



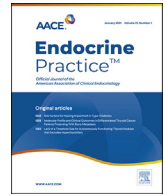
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Original Article

Increase in the Number of Pediatric New-Onset Diabetes and Diabetic Ketoacidosis Cases During the COVID-19 Pandemic

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ABSTRACT

Objective: Infection with SARS-CoV-2 induces a proinflammatory state that causes hyperglycemia and may precipitate diabetic ketoacidosis (DKA) in patients with known or new-onset diabetes. We examined the trends in new-onset diabetes and DKA prior to and following the onset of the COVID-19 pandemic. **Methods:** This single-center retrospective observational study included pediatric patients (aged 0 to <18 years) hospitalized with new-onset type 1 diabetes or type 2 diabetes (T2D) before (March 1, 2018, to February 29, 2020) and after (March 1, 2020 to December 31, 2020) the pandemic onset. Demographic, anthropometrics, laboratory and clinical data, and outcomes were obtained.

Results: Among 615 children admitted with new-onset diabetes during the entire study period, 401 were admitted before the pandemic onset, and 214 were admitted after the pandemic onset. Children admitted with new-onset diabetes in the postpandemic period were significantly more likely to present with DKA (odds ratio, 1.76; 95% confidence interval, 1.24–2.52) than in the prepandemic phase. Children with DKA after the pandemic onset had higher lengths of hospitalization and were significantly more likely to experience severe DKA (odds ratio, 2.17; 95% confidence interval, 1.34–3.52). A higher proportion of children with DKA admitted to the pediatric intensive care unit required oxygen support after the pandemic onset than before the pandemic onset (8.85% vs 1.92%). Most cases of T2D with DKA occurred following the onset of the pandemic (62.5%).

Conclusion: A significant increase in T2D cases occurred following the onset of the COVID-19 pandemic with a greater risk of DKA and severe ketoacidosis. Racial disparity was evident with a higher proportion of Black and American Indian children presenting with ketoacidosis following the pandemic onset.

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Introduction

The first reported cases of COVID-19 caused by infection with SARS-CoV-2 were from Wuhan, China. However, with the rapid global spread of the novel coronavirus infection, the World Health Organization declared COVID-19 a pandemic in March 2020.¹ During the early phases of the pandemic, the rates of COVID-19

among children were lower, and disease manifestation was less severe, than in adults both in the United States and globally.^{2–5} Almost 2-years have elapsed since then, and pediatric cases and hospitalizations are now increasing in the United States likely due to the surge in the highly contagious B.1.1.529 (Omicron) and B.1.617.2 (Delta) variants of the SARS-CoV-2.^{6,7}

Unlike in the adult population, there is yet no clear evidence that children with known diabetes are at increased risk of COVID-19-related hospitalization compared with the general pediatric population.⁸ However, in a prior study among children with serious COVID-19 admitted to 46 pediatric intensive care units (PICUs) across North America, 84% of these critically ill children had underlying comorbidities.⁹ Among them, obesity was an important comorbidity, especially in older children, and diabetes was prevalent in 8% of patients in this PICU cohort.⁹ Several recent studies have also shown an increase in severity at presentation of

Abbreviations: BMI, body mass index; CI, confidence interval; DKA, diabetic ketoacidosis; HbA1C, hemoglobin A1C; IQR, interquartile range; OR, odds ratio; PICU, pediatric intensive care unit; RT-PCR, reverse transcription-polymerase chain reaction; T1D, type 1 diabetes; T2D, type 2 diabetes.

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new-onset diabetes with a higher proportion of children presenting with diabetic ketoacidosis (DKA) during the pandemic than during the earlier time periods.^{10–14} The majority of these studies report on children with primarily type 1 diabetes (T1D) who presented with an increased severity of illness since the onset of the pandemic.^{10–14} Preliminary reports are also emerging of an increase in the hospitalization rates of pediatric cases with new-onset type 2 diabetes (T2D).¹⁵

Further, the COVID-19 pandemic has exposed health inequities in minority communities with a larger burden of underlying chronic diseases such as obesity and diabetes who have also experienced higher coronavirus infection rates and subsequent poor clinical outcomes than the general population, among both children and adults.^{16,17} In a study examining the prevalence of DKA among children and adults with T1D and laboratory-confirmed COVID-19 infection across 52 clinical sites in the United States, Ebekeozien et al¹⁸ found that non-Hispanic Black patients were at almost fourfold higher risk of presenting with DKA than their non-Hispanic White peers after adjusting for potential confounders. The novel coronavirus pandemic seems to have compounded the problem that minority youth already have of exhibiting poor prognostic clinical markers of diabetes at the time of diagnosis that places them at even higher risk of diabetes-associated complications in the future.¹⁹

In this single-center surveillance, we examined the trends, clinical characteristics, and outcome of pediatric patients with new-onset diabetes and DKA, within 2 time periods, prior to the onset of the COVID-19 pandemic, and following the onset of the COVID-19 pandemic. We also examined the predictors of DKA and severe DKA in this cohort of children with new-onset diabetes.

Materials and Methods

This study included pediatric patients aged 0 to <18 years who required inpatient admission for new-onset diabetes (T1D and T2D) management at a tertiary care children's hospital between March 2018 and December 2020. Demographic data, anthropometric measurements, clinical history, laboratory tests at presentation including the results of the reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 if available, medical management, and outcomes were obtained by detailed review of medical records. Eligible patients were categorized into 2 groups for comparison of the severity of clinical characteristics and outcomes based on their time of admission. The first group included children and adolescents who were admitted to the hospital between March 1, 2018, and February 29, 2020, prior to the onset of the COVID-19 pandemic (pre-COVID-19 group), and the second group included those patients who were admitted after March 1, 2020, following the onset of the COVID-19 pandemic (post-COVID-19 onset group). Although the official declaration of the COVID-19 pandemic by the World Health Organization's Director-General occurred on March 11, 2020,¹ in this study, we have included all new-onset diabetes cases presenting on March 1, 2020, or later, in the post-COVID-19 onset group. To assess temporal trends in cases on new-onset diabetes and DKA, the time periods at presentation were reported in quarterly intervals.

On inpatient admission of a patient with new-onset diabetes, diabetes type was determined based on standard criteria.²⁰ A diagnosis of T1D was made if a patient showed the presence of pancreatic islet cell autoantibodies. A patient with a negative insulinoma-associated-2 autoantibodies and glutamic acid decarboxylase 65-kilodalton isoform antibody was suspected as a T2D case. If glutamic acid decarboxylase 65-kilodalton isoform and insulinoma-associated-2 autoantibodies were negative, then additional confirmatory testing was performed in the outpatient setting

with testing for zinc transporter-8 autoantibodies, insulin autoantibodies, and islet cell cytoplasmic autoantibodies. A final diagnosis of T2D was made if these antibodies tested negative and clinical phenotype and family history were consistent with T2D.²⁰ Testing for maturity-onset diabetes of the young (a form of inherited diabetes caused by impairment of insulin production that is not autoimmune in nature)²¹ was performed on a case-by-case basis if clinical (presentation and/or family history) or biochemical evidence suggested possible presence. These children were removed from the data set and are not included in our current analysis.

Children in both the pre-COVID-19 and post-COVID-19 onset groups were also categorized based on the presence or absence of DKA (hyperglycemia, blood glucose level > 200 mg/dL [>11.1 mmol/L], and venous pH < 7.3 or serum bicarbonate level < 15 mEq/L [<15 mmol/L]) and its severity (mild [venous pH 7.2–7.3], moderate [venous pH 7.1–7.2], and severe [venous pH < 7.1] DKA).²² The study was approved by the Institutional Review Board.

Statistical Analysis

The demographic and clinical characteristics were summarized as means and standard deviations or medians and interquartile ranges (IQRs, Q1–Q3) for non-Gaussian variables. We compared the means using the unpaired Student *t* test and the medians using the Mann-Whitney test. Categorical variables were summarized using frequency distributions and were compared using the chi-square test or Fisher exact method. A multivariable logistic regression model was fit to determine whether the time of hospitalization with new-onset diabetes (before or after the onset of the pandemic) was associated with the presence or absence of DKA in the whole cohort (children admitted with new-onset diabetes). A separate logistic regression model was fit in patients admitted with new-onset diabetes and DKA to determine whether the time of hospitalization was associated with the presence or absence of severe DKA (venous pH < 7.1). The adjusted odds ratio (OR) for the presence of DKA and its severity were calculated with 95% confidence intervals (CIs) from these models. All analyses were performed using SAS. A two-sided *P* value of <.05 was considered statistically significant.

Results

New-Onset Diabetes, Both T1D or T2D, Before and After the Pandemic Onset

There were 619 children admitted to our institution with new-onset diabetes, T1D or T2D, between March 1, 2018, and December 31, 2020. Of them, 4 cases with secondary diabetes were excluded from the analysis. Of the remaining 615 patients, 401 were admitted prior to the onset of the COVID-19 pandemic (March 1, 2018, to February 29, 2020), and 214 were admitted following the onset (March 1, 2020, to December 31, 2020). In the whole cohort, 52% of children admitted with new-onset diabetes were male; the majority were non-Hispanic White (49%), and 35% were Hispanic or Latino, with a median age of 11.5 years (IQR, 8.4–14.3 years). The clinical characteristics of the whole cohort included a median body mass index (BMI) of 18.0 kg/m² (IQR, 15.2–25.3 kg/m²), blood glucose at admission of 404 mg/dL (IQR, 311–522 mg/dL), median pH at admission of 7.3 (IQR, 7.1–7.4), median level of bicarbonate from serum electrolytes of 15 mEq/L (IQR, 8–22 mEq/L) and from venous blood gas of 15 mEq/L (IQR, 7–23 mEq/L), and median hemoglobin A1C (HbA1C) level of 11.9% (IQR, 10.6%–13.3%). **Table 1** presents descriptive statistics for the whole cohort stratified by admission period (before or after the onset of the COVID-19 pandemic). **Figure 1 A** shows the relative frequencies of

Table 1
The Characteristics of Children Hospitalized With New-Onset Diabetes

Characteristic	Before the COVID-19 pandemic (n = 401)	During the COVID-19 pandemic (n = 214)	P value
Age (years)	11.3 (8.3-14.2)	11.9 (9.0-14.6)	.0884
Height (cm)	149 (131-162)	153 (133-165)	.0684
Weight ^a (kg)	42.3 (26.8-60.5)	45.7 (28.3-75.0)	.0176
BMI ^a (kg/m ²)	17.5 (15.2-24.1)	18.7 (15.2- 28.8)	.0208
PICU length of stay ^a (days)	0 (0-1)	1 (0-1)	<.0001
Hospital length of stay ^a (days)	3 (2-3)	3 (3-4)	<.0001
Initial blood glucose ^a (mg/dL)	386 (303-518)	416 (335-522)	.0190
Initial pH ^a	7.3 (7.2-7.4)	7.2 (7.1-7.4)	.0008
Initial bicarbonate from serum electrolytes ^a (mEq/L)	17 (9-23)	11 (7-21)	.0001
Initial bicarbonate from venous blood gas ^a (mEq/L)	17 (9-24)	11.5 (6-22)	.0002
HbA1C (%) ^a	11.7 (10.4-12.9)	12.4 (11.0-14.0)	<.0001
Sex, N (%)			.6165
Male	207 (52)	115 (54)	
Female	194 (48)	99 (46)	
Race/ethnicity^a, N (%)			.0050
Non-Hispanic White	203 (50)	97 (45)	
Hispanic White	144 (36)	67 (31)	
Black or African American	31 (8)	23 (10)	
American Indian/Alaska Native	19 (5)	24 (11)	
Asian	4(1)	1 (1)	
Native Hawaiian/Pacific Islander	0 (0)	1 (1)	
Unknown	0 (0)	1 (1)	
Hispanic or Latino, N (%)			.3626
Yes	144 (36)	69 (32)	
No	257 (64)	145 (68)	
Diabetes type^a, N (%)			0.0142
Type I	320 (80)	152 (71)	
Type II	81 (20)	62 (29)	
Admitted at PICU^a, N (%)			0.0004
Yes	157 (39)	116 (54)	
No	244 (61)	98 (46)	
New-onset DKA^a, N(%)			0.0057
Yes	193 (48)	128 (60)	
No	208 (52)	86 (40)	
Disposition, N (%)			0.5760
Discharge at baseline	400 (99)	213 (99)	
Discharge with neurodeficits	1 (1)	1 (1)	

Abbreviations: BMI = body mass index; DKA = diabetic ketoacidosis; HbA1C = hemoglobin A1C; PICU = pediatric intensive care unit.

^a All continuous variables were nonnormal and are summarized as median (interquartile range).

new-onset T1D and T2D that occurred at each quarter after March 1, 2018. Both the relative frequencies of new-onset T1D and T2D showed variability before the onset of the COVID-19 pandemic. The relative frequencies of T2D cases were highest at quarters following the onset of the COVID-19 pandemic (June 2020 to August 2020 and September 2020 to November 2020).

A multivariable logistic regression analysis that adjusted for age, sex, BMI, race/ethnicity (non-Hispanic White vs Hispanic and/or non-White), new-onset diabetes type, and time of admission was fit to determine the factors associated with the presence of DKA during admission in the full cohort (615 children admitted with new-onset diabetes). Race/ethnicity ($P = .0103$), time period of hospitalization ($P = .0017$), and diabetes type ($P = .0002$) were significantly associated with the presence of DKA at presentation in the whole cohort. Non-Hispanic White children with new-onset diabetes had lower odds of presenting with DKA (adjusted OR, 0.61; 95% CI, 0.42-0.89) during the entire study period and after the pandemic onset (adjusted OR, 0.28; 95% CI, 0.13-0.58) than Hispanic and/or non-White children. Children with new-onset diabetes admitted following the onset of the pandemic had higher odds of presenting with DKA (adjusted OR, 1.76; 95% CI, 1.24-2.52) than those admitted before the onset of the COVID-19 pandemic.

New-Onset DKA, Both T1D or T2D, Before and After the Pandemic Onset

Between March 1, 2018, and December 31, 2020, a total of 321 children and adolescents aged 0 to <18 years who were admitted to

the children's hospital with new-onset diabetes had DKA at the time of presentation. Among those admitted for new-onset diabetes, the prevalence rates of DKA were 48% (193/401) before and 60% (128/214) after the pandemic onset, that is, the pandemic was associated with an increase in the prevalence of DKA among those admitted ($P = .0057$). Figure 1 B shows the relative frequency of new-onset DKA cases and T1D and T2D cases with DKA for each quarter after March 1, 2018. The relative frequencies of all new-onset DKA cases showed variability before the onset of the pandemic and were highest at the 3 quarters following the onset of the pandemic. T1D cases followed a similar pattern over time compared to the total new-onset DKA cases. Before the onset of the pandemic, T2D cases tended to be highest at the June-August quarters (in both 2018 and 2019) and lowest at the September-November quarters (in both 2018 and 2019). However, the relative frequencies of T2D cases increased sharply following the onset of the COVID-19 pandemic. Although the relative frequencies of T2D cases increased for both the whole cohort with new-onset diabetes and the cohort of children with DKA, they increased more dramatically in children with DKA. From March 2020 to December 2020, there were 43.36% cases of T2D in the whole cohort versus 62.50% in the DKA cohort (Supplementary Tables 1 and 2).

Table 2 shows the descriptive statistics for demographic and clinical characteristics for the new-onset DKA cohort separately by time period of presentation, before and after the pandemic onset. The median age at admission for the DKA cohort was 11.3 years (IQR, 8.4-13.8 years), and most of the children were male (56%) and

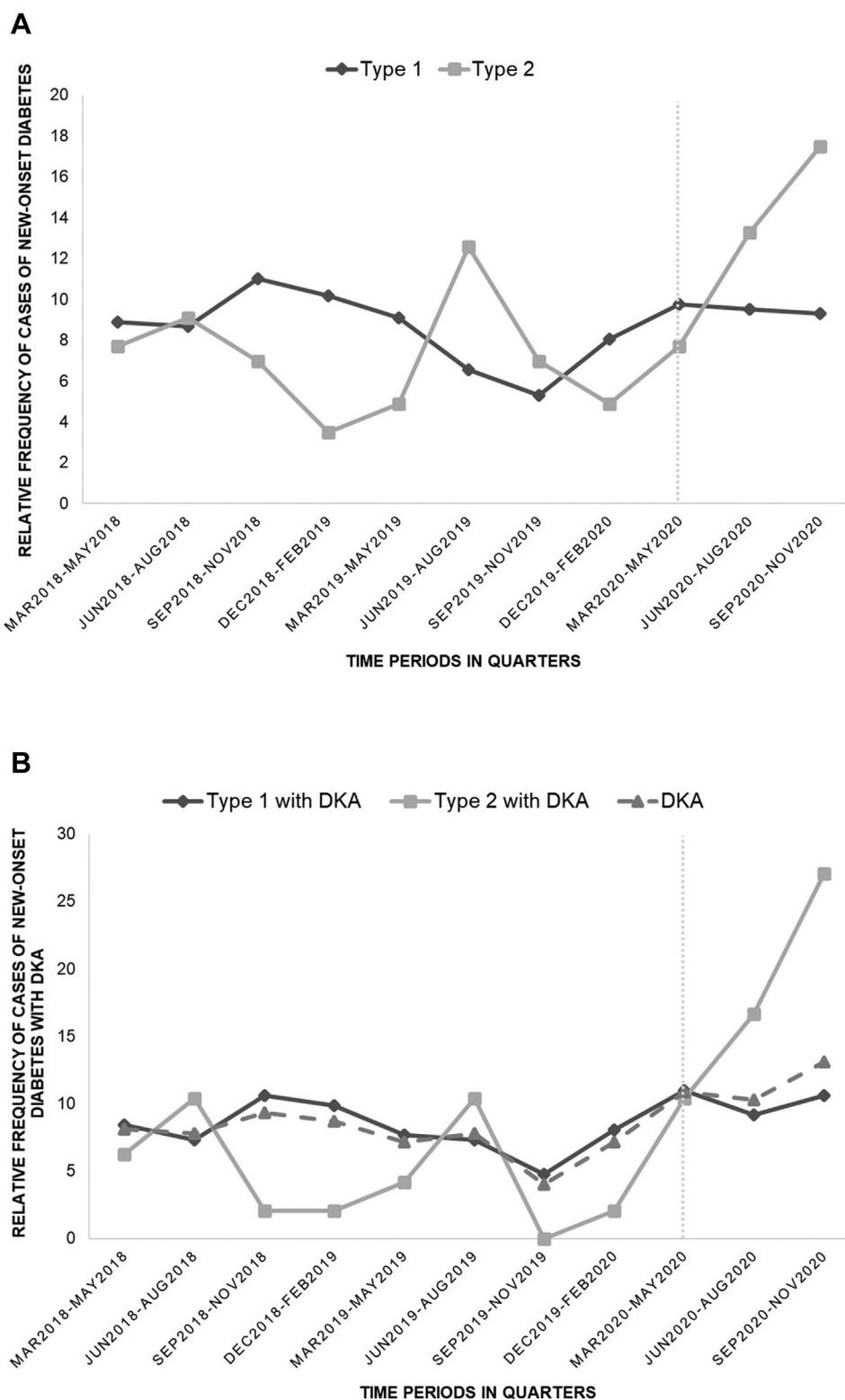


Fig. 1. A, Temporal trends in new-onset diabetes cases during the study period (March 1, 2018, and December 31, 2020) by diabetes type. B, Temporal trends in diabetic ketoacidosis (DKA) among children with new-onset diabetes during the study period (March 1, 2018, and December 31, 2020) in the full cohort and by diabetes type. December 2020 is not included in these figures because data for its quarter are incomplete; data used to create these tables are shown in [Supplementary Tables 1 and 2](#).

non-Hispanic White (49%). The clinical characteristics for the new-onset DKA cohort included the median BMI of 17.1 kg/m² (IQR, 14.8–22.9 kg/m²), median blood glucose at admission of 442 mg/dL (IQR, 364–562 mg/dL), median pH at admission of 7.15 (IQR, 7.03–7.23),

median level of bicarbonate from serum electrolytes of 8 mEq/L (IQR, 5–11 mEq/L) and from venous blood gas of 8 mEq/L (IQR, 5–11 mEq/L), and median HbA1C at admission of 12.3% (IQR, 11.1%–13.5%).

Table 2
The Characteristics of Children Hospitalized With New-Onset DKA

Characteristic	Before the COVID-19 pandemic (n = 193)	During the COVID-19 pandemic (n = 128)	P value
Age (years)	10.9 (8.4-13.8)	11.8 (8.4-13.7)	.2394
Height (cm)	146 (131-161)	153 (133-165)	.0490
Weight ^a (kg)	37.5 (25.4-51.8)	43.0 (26.5-71.0)	.0147
BMI ^a (kg/m ²)	16.7 (14.5-21.0)	18.0 (15.0-27.9)	.0119
Weight for age z-score ^a	-0.09 (-0.89 to 1.26)	0.56 (-0.57 to 1.89)	.0044
PICU length of stay (days)	1 (1-2)	1 (1-2)	.0695
Hospital length of stay ^a (days)	3 (3-4)	4 (3-5)	<.0001
Initial blood glucose (mg/dL)	441 (354-551)	443 (394-580)	.1425
Initial pH ^a	7.18 (7.06-7.25)	7.11 (7.00-7.21)	.0010
Initial bicarbonate from serum electrolytes ^a (mEq/L)	9 (6-12)	7 (5-11)	.0089
Initial bicarbonate from venous blood gas ^a (mEq/L)	8 (6-12)	7 (5-11)	.0257
HbA1C (%) ^a	12.1 (11.0-13.2)	12.5 (11.4-14.0)	.0031
Sex, N (%)			.0971
Male	101 (52)	79 (62)	
Female	92 (48)	49 (38)	
Race/ethnicity^a, N (%)			.0018
Non-Hispanic White	105 (54)	52 (41)	
Hispanic White	65 (34)	44 (34)	
Black or African American	14 (7)	14 (11)	
American Indian/Alaska Native	6 (3)	17 (13)	
Asian	3 (2)	1 (1)	
Hispanic or Latino, N (%)			.8974
Yes	65 (34)	44 (34)	
No	128 (66)	84 (66)	
DKA severity^a, N (%)			.0097
Mild	83 (43)	38 (30)	
Moderate	52 (27)	31 (24)	
Severe	58 (30)	59 (46)	
Diabetes type^a, N (%)			.0005
Type I	175 (91)	98 (77)	
Type II	18 (9)	30 (23)	
Admitted to PICU, N (%)			.0760
Yes	156 (81)	113 (88)	
No	37 (19)	15 (12)	
Disposition, N (%)			.6393
Discharge at baseline	192 (99)	127 (99)	
Discharge with neurodeficits	1 (1)	1 (1)	

Abbreviations: BMI = body mass index; DKA = diabetic ketoacidosis; HbA1C = hemoglobin A1C; PICU = pediatric intensive care unit.

^a All continuous variables were nonnormal and are summarized as median (interquartile range).

There was a significant association between race/ethnicity and time of new-onset DKA ($P = .0035$). The percentage of non-Hispanic White children with new-onset DKA was higher before the pandemic onset than after the pandemic onset (54% vs 41%), whereas the proportions of Black/African American and American Indian/Alaskan Native children were lower before the pandemic onset (7% vs 11% and 3% vs 13%, respectively). The percentages of Hispanic/Latino children remained the same in both time periods (34%). The median weight ($P = .0147$), BMI ($P = .0119$), weight for age z-score ($P = .0044$), and HbA1C (%) using high-performance liquid chromatography ($P = .0031$) values were significantly higher at the postpandemic time period than at the prepandemic time periods. At admission, the median values of venous pH ($P = .0010$), bicarbonate ($P = .0257$) obtained from a venous blood gas sample, and serum bicarbonate ($P = .0089$) were significantly higher for those admitted before the pandemic. The median length of hospital stay was significantly higher for subjects admitted following the onset of pandemic ($P < .0001$).

There were significant associations between diabetes type and time period of admission with DKA ($P = .0005$), between DKA severity and time period of admission ($P = .0097$), and between need for vasopressors and time period of admission ($P = .0424$). The percentages of subjects diagnosed with T2D (23% vs 9%) and/or with severe DKA (46% vs 30%) were higher after the onset of the pandemic than at the immediate prepandemic period. In subjects admitted with DKA before the pandemic onset, 1 (0.52%) patient was administered vasopressors compared with 5 (3.91%) patients

who presented in the postpandemic phase. There were 156 (81%) children admitted to the PICU before the onset of the pandemic and 113 (88%) following the onset. In those admitted to the PICU, the time period of admission significantly was associated with the need for oxygen support ($P = .0089$); in the prepandemic phase, only 3 (1.92%) children needed oxygen support versus 10 (8.85%) in the postpandemic phase. Of those admitted to the PICU with DKA before the pandemic, 3 (1.92%) underwent cerebral imaging, 9 (5.77%) were administered hyperosmolar agents, 1 (0.64%) received oxygen support by a facemask, and 2 (1.28%) required mechanical ventilation. Of those admitted to the PICU with DKA following the onset of the pandemic, 7 (6.19%) underwent cerebral imaging, 9 (7.96%) were administered hyperosmolar agents, 1 (0.88%) received oxygen support via a nasal cannula, 3 (2.65%) received oxygen support using a facemask, and 6 (5.31%) required mechanical ventilation.

We fit a logistic regression model that adjusted for sex, age, BMI, race/ethnicity (non-Hispanic White vs Hispanic and/or non-White), and new-onset diabetes type to determine whether time period was associated with experiencing severe DKA. Children hospitalized following the onset of the COVID-19 pandemic had higher odds of (OR, 2.170; 95% CI, 1.337-3.520; $P = .0017$) experiencing severe DKA than subjects admitted prior to March 2020. No other factors were associated with the presence of severe DKA.

The clinical and demographic characteristics of children with new-onset T1D and T2D before (Supplementary Table 3) and after (Supplementary Table 4) the onset of the COVID-19 pandemic were

compared. In both time periods, children with new-onset T2D were significantly older and had higher BMI and weight for age z-score. Race/ethnicity was significantly associated with diabetes type in both time periods. Before the onset of the COVID-19 pandemic, the PICU length of stay was significantly lower for children with T2D than for children with T1D ($P = .0268$). There was a significant association between diabetes type and DKA severity after the onset of the pandemic ($P = .0105$); the percentages of mild DKA were similar for both types of diabetes, while the percentage of moderate DKA was lower in T1D than in T2D (18% vs 43%), and the percentage of severe DKA was higher in T1D than in T2D (52% vs 27%).

A total of 153 (72%) children underwent RT-PCR testing for SARS-CoV-2 in the postpandemic new-onset diabetes cohort. Of those, 91 children also presented with DKA. In the postpandemic new-onset diabetes group with DKA, 11 (12%) children tested positive for COVID-19 using the RT-PCR test during hospitalization, and of them, 7 (64%) had unknown exposure, and 4 (36%) were exposed by a family member. The average temperature at admission for these 11 children was 37.0 °C. The nonmutually exclusive presenting symptoms of COVID-19 in these 11 children with DKA included abdominal pain in 4 (36%), breathing difficulty in 5 (45%), fatigue in 3 (27%), cough in 2 (18%), and sore throat, vomiting, headache, fever, and myalgia in 1 (9%). Of these 11 children, 7 (64%) had severe DKA upon admission, 3 (27%) had new-onset T2D, and all of them (100%) were admitted to the PICU. None of the patients in the postpandemic new-onset diabetes cohort underwent COVID-19 antibody testing.

Discussion

In this retrospective study, we observed an alarming increase in the cases of new-onset T2D and DKA in a pediatric cohort admitted to a children's hospital in the southwestern United States following the outbreak of the COVID-19 pandemic. DKA severity was also higher during the postpandemic phase. Children with new-onset diabetes and DKA admitted for inpatient management following the pandemic onset presented with more profound acidosis, required vasopressors more frequently, had a higher need for oxygen supplementation, and experienced a significantly longer period of hospitalization than the prepandemic cohort. The relationship between COVID-19 infection and diabetes is complex and multifactorial. An acute infection with SARS-CoV-2 in patients with known diabetes may result in a higher rate of complications and precipitate ketoacidosis, which is primarily due to its negative effects on β -cell function. COVID-19 infection also has the potential of causing acute hyperglycemic episodes in subjects with no prior history of diabetes and may result in new-onset diabetes.²³ Other metabolic and mechanistic links between diabetes and COVID-19 have also been proposed. These include an underlying chronic inflammatory state that generates an exaggerated response to infection with excess cytokine release and immune dysregulation²⁴ as well as selective infection of the pancreatic β -cell by the novel coronavirus leading to cell apoptosis impacting pancreatic insulin levels and secretion.²⁵ Since all patients with new-onset diabetes in this study cohort who were admitted after March 2020 did not routinely undergo RT-PCR testing for SARS-CoV-2 or routine antibody testing, the higher rates of new-onset diabetes and DKA cannot be directly attributed simply to a coronavirus-induced β -cell impairment. However, all children who tested positive for SARS-CoV-2 in this study required PICU admission for a higher level of care.

In the last 2 decades, the incidence and prevalence of youth-onset T2D have increased contemporaneously with the epidemic of obesity especially among minority youth in the United States.^{26,27} In our cohort, the prevalence of obesity in children with

new-onset T2D and new-onset DKA was 87.50%. It is also known that social determinants of health play a key role in the risk of chronic diseases such as diabetes and cardiovascular disease and their outcomes.²⁸ Minority youth with T1D diabetes have poorer prognostic factors for complications and experience worse outcomes than their non-Hispanic White peers during the early years following their diabetes diagnosis.¹⁹ In the current study, the number of cases of new-onset diabetes presenting with DKA was higher among children of minority race including in Black and American Indian/Alaskan Native patients. Children in the postpandemic onset DKA group also exhibited higher adiposity and had higher glycated hemoglobin levels indicating longer exposure to hyperglycemia prior to presentation that could be due to higher baseline obesity prevalence as well as a delay in seeking care or other factors related to health disparities that are often pervasive in vulnerable populations. With the sudden advent of a catastrophic public health crisis, the COVID-19 global pandemic, we can only speculate that these disparities and health inequities may have been further accentuated that subsequently led to a higher number of children presenting with DKA and severe ketoacidosis.

Our study has limitations. This is a single-center study, and the study population due to its geographic location may not be entirely representative of the general population of the United States. In addition, we included all patients with new-onset diabetes irrespective of their SARS-CoV-2 testing status; hence, a definitive causal relationship between COVID-19 infection and new-onset diabetes cannot be inferred. More detailed history such as a history of diabetes in first-degree and second-degree relatives, detailed clinical findings, and additional laboratory tests such as C-peptide levels were not available in all patients and were not included in the final analysis. However, ours is one of the few studies in children that showed a striking increase in the number of cases of T2D after the pandemic onset with more severe DKA at presentation. As the COVID-19 pandemic rages on and with the fear of similar public health emergencies looming in the future, it is important to address the urgent problem of childhood obesity and mitigate the associated metabolic risks through vigorous lifestyle measures and make these interventions accessible to children universally and to children in vulnerable communities where the need is acute.

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The authors have no multiplicity of interest to disclose.

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