-calcitonin (ng/mL)	0.97 (4.2)	0.61 (3.18)	< 0.001
Pro-BNP (pg/mL)	1948.56 (4602.46)	1533.62 (6449.57)	0.008
Ferritin (mcg/L)	1526.7 (2153.81)	1231.68 (3268.65)	< 0.001
LDH (U/L)	444.93 (371.05)	355.55 (243.98)	< 0.001
LDH-Peak (U/L)	429.27 (393.39)	366.62 (585.83)	< 0.001
CPK peak (U/L)	597.8 (1090.39)	505.5 (2055.57)	0.022
Creatinine (mg/dL)	1.87 (2.12)	1.16 (1.44)	< 0.001
D: Chest radiographs, ventilation and disease outcome [No (%)]			
Normal chest radiograph	16 (3.8)	99 (16.5)	< 0.001
Mild consolidation [1-2 zones]	174 (41.7)	342 (57.1)	
Moderate consolidation [2-3 zones]	183 (43.9)	125 (20.9)	
Severe consolidation [3-4 zones]	44 (10.6)	33 (5.5)	
E: SpO$_2$ on admission			
≤ 94	84 (19.7)	64 (9.8)	< 0.001
> 94	343 (80.3)	592 (90.2)	
F: Ventilation and/or intubation			
O$_2$ mask	58 (13.6)	43 (6.6)	< 0.001
Nasal canula	311 (72.8)	361 (55)	< 0.001
Intubation	42 (9.8)	15 (2.3)	< 0.001
G: Complications & Outcomes			
Diabetic keto acidosis	7 (4.5)	0	0.01
Chronic kidney failure	37 (10.5)	16 (3)	< 0.001
Length of hospital stay, mean (days)	14.90 (17.31)	7.49 (10.22)	< 0.001
Death: No (%)	63/427 (14.8)	32/656 (4.9)	< 0.001

[a]*t*-test, Mann-Whitney and Chai Square.
COPD: Chronic obstructive pulmonary disease; WBC: White blood cell; CRP: C-reactive protein; LDH: Lactate dehydrogenase; T2D: Type 2 diabetes; MCV: Mean corpuscular volume; POCT: Point of care testing; CPK: Creatine phospho-kinase.

Among the eight clinical and 12 Laboratory risk factors (Table 2), significant associations of mortality of COVID-19 in patients with and without T2D were identified with advanced age, increased total white blood cell (WBC) count, lymphopenia, and elevated serum troponin. In multivariate analysis, only lymphopenia was identified as a predictor of mortality in patients with T2D.

Survival analysis of COVID-19 patients based on T2D status using Kaplan-Meier estimates.

Kaplan-Meier analysis was used to compare survival against serial time to death between patients with and without T2D (Figure 1). The median time of death among patients without T2D is less than that among patients with T2D [42 d with 95%CI: 32.2–51.8 and 54 d with 95%CI (23.3–84.7)]; respectively. This difference was not statistically significant because 95% of the CIs overlapped. However, the number of deaths was significantly higher among patients with T2D [63 (14.8%)] than among patients without T2D [36 (5.5%)], with *P* < 0.001 (Table 3).

Table 2 The association between demographic characteristics, comorbidities, symptoms, signs, laboratory measurements, radiographic and severity indices of chest infection and disease outcome observed in coronavirus disease 2019 patients with and without type 2 diabetes in Dubai

Characteristics	T2D (*n* = 427)			Without T2D (*n* = 656)		
	Survivors (*n* = 364)	Non-survivors (*n* = 63)	*P* value	Survivors (*n* = 624)	Non-survivors (*n* = 32)	*P* value[a] < 0.001
A: Demographics and comorbidities [*n* (%)]						
Males: No (%)	325 (86)	53 (14)	0.164	484 (94.1)	30 (5.9)	0.072
Females: No (%)	39 (79.6)	10 (20.4)		140 (98.6)	2 (1.4)	
Age: Yr (± SD)	50.76 (10.92)	54.86 (12.58)	0.02	38.83 (13.42)	48.58 (12.43)	< 0.001
BMI (±SD)	28.81 (5.53)	28.69 (5.08)	0.841	27.15 (4.95)	28.03 (5.05)	0.400
Hypertension, No (%)	137 (37.6)	28 (44.4)	0.188	77 (12.4)	11 (30.6)	0.005
B: Symptoms and signs [*n* (%)]						
Fever	306 (86.4)	52 (82.5)	0.26	502 (82.8)	26 (81.0)	0.484
Cough	256 (72.3)	47 (74.6)	0.418	359 (59.2)	29 (90.6)	< 0.001
Sore throat	50 (14.1)	2 (3.2)	0.007	146 (24.1)	4 (12.5)	0.093
Dyspnea	224 (63.3)	52 (82.5)	0.002	222 (36.6)	28 (87.5)	< 0.001
Headache	23 (6.5)	1 (1.6)	0.097	73 (12)	1 (3.1)	0.095
C: Laboratory measurements [mean (± SD)]						
Hemoglobin (g/dL)	12.69 (2.06)	10.95 (1.36)	< 0.001	13.6 (1.7)	10.7 (1.2)	< 0.001
MCV (fL)	85.98 (41)	83.95 (7.28)	0.815	84.4 (7.6)	86.2 (10)	0.223
WBC (10^9/L)	9.02 (6.56)	12.86 (12.41)	< 0.001	7.6 (4.75)	18.9 (20.4)	< 0.001
Lymphocytes (%)	15.48 (8.59)	9.55 (6.1)	< 0.001	18.79 (9.7)	13.1 (13.3)	< 0.001
Absolute lymphocyte	1.13 (0.84)	0.57 (0.5)	< 0.001	1.3 (0.7)	1.2 (1.6)	< 0.001
Random glucose (mg/dL)	221.52 (115.69)	227.94 (109.3)	0.442	118.8 (43.6)	124.4 (62.3)	0.026
Fasting glucose (mg/dL)	107.46 (114.85)	118.1 (121.74)	0.191	118.8 (43.6)	52.5 (68)	< 0.001
Hb$_{A1C}$ (%)	9.32 (2.4)	8.87 (2.64)	0.13	5.73 (0.5)	5.9 (0.4)	0.586
CRP (mg/L)	76.23 (77.72)	141.1 (116.77)	< 0.001	44.6 (56)	138 (108)	< 0.001
Troponin (ng/mL)	167.19 (990.22)	238.21 (470)	< 0.001	15.9 (64.5)	37.6 (58.4)	< 0.001
D-Dimer (mcg/mL)	3.09 (4.53)	9.56 (10.79)	< 0.001	1.78 (3.84)	8.9 (9.1)	< 0.001
Procalcitonin (ng/mL)	0.83 (4.32)	1.75 (3.45)	< 0.001	0.51 (3.01)	1.9 (4.72)	< 0.001
Pro-BNP (pg/mL)	1225.01 (3572)	3862.9 (6248.31)	0.007	1324.5 (7323)	2109.1 (2985.8)	< 0.001
Ferritin (mcg/L)	1277.9 (1599.2)	2888 (3749)	< 0.001	856.2 (1179)	5549.9 (10016)	< 0.001
LDH (U/L)	416.41 (365.96)	611.04 (360.04)	< 0.001	321.1 (164.7)	785 (521.5)	< 0.001
LDH-Peak (U/L)	402.02 (394.6)	605.2 (339.82)	< 0.001	346.3 (587.3)	644.1 (491.3)	< 0.001
CPK peak (U/L)	464.9 (970.7)	1163.5 (1369.5)	< 0.001	432.8 (2145.6)	1041.2 (1085)	< 0.001
Creatinine (mg/dL)	1.61 (2.01)	3.22 (2.17)	< 0.001	1.02 (1.22)	3.2 (2.55)	< 0.001
D: Chest radiographs, ventilation and disease outcome [*n* (mean ± SD)]						
E: Chest radiograph						
Normal X-ray	15 (4.2)	1 (1.6)	0.021	99 (17.4)	0	< 0.001
Mild	156 (43.9)	18 (29)		335 (59)	7 (22.6)	
Moderate	152 (42.8)	31 (50)		11 (19.5)	14 (45.2)	

Severe	32 (9)	12 (19.4)		23 (4)	10 (32.3)	
F: SpO$_2$ on admission						
≤ 94	56 (15.4)	28 (44.4)		574 (92.6)	18 (50)	< 0.001
> 94	308 (84.6)	35 (55.6)	< 0.001	46 (7.4)	18 (50)	
G: Ventilation and/or intubation						
O$_2$ mask	32 (8.8)	26 (41.3)	< 0.001	23 (3.7)	20 (55.6)	< 0.001
Nasal canula	269 (73.9)	42 (66.7)	0.15	340 (54.8)	21 (58.3)	0.408
Intubation	21 (5.8)	21 (33.3)	< 0.001	6 (1.0)	9 (25)	< 0.001
H: Complications & outcomes						
Diabetic ketoacidosis	3 (2.3)	4 (14.3)	0.02			
Chronic kidney failure	19 (6.4)	18 (31)	< 0.001	11 (2.2)	5 (15.2)	0.002
Length of hospital stay: Mean (SD)	14.47 (17.9)	17.02 (14)	0.005	6.47 (8.53)	32 (20.06)	< 0.001

[a]*t*-test, Mann-Whitney and Chai Square.

BMI: body mass index; WBC: White blood cell; CRP: C-reactive protein; LDH: Lactate dehydrogenase; T2D: Type 2 diabetes; MCV: Mean corpuscular volume; CPK: Creatine phospho-kinase.

Table 3 Comparison of the rate of mortality of COVID-19 patients, with and without type 2 diabetes; in successive 5-day intervals of hospital admission, in Dubai

|	Total number of patients (*n* = 1083)	Patients with T2D (*n* = 427)	Patients without T2D (*n* = 656)	Ratio: T2D:Non-T2D
0-5 d	15	10	5	3.1
6-10 d	18	12	6	3.1
11-15 d	20	15	5	4.6
16-20 d	8	4	4	1.53
21-25 d	13	9	4	3.5
26-30 d	8	7	1	10.8
> 30 d	13	6	7	1.3
Total	95	63	32	3.1

T2D: Type 2 diabetes.

Rate of mortality of patients with COVID-19 with and without T2D

The overall ratio of COVID-19 patients who died among patients with T2D was three times that of patients without T2D (Table 3). The ratio remained high in each successive 5-d interval for the first 4 wk of admission but decreased thereafter.

DISCUSSION

In this cross-sectional nested case-control study, we determined the risk factors and predictors that drove higher disease severity and mortality among in-hospital patients with COVID-19 and T2D during the first wave of the pandemic in Dubai, United Arab Emirates. Patients with T2D and COVID-19 seem to have higher rates of comorbidities such as hypertension, ischemic heart disease, and heart failure compared to patients with COVID-19 without T2D. Older men with T2D and high BMI were more prone to severe COVID-19. Dyspnea, cough, sore throat, and headache were significantly more frequent in patients with T2D. All laboratory measurements indicative of disease severity were significantly higher in patients with T2D. On chest radiographs, patients with COVID-19 infection with T2D showed significantly more lung consolidation, glassy appearance, and severity than patients without T2D. Consequently, patients with COVID-19 with T2D had significantly lower SpO$_2$ saturation and required more noninvasive assisted ventilation as well as frequent mechanical ventilation. They also had more life-threatening complications, such as diabetic ketoacidosis and acute kidney failure. Therefore, these patients had more ICU admissions, longer hospital stays, and significantly higher mortality rates.
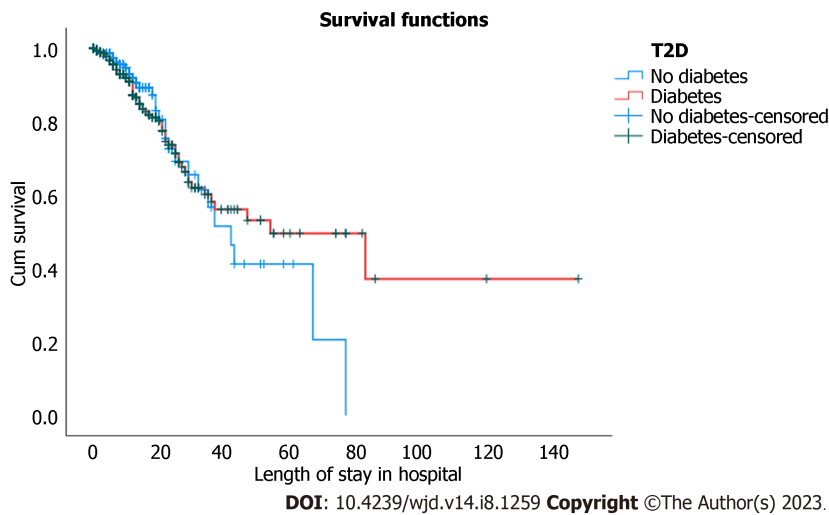
Figure 1 The Kaplan-Meier plot relating survival against serial time to death between coronavirus disease 2019 patients with and without type 2 diabetes. T2D: Type 2 diabetes.

Most laboratory indicators and radiographic and severity indices of chest infection in non-survivors were equally high in patients with COVID-19 with and without T2D. Therefore, we used Kaplan-Meier analysis to explain survival against serial time to death between patients with and without T2D. Although the median time of death among patients without T2D is lower than that among patients with T2D (42 *vs* 54 d), the number of deaths was significantly higher among patients with T2D [63/427 (14.8%)] than among patients without T2D [32/656 (4.9%)]. The overall ratio of patients with T2D dying is three times higher than that of patients without T2D. The ratio remained high in each successive 5-d interval for the first 4 wk of admission, but, decreased thereafter.

In addition to Kaplan-Meier analysis of the effect of T2D on survival, univariate and multivariate analyses were performed, including all the variables that differed statistically between survivors and non-survivors, to identify independent predictors of mortality among patients with COVID-19. Initially, predictors of mortality were examined using univariate analysis. Among eight clinical and 12 Laboratory risk factors, significant associations of mortality of COVID-19 in patients with and without T2D were identified with advancing age, increased total WBC count, lymphopenia, and elevated serum troponin. In multivariate analysis, only lymphopenia was identified as a predictor of mortality in patients with T2D.

In this study, we found no relationship between glycemic control and mortality. It cannot be implied that the poorer the glycemic control, the higher the mortality rate. Hyperglycemia *per se* is not an independent predictor of mortality. In contrast, it seems that the mortality of patients with T2D is driven by a much higher inflammatory response to COVID-19 as evidenced by higher CRP levels, higher WBC counts, and lymphopenia. It is also possible that mortality is associated with cardiac damage as evidenced by elevated serum troponin and synergized by the large number of comorbidities and complications observed in patients with T2D[30].

Similar investigations conducted overseas[1-20] and in the United Arab Emirates[21-26], have reported that the prevalence of diabetes in patients with COVID-19 does not differ from that in the general population, indicating that the primary risk of COVID-19 infection is not increased in patients with diabetes. It seems that the increased risk of COVID-19 severity and mortality in patients with diabetes is due to older age and comorbidities, such as hypertension, CVD, CKD, and obesity, in addition to a severe proinflammatory state and cardiac involvement. The risk that patients with diabetes face is that they are more likely to have worse complications and not have a greater chance of contracting the virus[31].

This study demonstrated that patients with COVID-19 with T2D had more comorbidities, higher disease severity, and died at three times the rate of patients without T2D. Identifying the predictors of mortality may allow healthcare workers to prioritize vaccination and implement early management strategies for patients with COVID-19 patients and T2D to offset this calamity.

Limitations

The authors acknowledge the several limitations of this study. It is possible that there was a selection bias in this study, as it was a short-term cross-sectional nested case-control study in which data were collected over a short period in a pandemic environment. In this cross-sectional study, it was not possible to establish causal inferences or analyze temporal changes. Patients could not be followed-up with after discharge, limiting the possibility of further outcomes. Despite these limitations, this study provided data on a large cohort of patients with COVID-19 and T2D with results similar to those of many internationally acknowledged studies.

CONCLUSION

Patients with COVID-19 and T2D were older with higher BMI, more comorbidities, higher disease severity indices, more severe proinflammatory state with cardiac involvement, and died from COVID-19 at three times the rate of patients without T2D. The identified mortality predictors will help healthcare workers prioritize the management of patients with COVID-19.

ARTICLE HIGHLIGHTS

Research background

Patients with diabetes suffer higher morbidity and mortality from corona virus disease 2019 (COVID-19). Despite better outcomes due to vaccination, many patients with diabetes continue to suffer from the disease. It is imperative therefore, to continue investigating the risk and predictors of COVID-19 severity in this vulnerable group, to help shaping better management of the disease.

Research motivation

Identifying independent predictors of mortality from COVID-19 will allow healthcare workers to prioritize vaccination, implement early management strategies for patients with COVID-19 and type 2 diabetes (T2D), and offset disease severity and mortality.

Research objectives

To identify independent mortality predictors among in-hospital patients with COVID-19 and T2D during the first wave of the pandemic (March–September 2020) in Dubai, United Arab Emirates.

Research methods

In this cross-sectional nested case-control study, a total of 1083 patients with COVID-19 were recruited. Of these, 427 had T2D and 656 were non-diabetic. The clinical, radiographic, and laboratory data of the patients with and without T2D were compared. Independent predictors of mortality in COVID-19 non-survivors were identified in patients with and without T2D.

Research results

Patients with T2D and COVID-19 were older and had a higher body mass index than patients without T2D. They had higher rates of comorbidities such as hypertension, ischemic heart disease, heart failure, and more life-threatening complications. All laboratory parameters of disease severity were significantly higher than in those without T2D. Therefore, these patients had a longer hospital stay and a significantly higher mortality rate. These patients died from COVID-19 at three times the rate of patients without T2D. In the univariate analysis of the independent predictors of mortality among all COVID-19 non-survivors, significant associations were identified with old age, increased white blood cell count, lymphopenia, and elevated serum troponin levels. In multivariate analysis, only lymphopenia was identified as an independent predictor of mortality among T2D non-survivors.

Research conclusions

It seems that the increased severity and mortality of patients with COVID-19 and T2D is due to older age and comorbidities such as hypertension, cardiovascular disease, chronic kidney disease, and obesity, with an added severe proinflammatory state.

Research perspectives

It is necessary to further investigate the factors that heighten the pro-inflammatory state, driving higher mortality among patients with T2D and COVID-19.

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FOOTNOTES

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