Diabetes mellitus as an independent predictor of COVID-19 outcomes
Le diabète sucré en tant que facteur prédictif indépendant du pronostic de l'infection au COVID-19

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Abstract

Introduction: COVID-19 is a respiratory disease that can range from asymptomatic to critical or fatal. The severity of the clinical presentation depends on various factors, including comorbidities such as diabetes, which has been shown to be strongly associated with a more severe course and higher mortality rate.

Objectives: This study aims to describe the particularities of COVID-1 infection in diabetic patients, and analyze its prognostic implications.

Methods: This retrospective cross-sectional study analyzed all admitted patients with confirmed COVID-19 in the emergency department of the Farhat Hached University Hospital in Sousse from April 1, 2020, to December 31, 2021.

Results: Out of the 2106 COVID-19 patients, 688 (32.66%) had diabetes. Among these patients, diabetes was pre-existing in 88.1% of cases, while it was inaugural in 11.9%. Our study revealed that diabetes was a poor prognostic factor in COVID-19 cases, associated with up to 1.72 (95% CI 1.41-2.1) times greater risk of severe or fatal forms. This may be due to several factors associated with the diabetic population, including advanced age (p=0.001), the presence of underlying comorbidities (p=0.001), and the presence of hemodynamic instability upon admission (p=0.001). they also exhibited an increased risk of respiratory acidosis (p=0.001) and AKI (p=0.0001). outcomes were less favorable in diabetic patients, with a final hospital mortality rate of 33.9% vs 22.9% in non-diabetic patients (p=0.0001).

Conclusion: Diabetes is one of the comorbidities most associated with the severity of COVID-19 infection. Careful management of diabetic patients with COVID-19 is essential to prevent complications and reduce adverse outcomes.

Keywords: covid19; outcomes; diabetes mellitus; mortality

Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has significantly affected millions of lives worldwide, with its repercussions extending beyond the realm of public health to encompass socioeconomic, psychological, and healthcare delivery aspects.

The emergence of the pandemic has not only posed unprecedented challenges to global healthcare systems but has also exposed the vulnerability of certain populations, including individuals with pre-existing health conditions such as diabetes.

As the world continues to grapple with the multifaceted impacts of the ongoing pandemic, understanding the intricate relationship between COVID-19 and diabetes has become increasingly imperative.

This heightened vulnerability highlights the need for targeted research to guide effective public health responses and clinical management strategies. While existing studies have shed light on the epidemiology and clinical outcomes of COVID-19 in diabetic patients, many questions remain unanswered—particularly regarding risk factors, disease progression, therapeutic approaches, and long-term sequelae specific to this population.

Therefore, this study aims to fill those knowledge gaps by examining the epidemiological, clinical, paraclinical, therapeutic, and prognostic aspects of COVID-19 in people with diabetes. Through detailed data analysis, it seeks to identify key prognostic factors uniquely affecting this high-risk group, and to support more effective, tailored care strategies that can reduce complications and improve outcomes.

Methods

This is a cross-sectional study designed to investigate the clinical outcomes of patients with RT-PCR-confirmed COVID-19, including those with diabetes, at the emergency department of the Farhat Hached university hospital from April 1, 2020, to December 31, 2021.

Patients aged 15 years or older hospitalized for severe acute respiratory syndrome related to SARS-CoV-2 infection associated with known or newly diagnosed diabetes, confirmed by detection of the SARS-CoV-2 viral genome in the upper airways by RT-PCR and/or chest CT findings suggestive of COVID-19 infection, and requiring hospitalization for the treatment for COVID-19 infection were included in the study. Patients with multiple missing data were excluded.

Data were collected using a data processing form from the patients' medical records.

The study collected data on sociodemographic characteristics (age, sex, comorbidities such as diabetes and hypertension, and lifestyle factors), clinical data (symptoms, physical examination findings and severity scores), paraclinical parameters (laboratory results, imagery findings, and biomarkers), therapeutic interventions (oxygen therapy, intubation, medications, and fluid management), and patient outcomes (length of stay, emergency department course, and final hospital disposition).

Statistical Data Analysis The data was analyzed using IBM SPSS software version 23.0 for windows.

Descriptive analysis included calculating frequencies and percentages for qualitative variables and means, standard deviations, medians, and ranges for quantitative variables. Analytical analysis consisted of Student's t-test for comparing means of two independent groups and Pearson's Chi-square test for frequency comparisons. Multivariate analysis was conducted using binary logistic regression to identify independent risk factors associated with disease severity in diabetic patients, incorporating variables with a univariate p-value < 0.2. The significance threshold for all tests was set at $p < 0.05$.

Results

A total of 2106 patients were enrolled in this study. The mean age was 64.48±13.53 years, with extreme ages ranging from 16-95. The most prevalent age group was that of elderly patients aged >65 years (54.30%).The study population showed a male predominance (sex ratio 1.26) and a high prevalence of comorbidities, particularly hypertension (42.1%) and diabetes (32.8%). (table1)

(54.30%). The study population showed a male predominance (sex ratio 1.26) and a high prevalence of comorbidities, particularly hypertension (41.9%) and diabetes (32.7%). (table1)

Table 1: characteristics of the study population

Age (years)		n(%)
	Mean ± SD	66.25±12.15
	Min-max	25-92
Sex ratio (M/F)		1.11
Comorbidities		1506(74.1)
	Diabetes	606(88.1)
	Hypertension	436(63.4)
	Coronary disease	117(17)
	Obesity	122(17.7)
	Smoking	107(15.6)
	Chronic respiratory failure	91(13.2)
	Chronic kidney disease	69(10)
	Tumors	31(4.5)
	Immunosuppressor therapy	18(2.6)
Presenting symptoms		
	Dyspnea	545(79.2)
	Fatigue	477(69.3)
	Cough	475(69)
Respiratory exam		
RR (cpm)	Mean ± SD	24.24 ± 5.63
	Min-max	13-50
spO2 (%)	Mean ± SD	86.96±10.238
	Min-max	40-100
Hemodynamic assessment		
SAP (mm Hg)	Mean ± SD	132.13±17.675
	Min-max	70-240
HR (bpm)	Mean ± SD	89.77±16.682
	Min-max	54-170
GCS	15-14	648(94.2)
	≤13	40(5.8)
EKG abnormalities		330(15.7)
Gasometrical values		
pH	Mean ± SD	7.4±0.1
	Min-max	6.8-7.6
paO2	Mean ± SD	76.8±37.5
	Min-max	40-217
pCO2	Mean ± SD	30.9±7.5
	Min-max	25-66
HCO3-	Mean ± SD	21.4±5.0
	Min-max	3-35.5
Chest CT lesion extent	50-75%	467(22.20)
	<25%	1339(63.60)
	25-50%	177(8.40)
	>75%	123(5.80)
Oxygen Therapy/Ventilation		
Nasal Cannulas		320 (46.5)
High-Concentration Mask		238 (34.6)
Optiflow		25 (3.6)
Non-invasive Ventilation		231 (33.6)
Intubation		8 (1.2)
ED LOS (days)	Mean ± SD	2.45 ± 2.19
ED mortality		132 (19.2)
In-hospital referral		688(77.2)
ICU need		108 (15.7)
Final Outcome		
Discharge		455 (66.1)
Total in-hospital mortality		233 (33.9)

In a comparative analysis between 688 diabetic and 1418 non-diabetic patients admitted to our emergency department, diabetic individuals tended to be older, while non-diabetics were predominantly male. Moreover, diabetic patients exhibited a higher prevalence of comorbidities (74.1% vs 60.4%), particularly hypertension and renal failure, compared to their non-diabetic counterparts. Symptomatically, diabetics displayed a greater occurrence of respiratory distress such as dyspnea, cough, fever, and fatigue, while non-diabetics reported more issues related to smell and taste. Physiologically, diabetics typically had higher blood pressure levels, whereas non-diabetic patients showed more electrocardiogram abnormalities except for arrhythmias, which were more common in diabetics. Medical complications further distinguished the two groups, with diabetics being more prone to acute renal failure and non-diabetics to respiratory acidosis. Interestingly, imaging findings did not significantly differ between the groups. Treatment-wise, diabetic patients often required higher oxygen flow rates through a high-flow mask and were more likely to need curative and preventive anticoagulation, Calciparin, and antibiotic therapy. The mean and range of emergency department visits were similar between the two groups (p=0.113 and p=0.599, respectively). However, the course of the emergency department hospitalization was less favorable for diabetic patients, with a worsening in diabetic patients (p=0.0001) and a mortality rate of 19.2% compared to 10.4% for non-diabetic patients (p=0.0001). The final outcome showed a higher mortality rate in diabetic patients (33.9%) compared to non-diabetic patients (22.9%) (p=0.0001) (table 2).

In the multivariate analysis, diabetes was associated with up to 1.72 times higher risk of severe or fatal disease when comparing survival and death rates between diabetic and non-diabetic patients (CI95%=1.41-2.10, p=0.001) (table 3).

Discussion

Coronavirus disease (COVID-19), caused by SARS-CoV-2, exhibits a wide spectrum of severity, from asymptomatic to life-threatening respiratory distress. Elderly individuals and those with certain underlying conditions, notably diabetes, face an elevated risk of severe illness and mortality(1,2). Diabetes mellitus is prevalent among COVID-19 patients and is associated with higher rates of hospitalization, ICU admissions, complications, and mortality(3–7). Our study, encompassing 688 diabetic COVID-19 patients, revealed that advanced age, preexisting comorbidities along with clinical indicators are predictive of severity. Comparison with non-diabetic counterparts highlighted that diabetic patients were older with more comorbidities, particularly coronary artery disease , hypertension , and renal failure , and presented with more severe symptoms including dyspnea, cough , fever , and fatigue (8). They also exhibited higher rates of acute renal failure and required more aggressive therapeutic interventions, anticoagulation, and antibiotics. Notably, diabetic patients experienced a significantly higher case fatality rate both in the emergency department and throughout hospitalization, emphasizing the heightened risk associated with diabetes in the.

Table 2: Results of the univariate analysis

			Diabetic patients n= 688 (%)	Non diabetic patients n=1418 (%)	p
Comorbidities			510(74.1)	857(60.4)	0.001
Coronaropathy			117(17.0)	127(9.0)	0.001
Hypertension			436(63.4)	446(31.5)	0.001
CKD			69(10.0)	71(5.0)	0.001
Smoking			107(15.6)	271(19.1)	0.046
		Physical exam			
Dyspnea			545(79.2)	1033(72.8)	0.002
Cough			475(69.0)	910(64.2)	0.027
Fever			379(55.1)	658(46.4)	0.001
Fatigue			477(69.3)	887(62.6)	0.002
Anosmia/Dysgeusia			53(7.7)	169(11.9)	0.003
BP	Mean		132.13±17.675	129.56±15.394	
	Min-max		80-240	90-200	0.001
EKG	Normal		580(84.3)	1137(80.2)	0.022
	Sinus tachycardia		42(6.1)	149(10.5)	
	Repolarization disorders		33(4.8)	65(4.6)	
	Conduction disorders		23(3.3)	51(3.6)	
	Arrythmia		10(1.5)	16(1.1)	
Respiratory acidosis			26(3.8)	64(4.5)	0.001
AKI			198(28.8)	219(15.4)	0.001
Oxygen therapy	HFM		238(34.6)	422(29.8)	0.025
Anti coagulation	No		50(7.3)	151(10.6)	0.007
	Enoxaparin	curative	419(60.9)	850(59.9)	
		preventive	201(29.2)	395(27.9)	
	Calciparin		15(2.2)	11(0.8)	
	HNF		3(0.4)	11(0.8)	
Antibiotherapy	No		67(9.7)	232(16.4)	0.001
	3GC-ofloxacin		363(52.8)	719(50.7)	
	3GC		246(35.8)	455(32.1)	
	Amoxicillin-clavulanic acid		12(1.7)	12(0.8)	
Outcomes	Stable		318(46.2)	604(42.6)	0.001
	Improvement		212(30.8)	575(40.6)	
	Aggravation		158(23)	239(16.9)	
In-hospital referral			351(77.2)	1212(85.4)	0.001
Discharge			25(3.6)	58(4.1)	0.001
Emergency mortality rate			132(19.2)	148(10.4)	0.001
Final outcome	Death		233(33.9)	325(22.9)	0.001
	Discharge		455(66.1)	1093(77.1)	

Table3: Results of the multivariate analysis

	Surviving(%)	Deceased(%)	OddsRatio	IC 95%	P
Age>65	64.5	35.5	5.54	2.07 - 9.10	<10-3
Cardiopathy	64.6	35.4	1.64	1.29-2.09	0.01
Diabete mellitus	65.8	34.2	1.72	1.41 - 2.10	0.01
Choc signs	21.5	78.50	1.32	1.11-2.88	0.01
Glasgow coma score <13	33.9	66.10	2.22	1.71-2.88	0.01
Acidosis	50.9	49.10	1.52	1.37-1.69	0.01
Acute renal failure	49.4	50.60	3.89	3.11-4.87	0.01
Chest CT lesions extent>50%	57.7	42.30	3.88	2.45-6.87	<10-3

context of COVID-19. Multivariate analysis confirmed diabetes as an independent risk factor for severe or fatal disease.

With regard to average age, several studies of the diabetic population reported similar results, with diabetic patients being statistically older than non-diabetic patients(9–11).

Numerous studies have shown advanced age increases the risk of mortality (12–14). In regards to gender, studies show a male predominance(15,16). The male-related severity observed may be attributed to hormone-dependent modulation of ACE2 and TMPRSS2 expression, facilitating SARS-CoV-2 cellular entry, as well as higher prevalence of comorbidities like cardiovascular disease in males(17,18).

When it comes to comorbidities, diabetic patients exhibited higher comorbidity rates across multiple studies, particularly for hypertension and cardiovascular disease (19,20). Our study corroborates these findings, indicating significantly higher rates of hypertension and cardiovascular disease among diabetic patients (p=0.0001).

Numerous studies have highlighted the association between comorbidities and the severity of COVID-19, with diabetes and hypertension being significant predictors of mortality in many cases, with multipliers ranging from 1.2 to 8.96 (21–25).

The initial finger-prick blood glucose levels upon admission in COVID-19 patients have been found to exhibit a range of diabetic decompensations including inaugural diabetes (26–29).

Numerous studies have demonstrated the prognostic significance of glycemic control in COVID-19 patients. Hyperglycemia upon admission is associated with higher mortality rates and increased risk of complications such as acute respiratory distress syndrome(8,28,30).

In our study, diabetic decompensation upon admission was significantly associated with mortality in univariate analysis (p=0.02), consistent with findings from other studies.

The biological data analysis in COVID-19 patients widely reported the presence of lymphopenia (106). Studies have reported varying prevalence rates, ranging from 29.8% to 55.4% in diabetic patients(8,10,31–34). Comparing diabetic and non-diabetic groups, lymphopenia was significantly more prevalent in the diabetic group (8,35).

Gazometric abnormalities, including respiratory alkalosis, respiratory acidosis, and metabolic alkalosis, have been frequently observed in COVID-19 patients. Studies have reported varying distributions of these abnormalities, with respiratory alkalosis being the most common(36–39). However when comparing gazometric values between diabetic and non-diabetic patients, literature results have been inconsistent(19).

Other biological data were analyzed, including renal function, liver function, pancreatic enzymes, and inflammatory markers concluding that the diabetic group had higher rates of AKI compared

to non-diabetics while no statistically significant difference was found in liver function (8,11,12).Elevated inflammatory markers were noted in various studies(32,43,44). Patients with COVID-19 showed higher levels of CRP (p=0.06) and interleukin-6 (IL-6) (p=0.07) compared to non-diabetic patients(35,45).

CT scan findings have reportedly shown more severe lung lesions in diabetic patients(35,44,46–50), however our study did not find a significant difference (p=0.863).

When it comes to oxygenation and ventilation, diabetic patients exhibited higher NIV usage compared to non-diabetics with usage rates ranging from 13.3% to 30.3% across different studies (19,28).Although some studies suggested greater intubation rates in diabetic patients(15), our study found similar rates between the two groups (p=0.944).

Corticosteroid therapy remains controversial in COVID-19 treatment due to concerns about immunosuppression, delayed viral clearance, bacterial infections, and acute hyperglycemia(51,52). Their usage did not significantly differ between diabetic and non-diabetic patients in our study, consistent with findings from previous research(53). However, in diabetic patients, careful monitoring of blood glucose levels is essential due to their hyperglycemic potential (54,55).

Length of hospital stay is an important factor in COVID-19 outcomes, with prolonged stays associated with increased mortality risk(56). Studies differ on this finding , while length of stay was statistically more prolonged in diabetic patients than in non-diabetic patients in some (8,28,57), it was comparable in others(19).

Regarding the outcome of COVID-19, diabetes significantly impacts the prognosis and progression of COVID-19, with studies consistently showing it as one of the most important comorbidities linked to disease severity. Early data from Wuhan, China, and international studies reported a prevalence of diabetes ranging from 12% to 25% in COVID-19 patients, with diabetes being associated with increased morbidity and mortality during previous viral pandemics(8,58).

Diabetes is associated with critical complications of COVID-19, such as acute respiratory distress syndrome (ARDS), the need for ICU admission, mechanical ventilation, and increased mortality rates. Studies comparing diabetic and non-diabetic COVID-19 patients consistently show a higher percentage of severe forms and ICU admissions among diabetics. Additionally, diabetic patients have a higher percentage of mortality following COVID-19 compared to non-diabetic patients(32,33,59–65).

Conclusion

Our study found a substantial increase in the risk of critical COVID-19 infection among individuals with diabetes. The mortality rate was also significantly higher. Therefore, it is crucial to implement customized prevention and control measures to reduce the risk of viral transmission among vulnerable populations, and to tailor in hospital treatments to reduce mortality.

Chatbot use: *An AI program (DeepL write) was used for linguistic correction and improving coherence of the manuscript.*

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