Diabetic Ketoacidosis in Patients With COVID-19

Diabetic ketoacidosis (DKA) is a common condition causing hospitalization and mortality in patients with Type 1 and Type 2 diabetes mellitus. In the current COVID-19 pandemic, diabetes is a risk factor for poor outcomes in hospitalized patients. Increased glucose levels on admission to the hospital (greater than 180 mg/dL) also predict poor outcomes in these patients.[1] Early reports have indicated that COVID-19 patients with Type I diabetes and DKA had longer lengths of stay, increased rates of acute respiratory distress syndrome, and higher mortality rates.[2] We reviewed patients with COVID-19 presenting with DKA to determine relevant demographic parameters, laboratory values, and outcomes in patients admitted to a tertiary care hospital in West Texas.

The Infectious Disease and Control office at University Medical Center in Lubbock, Texas, provided a list of patients with COVID-19 infections hospitalized between March 1, 2020, and July 20, 2020. Medical records were reviewed to identify patients with a discharge diagnosis of DKA. Seven patients were identified, and their medical records were reviewed to collect information on age, gender, history of diabetes, laboratory tests pertinent to DKA, and outcomes.

These 7 patients had a median age of 39 years; 3 patients were males (Table 1). The median admission body mass index was 29.44 kg/m^2. Six patients had a history of diabetes mellitus; 6 patients had type 2 diabetes and 1 had type 1. The median hemoglobin A1c was 12.8% (available in 5 patients). The median admission glucose level was 311 mg/dL, and the median anion gap was 21 meq/L (Table 2). The median pH was 7.25 (7 patients). All patients were managed with insulin infusions. The median total insulin infusion was 319 total units during the DKA protocol; the individual insulin infusion doses were 45, 69, 83, 319, 529, 1199, and 1541 units. The median time until the anion gap closed twice was 48 h; the individual times were 24, 24, 48, 48, 48, 48, and 144 h. The median fluid balance during insulin infusion was 5660 mls; the individual fluid balances were 3620, 4692, 5427, 5660, 8349, 21,447, and 37,105 ml. Two patients required mechanical ventilation during their hospitalization. No patients required vasopressors or renal replacement therapy. The median length of hospital stay was 4 days; the individual lengths of stay were 3, 3, 4, 4, 5, 22, and 48 days. The mortality rate was 14.3%.

Most patients with DKA and COVID-19 in this study had poorly controlled diabetes. They presented with typical laboratory results seen in other patients with DKA without COVID-19 and responded well to intravenous insulin and fluids. Except for two patients, the length of stay was relatively short. This study suggests that patients with diabetes admitted to the hospital with COVID-19, especially patients with poorly controlled diabetes, should be screened for DKA and monitored for its development during hospitalization.

There is a bidirectional relationship between diabetes and COVID-19.[3] Diabetes increases the risk of severe COVID-19, and COVID-19 increases the risk of hyperglycemia and possibly the development of diabetes. Rao et al. analyzed admission glucose levels in patients hospitalized with COVID-19 infections.[1] This study included 61 patients with a mean age of 62 ± 14 years. The mean admission glucose level was 129.4 ± 57.1 mg/dL in patients who survived and 189.6 ± 112.2 mg/dL in patients who died during hospitalization. An admission glucose greater than 180 mg/dL predicted mortality in a model adjusted for diabetes, age, and male gender. This study suggested that the admission glucose level reflects the overall level of stress in patients with a COVID-19. Alternatively, high glucose levels have metabolic effects which influence outcomes.

Pal et al. published a systematic review of the literature reporting the clinical profiles and outcomes in COVID-19 patients with diabetic ketoacidosis.[2] This report included 110 patients; 63% of the patients were male and 36% were Black. The median age ranged from 45.5 to 59.0 years, and most patients had pre-existing type 2 diabetes. The median glucose levels at presentation ranged from 486 to 569 mg/dL. The in-hospital mortality rate was 45%. The pH was lower in patients who died than in patients who survived.

Patients with COVID-19 often present with significant stress, which may influence the metabolism of glucose resulting from decreased insulin secretion and/or increased insulin resistance associated with increased production of counter regulatory hormones. In addition, pancreatic alpha and beta cells have ACE 2 receptors which could allow the SARS-CoV-2 to bind to the cell surface and directly damage the beta cells.[4] This would reduce insulin secretion. Studies with a nonobese murine model for diabetes demonstrate that these animals develop high levels of circulating ACE 2.[5] Insulin reduces these ACE 2 levels in the serum and in the urine. These animals have increased ACE 2 levels in the lung during the early phase of the development of diabetes, and insulin decreases of these levels. Consequently, it is possible that insulin could limit coronavirus 2 infection in certain tissues. Nakhleh and Shehadeh have argued that patients with type 2 diabetes and COVID-19 requiring hospitalization should have early insulin therapy.[6] They suggested that this approach could control hyperglycemia and, in turn, have positive immunomodulatory effects. The complex interactions among ACE 2 cellular

TABLE 1. Demographics.

Parameter	Median/Number	Individual values
Age, years	39	20, 20, 20 39, 53, 54, 55
Gender	M-3, F-4	
Ethnicity	W-4, H-3	
Hx of DM	Y-6, N-1	
DM type	Type 1−1 Type 2−6	
BMI, kg/m^2	29.44	18.5, 26.8, 27.5, 28.6, 29.4, 34.0, 52.8

M-male; F-female; W-white; H-Hispanic; Y-yes; N-no; Hx-history; DM-diabetes mellitus; BMI-body mass index.

TABLE 2. Laboratory data.

Laboratory test	Median	Individual values
Glucose, mg/dL	311	181, 282, 291, 311, 485, 596, 661
K, meq/L	4.6	3.7, 4.0, 4.3, 4.6, 4.7, 5.1, 6.3
HCO3, meq/L	13	4, 9, 11, 13, 17, 19, 22
AG, meq/L	21	15, 19, 21, 21, 27, 33, 33
BUN, mg/dL	21	6, 14, 18, 21, 26, 36, 52
Cr, mg/dL	0.9	0.4, 0.5, 0.8, 0.9, 1.0, 1.3, 5.2
pH, units	7.25	7.02, 7.18, 7.25, 7.24, 7.3, 7.37, 7.52
PaCO$_2$, mmHg	26.7	11.2, 18.0, 18.9, 26.7, 27.5, 32.5, 41
HA1C,%	12.8	8.0, 12.2, 12.8, 13.7, 14.2

AG-anion gap.

receptors and their varying levels in different tissues, circulating ACE 2 released from cellular membranes, angiotensin II, angiotensin 1−7, and SARS-CoV-2 potentially contribute to both viral infection and associated tissue injury and to host defenses.[7] In addition, elevated glucose levels could cause glucose toxicity and inhibit host defenses.[8]

In summary, patients with COVID-19 and diabetes can present in diabetic ketoacidosis. These patients have the typical laboratory parameters associated with this diagnosis and respond relatively well to intravenous fluids and insulin. In our study, the mortality rate was reasonably low. This might suggest that the presence of diabetic ketoacidosis creates a more focused management strategy or that the use of intravenous insulin limits viral infection. The latter possibility warrants clinical study.

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