Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor: Unexpected high mortality in COVID-19 and diabetic ketoacidosis

To the Editor

Patients with diabetes mellitus (DM) appear to be at a greater risk for severe symptoms and complications, including death from COVID-19 [1,2]. DM is a common comorbidity in patients affected with COVID-19 and may cause ketosis, ketoacidosis, and diabetic ketoacidosis (DKA) [3]. In patients with DM, acute hyperglycemic crises such as DKA and hyperosmolar hyperglycemic state can be precipitated by an acute illness such as COVID-19 and it can result in catastrophic outcomes. At Jacobi Medical Center, an epicenter of the COVID-19 pandemic crisis, we noted that a significant proportion of patients with COVID-19 also presented with DKA. We identified 50 such patients admitted with COVID-19 from March 10th to April 30th of 2020 who concomitantly had DKA upon admission or developed DKA during their hospital course. DKA was defined as blood glucose >250 mg/dL, an elevated anion gap, and positive ketones in blood or urine. COVID-19 was confirmed by real-time reverse-transcription polymerase chain reaction (PCR) assay (BioReference Laboratories, Elmwood Park, NJ).

Among the evaluated patients, 32 (64%) were male, the median age was 59 years (IQR 42.3–70), 16 (31%) were Hispanic, 15 (30%) were African American, and the median body mass index (BMI) was 27.15 kg/m^2 (see Table 1). Six of the 50 patients (12%) had a previous diagnosis of Type 1 DM with a median hemoglobin A1C (HbA1C) before the admission of 11%. Forty-four (88%) patients had previously diagnosed type 2 DM and their median HbA1c before the admission was 8.05%. Eight patients (16%) had previously undiagnosed DM. Twenty (40%) patients were on oral hypoglycemic agents with only 2 on SGLT2 inhibitors (which are known to increase the risk of ketoacidosis), 24 (48%) were on a home insulin regimen, and 4 (8%) patients were receiving treatment with GLP-1 agonists.

The median value of the initial glucose on presentation in our sample population was 506.5 mg/dL (252.0–1485.0 mg/dL). Forty-three (86%) patients were treated with intravenous insulin infusion protocol and 7 (14%) were treated with subcutaneous insulin protocol. The mean insulin and the intravenous fluids requirements in the first 24 h were 115. 5 units and 3000 mL respectively. Thirty-eight (76%) patients developed acute kidney injury (AKI) during admission, 11 (22%) patients required renal replacement therapy, 26 (52%) required intensive care unit (ICU) admission, 21 (42%) were intubated, and 25 (50%) patients died. The median length of stay was 9 days (range 1–31); one patient was still admitted at the time of data evaluation.

In general, patients who died (50%) were older than those who survived (mean age 65.2 vs. 49 years), had higher ferritin (mean 8229.6 vs. 3373.4 ng/mL), and higher C-reactive protein levels (mean 355.3 vs. 167.2 mg/L). Mortality was higher in males than females (65.6% vs. 22.2%), and in patients who developed AKI (60.5%), who required dialysis (90.9%), and intubation (80.9%) (see Table 2).

In conclusion, mortality in patients with COVID-19 and DKA at our institution was higher than expected when compared with patients admitted historically with DKA in the United States [4] and the mortality for hospitalized COVID-19 patients in our area [5,6]. Many of these patients developed AKI which likely contributed to the increased risk of adverse outcomes. As has been previously described, in our analysis, age and male sex were associated with higher mortality in patients with COVID-19 and DKA [7,8]. Moreover, majority of our patients were Hispanic or African American, and it has been proposed that these patients have a higher risk of mortality from COVID-19 [9,10]. Interestingly, majority of these patients with DKA had type 2 diabetes and contrary to expectation many did not have poorly controlled diabetes mellitus before admission [11,12]. This suggests that COVID-19 can contribute to the development of hyperglycemic crisis in patients with diabetes irrespective of glycemic control. Previous studies with the related virus SARS CoV have suggested a role of pancreatic beta cell damage in worsening hyperglycemia [13,14] [15]. Future research is needed to explore mechanisms for why COVID-19 infection leads to the development of DKA and high mortality rates.

Author contributions

NCP, SP, JA, and PK contributed to the design and implementation of the data collection, and to the analysis of the results. All author's discussed the results and contributed to the final manuscript.

Declaration of competing interest

Authors' have no conflict of interest and this work was not supported by any external funding.

Abbreviations: DM, diabetes mellitus; DKA, diabetes ketoacidosis; PCR, reverse-transcription polymerase chain reaction; BMI, body mass index; HbA1C, hemoglobin A1C; ICU, intensive care unit.

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Table 1
Characteristics of the study population.

Demographics
Gender – no./total no. (%)
Male 32/50 (64)
Female 18/50 (36)
Race – no./total no. (%)
Asian 1/50 (2)
Black 15/50 (30)
Hispanic 16/50 (32)
Other 8/50 (16)
Unknown 7/50 (14)
White 3/50 (6)
Age (years)
Median 59
Interquartile range (IQR) 42.3–70.0
BMI (kg/m^2)
Median 27.15
Interquartile range (IQR) 23.2–33.0
Diabetes history – no./total no. (%)
Previously undiagnosed diabetes 8/50 (16)
Type 1 DM 6/50 (12)
Type 2 DM 44/50 (88)
Home antidiabetic regimen – no./total no. (%)
Insulin 24/50 (48)
Oral hypoglycemic agents 20/50 (40)
Metformin 17/50 (34)
Sulfonyl urea 4/50 (8)
DPPIV inhibitors 3/50 (6)
SGLT2 inhibitors 2/50 (2)
GLP-1 agonist 4/50 (8)
Laboratory values
Most recent HbA1c before admission (%) no./total no. (%)
HbA1c ≥ 8 14/50 (28)
HbA1c < 8 10/50 (20)
HbA1c unknown 26/50 (52)
HbA1c on admission (%)- no./total no. (%)
HbA1c ≥ 8 30/50 (60)
HbA1c < 8 4/50 (8)
HbA1C unknown 16/50 (32)
Initial glucose level upon presentation
Median (range) – mg/L 506.5 (252.0–1485.0)
Anion gap
Median (range) – mEq/L 28.1 (14.3–41.2)
Ketones
Median (range) – mmol/L 2.22 (0.44–11.7)
Ferritin
Median (range) – ng/mL 1215.0 (50.0 to >100,000.0)
C-reactive protein
Median (range) – mg/L 246.7 (3.4–620.8)
D-Dimer
Median (range) – ng/mL 33,369.0 (164.0- >69,000.0)
Therapy
Insulin – no./total no. (%)
Subcutaneous 7/50 (14)
Intravenous Infusion 43/50 (86)
Insulin needs/24 h
Median (range) – units 115.5 (9.0–240.0)
Fluids/24 h
Median (range) – mL 3000.0 (1000.0–8000.0)
Outcomes at a median of 9 days (range, 1–31) – no./total no. (%)
Acute kidney injury 38/50 (76)
Renal replacement therapy 11/50 (22)
Intubation 21/50 (42)
ICU care 26/50 (52)
Death 25/50 (50)
Remained hospitalized 1/50 (2)
Discharged from hospital 24/50 (48)

Table 2
Comparison of variables between deceased vs non-deceased patients.

Characteristics	Deceased	Non-deceased
Age – years		
Mean (SD)	65.2 (15.0)	40.0 (17.5)
Male		
No./total no. (%)	21/50 (42)	11/50 (22)
Female		
No./total no. (%)	4/50 (8)	14/50 (28)
BMI – kg/m^2		
Mean (SD)	28.8 (7.0)	28.7 (7.9)
Initial glucose – mg/dL		
Mean (SD)	544.3 (211.9)	575.6 (304.8)
Ferritin – ng/mL		
Mean (SD)	8229.6 (21,416.0)	3373.4 (7505.4)
C-reactive protein – mg/L		
Mean (SD)	355.3 (109.9)	167.2 (120.2)
D-Dimer – ng/mL		
Mean (SD)	13,201.4 (20,578.2)	13,698.3 (20,817.3)
Anion gap – mEq/L		
Mean (SD)	26.0 (7.4)	28.3 (7.9)
Insulin requirements/24 h – units		
Mean (SD)	111.3 (64.1)	96.8 (60.2)
Fluids requirements/24 h – mL		
Mean (SD)	2937.0 (1235.5)	3776.5 (1842.1)
Outcomes		
Acute kidney injury (AKI) – no./total no. (%)	23/50 (46)	15/50 (30)
Renal replacement therapy – no./total no. (%)	10/50 (20)	1/50 (2)
ICU care – no./total no. (%)	15/50 (30)	11/50 (22)
Intubation – no./total no. (%)	17 /50(34)	4/50 (8)

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