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### Authors

Ebekozien, Osagie  
Agarwal, Shivani  
Noor, Nudrat  
[et al.](#)

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# Inequities in Diabetic Ketoacidosis Among Patients With Type 1 Diabetes and COVID-19: Data From 52 US Clinical Centers

Osagie Ebeozien,<sup>1,\*</sup> Shivani Agarwal,<sup>2,\*</sup> Nudrat Noor,<sup>1</sup> Anastasia Albanese-O'Neill,<sup>3</sup> Jenise C. Wong,<sup>4</sup> Tossaporn Seeherunvong,<sup>5</sup> Janine Sanchez,<sup>5</sup> Daniel DeSalvo,<sup>6</sup> Sarah K. Lyons,<sup>6</sup> Shideh Majidi,<sup>7</sup> Jamie R. Wood,<sup>8</sup> Runa Acharya,<sup>9</sup> Grazia Aleppo,<sup>10</sup> Kathryn M. Sumpter,<sup>11</sup> Anna Cymbaluk,<sup>6</sup> Nirali A. Shah,<sup>12</sup> Michelle Van Name,<sup>13</sup> Lisa Cruz-Aviles,<sup>13</sup> Guy Todd Alonso,<sup>7</sup> Mary Pat Gallagher,<sup>14</sup> Srinath Sanda,<sup>4</sup> Alexis Jamie Feuer,<sup>15</sup> Kristina Cossen,<sup>16</sup> Nicole Riales,<sup>1</sup> Nana-Hawa Yayah Jones,<sup>17</sup> Manmohan K. Kamboj,<sup>18</sup> and Irl B Hirsch<sup>19</sup>

<sup>1</sup>T1D Exchange, Boston, MA 02111, USA; <sup>2</sup>Fleischer Institute for Diabetes and Metabolism, Albert Einstein College of Medicine, Bronx, NY 10461, USA; <sup>3</sup>University of Florida, Gainesville, FL 32610, USA; <sup>4</sup>Madison Clinic for Pediatric Diabetes, University of California San Francisco, CA 94158, USA; <sup>5</sup>Miller School of Medicine, University of Miami, Miami, FL 33136, USA; <sup>6</sup>Texas Children's Hospital/Baylor College of Medicine, Houston, TX 77030, USA; <sup>7</sup>Barbara Davis Center for Diabetes, University of Colorado, Denver, CO 80045, USA; <sup>8</sup>UH Rainbow Babies & Children's Hospital, Case Western Reserve University, Cleveland, OH 44106, USA; <sup>9</sup>SUNY Upstate Medical University, NY 13210, USA; <sup>10</sup>Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA; <sup>11</sup>Le Bonheur Children's Hospital, University of Tennessee Health Science Center, Memphis, Tennessee, TN 38103, USA; <sup>12</sup>Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA; <sup>13</sup>Yale School of Medicine, New Haven, CT 06510, USA; <sup>14</sup>Hassenfeld Children's Hospital, NYU Langone, New York, NY 10016, USA; <sup>15</sup>Division of Pediatric Endocrinology, Weill Cornell Medicine, New York, NY 10065, USA; <sup>16</sup>Children's Hospital of Atlanta, Emory University School of Medicine, Atlanta, GA 30329, USA; <sup>17</sup>Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229, USA; <sup>18</sup>Nationwide Children Hospital, Columbus, OH 43205, USA; and <sup>19</sup>University of Washington Diabetes Institute, Seattle, WA 98109, USA

\*Co-first authors.

**ORCID numbers:** 0000-0002-8473-249X (O. Ebeozien); 0000-0003-4506-3702 (S. Agarwal).

**Abbreviations:** CGM, continuous glucose monitoring; COVID-19, coronavirus disease 2019; DKA, diabetic ketoacidosis; HbA1c, glycated hemoglobin A1c; NH, non-Hispanic; T1D, type 1 diabetes; T2D, type 2 diabetes.

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## Abstract

**Objective:** We examined whether diabetic ketoacidosis (DKA), a serious complication of type 1 diabetes (T1D) was more prevalent among Non-Hispanic (NH) Black and Hispanic patients with T1D and laboratory-confirmed coronavirus disease 2019 (COVID-19) compared with NH Whites.

**Method:** This is a cross-sectional study of patients with T1D and laboratory-confirmed COVID-19 from 52 clinical sites in the United States, data were collected from April to August 2020. We examined the distribution of patient factors and DKA events across NH White, NH Black, and Hispanic race/ethnicity groups. Multivariable logistic regression analysis was performed to examine the odds of DKA among NH Black and Hispanic patients with T1D as compared with NH White patients, adjusting for potential confounders, such as age, sex, insurance, and last glycated hemoglobin A1c (HbA1c) level.

**Results:** We included 180 patients with T1D and laboratory-confirmed COVID-19 in the analysis. Forty-four percent (n = 79) were NH White, 31% (n = 55) NH Black, 26% (n = 46) Hispanic. NH Blacks and Hispanics had higher median HbA1c than Whites (%-points [IQR]: 11.7 [4.7],  $P < 0.001$ , and 9.7 [3.1] vs 8.3 [2.4],  $P = 0.01$ , respectively). We found that more NH Black and Hispanic presented with DKA compared to Whites (55% and 33% vs 13%,  $P < 0.001$  and  $P = 0.008$ , respectively). After adjusting for potential confounders, NH Black patients continued to have greater odds of presenting with DKA compared with NH Whites (OR [95% CI]: 3.7 [1.4, 10.6]).

**Conclusion:** We found that among T1D patients with COVID-19 infection, NH Black patients were more likely to present in DKA compared with NH White patients. Our findings demonstrate additional risk among NH Black patients with T1D and COVID-19.

**Key Words:** COVID-19, DKA, type 1 diabetes, inequities

The World Health Organization declared coronavirus disease 2019 (COVID-19) a global pandemic in March 2020. As of August 30, 2020, there have been over 186 000 deaths and 6 million people infected with COVID-19 in the United States (1, 2).

Like many diseases, COVID-19 has disproportionately affected racial/ethnic minority groups (3, 4). Non-Hispanic (NH) Black and Hispanic people are 3 times more likely to be infected with COVID-19 and 2 times as likely to die from COVID-19 compared with NH Whites (5). Racial-ethnic minorities also have increased odds of hospitalization compared with Whites after adjusting for age, sex, comorbidities, and income (6). Although NH Blacks comprise 13% of the US population, they represent up to 34% of the US mortality from COVID-19 (7). These data underscore the reality that social and health inequities predispose NH Blacks and Hispanics to adverse outcomes of the COVID-19 pandemic.

Type 2 diabetes (T2D) has been identified as a risk factor for worse COVID-19 outcomes, including mortality, especially among NH Black and Hispanic people (8, 9). However, there are limited data on patients with type 1 diabetes (T1D), despite having unique complications, such as diabetic ketoacidosis (DKA), which requires resource-intensive care in the hospital and tailored approaches distinct from T2D.

Most studies to date on diabetes and COVID-19 include population or cohort-based approaches, with predominantly T2D patients, and have shown that age, obesity, and other comorbidities are associated with increased risk of dying (10, 11). Given that the natural history, treatment regimens, and age of onset for T2D differ significantly from that of T1D, there is a critical need to understand how

COVID-19 modifies T1D-specific risks. Moreover, recent epidemiologic studies suggest that complications of T1D are higher among minority populations (12-14).

Prior T1D Exchange network data before the COVID-19 pandemic had demonstrated significant disparities in race and ethnicity among patients with T1D (12, 15-17).

We were interested in whether NH Black and Hispanic patients with T1D and laboratory-confirmed COVID-19 had a higher incidence of DKA compared with NH Whites, given that added risk for DKA may have grave consequences in hospitalization. We used a unique national registry of patients with T1D from 52 T1D Exchange clinical sites, which offered a racial/ethnic and geographically diverse cohort.

We describe the characteristics of the cohort and our use of multivariable logistic regression analyses to examine whether NH Black and Hispanic children and adults with T1D had higher rates of DKA compared with NH Whites, after adjusting for age, sex, insurance, and glycated hemoglobin A1c (HbA1c) levels.

## Methods

### Study procedures

This cross-sectional study was coordinated by the T1D Exchange, a Boston-based population health research organization focused on T1D. The study was reviewed and approved as non-human subjects' research with the need for informed consent waived by the Western Institutional Review Board. All participating centers also obtained local institutional approval.

As of August 30, 2020, 52 Endocrinology centers from the T1D Exchange clinical network sites participated in the multicenter surveillance study. Participating endocrinology clinics completed a retrospective chart review and were asked to submit information on all patients with T1D at their sites who tested positive for COVID-19 via an online questionnaire that was created and managed by the T1D Exchange. The questionnaire was administered using the Qualtrics survey platform ([www.qualtrics.com](http://www.qualtrics.com) version XM) and comprised 33 pre-coded and free text questions to collect data on patient and clinical attributes. Each participating center identified one team member for reporting to avoid duplicate patient submission. Each submission was reviewed for potential errors and incomplete information. The coordinating center verified the number of cases per site for data quality assurance.

Three of the co-authors (O.E., S.A., and N.N.) had full access to all the source data used for this analysis.

### Inclusion criteria

All NH Black, NH White, and Hispanic patients submitted by participating clinics to the registry with laboratory-confirmed COVID-19 were included in this study. An individual was entered into the registry as COVID-19 positive if they tested positive by molecular testing (reverse transcription-polymerase chain reaction) from nasopharyngeal swabs, throat swabs, sputum, or other bodily fluid testing. Preliminary reporting from the T1D COVID-19 registry has previously been described (18).

### Race-ethnicity

Participating Centers entered race/ethnicity information into the online questionnaire as a categorical variable, encoded as “Non-Hispanic White,” “Non-Hispanic Black,” “Hispanic,” “Asian,” “More than One Race,” or “Other” per US Census criteria (16). Clinical sites extracted this information from medical charts. For this analysis, we included Non-Hispanic White (NH White), Non-Hispanic Black (NH Black), and Hispanic race/ethnicity participants only.

We excluded 18 patients from this analysis because of missing race/ethnicity information or outside of the focus race/ethnicity groups (Asian  $n = 1$ , More than One Race  $n = 4$ , Other  $n = 5$ , Unknown  $n = 8$ ).

### Primary outcome

The primary outcome for this study was DKA. DKA was defined as blood glucose greater than 200 mg/dL (11 mmol/L), venous pH less than 7.3 or bicarbonate less than 15 mmol/L, ketonemia, and ketonuria. Patient medical charts were reviewed to confirm DKA status.

### Covariates

Information was collected on additional variables of interest which are pertinent to T1D and COVID-19, including sociodemographic information (age, sex, insurance), duration of T1D, use of insulin pump or continuous glucose monitoring (CGM), comorbidities, and presenting symptoms of COVID-19.

### Statistical analysis plan

The primary objectives of this analysis were to (i) examine the distribution of patient and diabetes-specific clinical characteristics across Black, Hispanic, and White patient groups with T1D and COVID-19 infection; (ii) compare the distribution of DKA events for Whites vs Blacks and Hispanics; and (iii) determine if the odds of DKA events in Black and Hispanic groups were greater relative to White patients.

Data were collected from April 7, 2020, to August 30, 2020, from 52 clinical sites that are members of the T1D Exchange Clinic Registry.

Descriptive statistics were used to summarize the data. Continuous data are represented as means (SD) or medians (interquartile range [IQR]). Summary statistics, including frequency and percentage for categorical variables, were calculated for all patient-related and clinical characteristics. Age in years was analyzed as both a continuous variable as well as a categorical variable ( $>19$  and  $\leq 19$  years). The age cutoff was chosen to be in line with the most common COVID19 state reporting practices since 36 of 49 reporting states use this age cutoff for delineating pediatric from adult patients (19). Patient sex was analyzed as Male or Female. Insurance status was analyzed as a categorical variable with Public (Medicare, Medicaid, or other public), Private (employer-based private, other private or military), Uninsured, and Unknown groups. HbA1c levels were reported as %-units, whereas data on comorbidities and medications were provided under free text questions. Information on comorbidities, specifically hypertension, obesity, and chronic kidney disease, were classified into categorical variables (Yes/ No) for analysis.

Patient characteristics were reported across race-ethnicity groups and stratified by racial-ethnic groups. Newly diagnosed patients were excluded from descriptive analysis. The difference in the distribution of categorical patient characteristics across race/ethnicity groups was examined by chi-square or Fisher Exact tests. Categorical variables with multiple groups were compared against a reference category, as noted in Tables 1 and 2. Median HbA1c values were compared between groups using the nonparametric Kruskal-Wallis test, given the nonnormal distribution of HbA1c.

**Table 1.** Participant Characteristics of Patients With Type 1 Diabetes and COVID-19, by Race-Ethnicity (N = 180)

	NH White N = 79	NH Black N = 55	Hispanic N = 46	P value NH White vs NH Black	P value NH White vs Hispanic
<b>Sex</b>				0.99	0.42
Male	40 (51%)	27 (49%)	18 (39%)		
Female	39 (49%)	28 (51%)	28 (61%)		
<b>Age, years</b>				0.18	0.94
≤19	27 (34)	26 (47)	23 (50)		
>19	52 (66)	29 (53)	23 (50)		
<b>New-diagnosis T1D</b>				0.01	0.08
Yes	1 (1)	7 (13)	6 (13)		
<b>Duration of T1D</b>				0.11	0.06
0-5 years	22	15	13		
6-10 years	8	11	10		
>11 years	47	22	17		
<b>Insurance<sup>a</sup></b>				0.001	0.001
Private	53 (67)	11 (20)	12 (26)		
Public	24 (30)	43 (78)	33 (72)		
Uninsured	2 (3)	1 (2)	1 (2)		
<b>HbA1c</b>				0.001	0.001
<7%	21 (27)	2 (5)	4 (9)		
7%-9%	35 (44)	13 (24)	16 (35)		
>9%	23 (29)	39 (71)	26 (57)		
<b>Median HbA1c %-points (IQR)</b>	8.3 (2.4)	11.7 (4.7)	9.7 (3.1)	0.001	0.01
<b>Median HbA1c % points (IQR)<sup>c</sup></b>	8.2 (2.2)	11.6 (4.8)	9.1 (3.0)	0.001	0.01
<b>Comorbidities (yes)</b>					
Obesity	10 (12)	11 (20)	8 (17)	0.3	0.51
Hypertension	13 (16)	16 (29)	8 (17)	0.9	0.09
CKD	11 (14)	8 (15)	6 (13)	0.9	0.93
<b>CGM use<sup>c</sup></b>					
Yes	49 (62)	7 (13)	17 (37)	0.001	0.004
<b>Insulin pump<sup>c</sup></b>					
Yes	43 (54)	4 (7)	10 (22)	0.001	0.001
<b>Presenting symptoms<sup>ba</sup> (yes)</b>					
Elevated temperature	31 (39)	26 (47)	23 (50)	0.5	0.31
Dry cough	25 (32)	22 (40)	17 (37)	0.4	0.68
Body ache	25 (32)	14 (25)	16 (35)	0.8	0.53
High blood glucose	23 (29)	31 (56)	25 (54)	0.002	0.009
Fatigue	27 (34)	19 (34)	14 (30)	0.98	0.81
<b>Medications<sup>b</sup> ( yes)</b>					
ACE inhibitors	3 (4)	3 (5)	5 (11)	0.8	0.82
Beta blockers	12 (15)	10 (18)	12 (26)	0.6/	0.91
Statins	15 (19)	8 (15)	8 (17)	0.8/	0.73
Antidepressants	7 (9)	6 (11)	6 (13)	0.7/	0.81
ARBs	7 (9)	10 (18)	6 (13)	0.2/	0.34
<b>Highest level of care</b>				<0.001	0.001
Home (ref)	36 (46)	4 (7)	13 (28)		
Clinic/urgent	15 (19)	6 (11)	0 (0)		
Emergency department	5 (6)	3 (5)	5 (11)		
Hospitalization/ICU	23 (29)	42 (76)	27 (59)		
<b>Adverse acute T1D outcomes (yes vs no adverse outcome)</b>					
DKA	10 (13)	30 (55)	15 (33)	<0.001	0.008
Severe hypoglycemia	3 (4)	2 (4)	0 (0)	0.61/	0.52
Death	1 (1)	0 (0)	3 (7)	0.001/	0.03

Data are presented as n (%) patients.

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CGM, continuous glucose monitoring; CKD, chronic kidney disease; DKA, diabetic ketoacidosis; HbA1c, glycated hemoglobin A1c; ICU, intensive care unit; IQR, interquartile range; NH, non-Hispanic; T1D, type 1 diabetes.

<sup>a</sup>Multiple responses per individual <sup>b</sup>Medical History chart review <sup>c</sup>Excludes new diagnosis

Multivariable logistic regression analysis was performed to examine the association between race/ethnicity status and DKA while adjusting for potential confounders, including age, sex, insurance, and HbA1c. Age and HbA1c were used as continuous variables in the model. Sensitivity analysis was performed by using HbA1c and Age as a categorical variable, which resulted in similar results. All statistical tests were 2-sided, with a type 1 error set at 5%. All analyses were performed using statistical software R version 3.6.2.

## Results

Of a total of 180 patients with T1D and confirmed COVID-19 in this analysis, 44% (n = 72) were NH White, 30% (n = 55) were NH Black and 26% (n = 46) were Hispanic (Table 1). There was no significant difference in the distribution of adults and young patients among the 3 race/ethnicity groups ( $P = 0.21$ ). Compared with NH White participants, more NH Black and Hispanic patients were publicly insured (78% NH Black and 72% Hispanic vs 30%

NH White) ( $P = 0.001$ ). HbA1c levels were also higher for NH Black and Hispanic patients, who had median HbA1c levels of 11.0% and 9.8%, respectively, compared with 8.3% for Whites ( $P < 0.001$ ). Compared with NH Whites, NH Black and Hispanic patients were less likely to be using an insulin pump or CGM and were more likely to be hospitalized for COVID-19 treatment (Table 1).

NH Blacks were more likely to present with DKA compared with NH White (55% vs 13%,  $P < 0.001$ ); all patients with DKA were hospitalized. Additionally, there were more cases of new-diagnosis T1D in the NH Black and Hispanic patients vs NH White patients (13% and 12% vs 1%, respectively;  $P = 0.001$ ).

Of those with DKA and known or newly diagnosed T1D, compared with NH Whites, both NH Black and Hispanic patients were more likely to be female, on public insurance, and had higher HbA1c levels (Table 2). Notably, in patients with known diabetes, there were similarly low rates of pump and CGM use across racial-ethnic groups. Table 3 shows results from logistic regression analyses

**Table 2.** Participant Characteristics of Patients With DKA Events, by Race-Ethnicity Status (N = 55)

	NH White (N = 10)	NH Black (N = 30)	Hispanic (N = 15)	P Value NH White vs NH Black	P Value NH White vs Hispanic
<b>Sex</b>				0.23	0.04
Male	7 (70%)	13 (43%)	3 (20%)		
Female	3 (30%)	17 (57%)	12 (80%)		
<b>Age, years</b>				0.22	0.28
≤19	3 (30)	18 (60)	9 (60)		
>19	7 (70)	12 (40)	6 (40)		
<b>New-onset T1D</b>				0.22	0.22
Yes	0 (0)	7 (23)	4 (27)		
<b>Insurance</b>				0.18	0.08
Private	4 (40)	6 (20)	1 (7)		
Public	5 (50)	23 (77)	13 (87)		
Uninsured	1 (10)	1 (3)	1 (7)		
<b>Median HbA1c [IQR]</b>	9.0 (1.3)	12.4 (3.3)	11.1 (4.0)	0.03	0.02
<b>Median HbA1c [IQR]<sup>d</sup></b>	9.0 (1.3)	13.0 (3.3)	11.0 (4.7)	0.03	0.02
<b>HbA1c<sup>d</sup></b>				0.17	0.28
<7% (ref)	0 (0)	0 (0)	0 (0)		
7%-9%	5 (50)	6 (20)	3 (20)		
>9%	5 (50)	26 (80)	12 (80)		
<b>CGM<sup>d</sup></b>				0.09	0.04
Yes	1 (10)	3 (10)	3 (20)		
<b>Pump<sup>d</sup></b>				0.52	0.62
Yes	2 (20)	3 (10)	2 (13)		
<b>Comorbidities</b>					
Obesity (yes)	2 (20)	4 (13)	3 (20)	0.67	0.91
Hypertension (yes)	3 (30)	6 (20)	2 (5)	0.69	0.32
CKD (yes)	1 (10)	2 (7)	1 (0.5)	0.98	0.99

Data are presented as n (%) patients.

Abbreviations: CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis; HbA1c, glycated hemoglobin A1c; NH, non-Hispanic; T1D, type 1 diabetes.

<sup>d</sup>Excludes new diagnosis

**Table 3.** Odds Ratios for DKA Comparing Racial-Ethnic Minority With NH White Patients With T1D and COVID-19 (N = 163; DKA = 55, no adverse Events = 108)

	Unadjusted OR (95% CI)	Adjusted model <sup>a</sup> OR (95% CI)	Adjusted model <sup>b</sup> OR (95% CI)
Race			
Hispanic vs NH White	3.7 (1.4-9.6) <sup>d</sup>	1.9 (0.7-5.7)	1.6 (0.5-4.9)
NH Black vs NH White	8.8 (3.8-22.0) <sup>d</sup>	3.7 (1.4-10.6) <sup>d</sup>	3.3 (1.2-9.6) <sup>d</sup>
Age (years)	-	1.0 (0.9-1.0)	1.0 (0.9-1.0)
Sex (M vs F)	-	0.8 (0.3-1.7)	0.8 (0.4-2.0)
HbA1c (%)	-	1.3 (1.1-1.5) <sup>d</sup>	1.2 (1.1-1.5) <sup>d</sup>
Insurance	-	2.7 (1.1-6.7) <sup>c</sup>	2.7 (1.1-7.0) <sup>c</sup>
Public vs private			
Newly diagnosed (yes vs no)		-	5.9 (1.5-30.1) <sup>c</sup>

<sup>a</sup>Adjusted for age, HbA1c (as continuous variables), sex, insurance

<sup>b</sup>Adjusted for age, HbA1c (as continuous variables), sex, insurance, and newly diagnosed T1D status

<sup>c</sup><0.05, <sup>d</sup><0.001

examining the association between racial/ethnic group and DKA events. The adjusted model was controlled for age, sex, HbA1c levels, and insurance (potential confounders). We found that NH Blacks had almost 4 times greater odds of presenting with DKA than NH Whites (adjusted odds ratio [OR] [95% CI]: 3.7 [1.4-10.6]). After adjustment, Hispanics had almost 2 times greater odds of presenting with DKA. However, this finding was not statistically significant (adjusted OR [95% CI]: 1.9 [0.7-5.7]).

## Discussion

We found that NH Black patients with T1D and confirmed COVID-19 were almost 4 times more likely to present with DKA compared to NH Whites, despite adjustment for age, sex, last HbA1c value, and insurance status among participants in this study. This study is the first systematic examination of racial-ethnic disparities for people with T1D and COVID-19 infection, using a diverse cohort, with equal representation from both NH Black and Hispanic groups. Our findings demonstrate that NH Black patients with COVID-19 and T1D have an additional risk of DKA beyond the risk already conferred from having longstanding diabetes or being of minority status. Data examining major US city COVID-19 estimates reveal that NH Black and Hispanic groups are more likely to contract COVID-19, ranging from 15% to 55% increased risk compared with NH Whites (7). Moreover, age-adjusted COVID-19 mortality is higher among Hispanics (187 per 100 000) and NH Black groups (184 per 100 000), compared with NH Whites (93 per 100 000). Compounding the risk of COVID-19 in Black and Hispanic patients, these groups are also known to have a higher risk of DKA and associated mortality (14, 17, 20, 21). Thus, the shared risk of COVID-19 and DKA

in T1D worsens the short-term and long-term prognosis for Black and Hispanic patients.

Previous studies have demonstrated an increased risk of DKA among minority populations with T1D (16, 17). Findings from this study confirm the persistence of these disparities during the COVID-19 pandemic and potential accentuation of these associations among COVID-19 positive patients. The increased risk of DKA in NH Black T1D patients with COVID-19 in this registry is likely due to a combination of factors, specifically, social determinants of health, including income level, education, and racial segregation, and inadequate healthcare access for NH Black and Hispanic communities (22-25). Moreover, severe viral infections, such as COVID-19, have been reported to reduce healthy behaviors, which can make it challenging to sustain essential self-management strategies, and lead to delays in accessing medical care (26-28). These social and structural risks must be identified and mitigated to prevent devastating complications with T1D and COVID-19. The evidence of an increased risk of DKA among Black patients with T1D and COVID-19 supports the case for restructuring healthcare systems to cater to the needs of underprivileged communities, and also to develop awareness programs for DKA recognition and treatment for the T1D patient population (26-28). While previous studies have demonstrated an increased risk of adverse diabetes related outcomes in the Hispanic population (29, 30), in this study, we found that Hispanic patients had greater odds of presenting with DKA compared with White patients, albeit these results were not statistically significant.

While our study has many strengths, we also acknowledge several limitations. First, this is a cross-sectional study from 52 centers and, therefore, cannot demonstrate causality or generalizable findings. Second, given the nature of medical chart extraction, we were not able

to collect data on a wide range of social determinants of health, which could have shed light on additional social indicators leading to racial or ethnic disparities in DKA. Third, while trained diabetes providers identified cases of COVID-19 with T1D for submission to this registry it is possible that some patients with T2D may have been included inadvertently. Further, despite diligent efforts to collect all cases of T1D with laboratory-confirmed COVID-19 in the participating centers, there is a chance some cases may have been missed for various reasons. However, this method of case ascertainment has been used in prior large registry-based studies and should not have led to systematic bias. Fourth, this study is based on a small sample size; however, patients with T1D and COVID-19 are a special population from whom data are exceedingly hard to collect in large numbers. Fifth, the timing of DKA relative to COVID-19 status was not collected in the study. Furthermore, while patients with DKA who tested positive for COVID-19 also exhibited one or more of the CDC listed symptoms, such as fever, it is likely that some DKA cases may have been asymptomatic carriers who were not screened for COVID-19 and, therefore, were not captured in this study. Sixth, as we did not collect information on levels of ketones in urine, we were unable to examine the association between COVID-19 and shock. Finally, we used HbA1c values

from different clinics in this analysis, which may add to variability in results. Prior research has estimated that HbA1c for NH Black population runs about 0.4% higher (31). We account for this observation in our analysis by adjusting for HbA1c levels in multivariable models.

In conclusion, this is the first multisite surveillance study of people with T1D and COVID-19 evaluating racial-ethnic disparities in T1D outcomes. Our findings underscore the high risk that racial-ethnic minorities face from COVID-19 and T1D, signaling to clinicians that further interventions are needed to prevent and provide a tailored approach to mitigate poor outcomes.

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## Additional Information

**Correspondence:** Osagie Ebeozien, MD, MPH, T1D Exchange, Boston, MA 02111, USA. Email: [oebeozien@t1dexchange.org](mailto:oebeozien@t1dexchange.org).

**Disclosures:** O.E. and S.A. are members of the Medtronic Diabetes Health Inequity Advisory Board.

**Data Availability:** Some or all datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

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