Differences in COVID-19 Outcomes Among Patients With Type 1 Diabetes: First vs Later Surges

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Background: Patient outcomes of COVID-19 have improved throughout the pandemic. However, because it is not known whether outcomes of COVID-19 in the type 1 diabetes (T1D) population improved over time, we investigated differences in COVID-19 outcomes for patients with T1D in the United States.

Methods: We analyzed data collected via a registry of patients with T1D and COVID-19 from 56 sites between April 2020 and January 2021. We grouped cases into first surge (April 9, 2020, to July 31, 2020, n = 188) and late surge (August 1, 2020, to January 31, 2021, n = 410), and then compared outcomes between both groups using descriptive statistics and logistic regression models.

Results: Adverse outcomes were more frequent during the first surge, including diabetic ketoacidosis (32% vs 15%, $P < .001$), severe hypoglycemia (4% vs 1%, $P = .04$), and hospitalization (52% vs 22%, $P < .001$). Patients in the first surge were older (28 [SD,18.8] years vs 18.0 [SD, 11.1] years, $P < .001$), had higher median hemoglobin A1c levels (9.3 [interquartile range {IQR}, 4.0] vs 8.4 (IQR, 2.8), $P < .001$), and were more likely to use public insurance (107 [57%] vs 154 [38%], $P < .001$). The odds of hospitalization for adults in the first surge were 5 times higher compared to the late surge (odds ratio, 5.01; 95% CI, 2.11-12.63).

Conclusion: Patients with T1D who presented with COVID-19 during the first surge had a higher proportion of adverse outcomes than those who presented in a later surge.

Keywords: TD1, diabetic ketoacidosis, hypoglycemia.

After the World Health Organization declared the disease caused by the novel coronavirus SARS-CoV-2, COVID-19, a pandemic on March 11, 2020, the Centers for Disease Control and Prevention identified patients with diabetes as high risk for severe illness.[1-7] The case-fatality rate for COVID-19 has significantly improved over the past 2 years. Public health measures, less severe COVID-19 variants, increased access to testing, and new treatments for COVID-19 have contributed to improved outcomes.

The T1D Exchange has previously published findings on COVID-19 outcomes for patients with type 1 diabetes (T1D) using data from the T1D COVID-19 Surveillance Registry.[8-12] Given improved outcomes in COVID-19 in the general population, we sought to determine if outcomes for cases of COVID-19 reported to this registry changed over time.

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Methods

This study was coordinated by the T1D Exchange and approved as nonhuman subject research by the Western Institutional Review Board. All participating centers also obtained local institutional review board approval. No identifiable patient information was collected as part of this noninterventional, cross-sectional study.

The T1D Exchange Multi-center COVID-19 Surveillance Study collected data from endocrinology clinics that completed a retrospective chart review and submitted information to T1D Exchange via an online questionnaire for all patients with T1D at their sites who tested positive for COVID-19.[13,14] The questionnaire was administered using the Qualtrics survey platform (www.qualtrics.com version XM) and contained 33 pre-coded and free-text response fields to collect patient and clinical attributes.

Each participating center identified 1 team member for reporting to avoid duplicate case submission. Each submitted case was reviewed for potential errors and incomplete information. The coordinating center verified the number of cases per site for data quality assurance.

Quantitative data were represented as mean (standard deviation) or median (interquartile range). Categorical data were described as the number (percentage) of patients. Summary statistics, including frequency and percentage for categorical variables, were calculated for all patient-related and clinical characteristics. The date August 1, 2021, was selected as the end of the first surge based on a review of national COVID-19 surges.

We used the Fisher's exact test to assess associations between hospitalization and demographics, HbA1c, diabetes duration, symptoms, and adverse outcomes. In addition, multivariate logistic regression was used to calculate odds ratios (OR). Logistic regression models were used to determine the association between time of surge and hospitalization separately for both the pediatric and adult populations. Each model was adjusted for potential sociodemographic confounders, specifically age, sex, race, insurance, and HbA1c.

All tests were 2-sided, with type 1 error set at 5%. Fisher's exact test and logistic regression were performed using statistical software R, version 3.6.2 (R Foundation for Statistical Computing).

Results

The characteristics of COVID-19 cases in patients with T1D that were reported early in the pandemic, before August 1, 2020 (first surge), compared with those of cases reported on and after August 1, 2020 (later surges) are shown in **Table 1**.

Patients with T1D who presented with COVID-19 during the first surge as compared to the later surges were older (mean age 28 [SD, 18.0] years vs 18.8 [SD, 11.1] years; $P<.001$) and had a longer duration of diabetes ($P<.001$). The first-surge group also had more patients with >20 years' diabetes duration (20% vs 9%, $P<.001$). Obesity, hypertension, and chronic kidney disease were also more commonly reported in first-surge cases (all $P<.001$).

There was a significant difference in race and ethnicity reported in the first surge vs the later surge cases, with fewer patients identifying as non-Hispanic White (39% vs, 63%, $P<.001$) and more patients identifying as non-Hispanic Black (29% vs 12%, $P<.001$). The groups also differed significantly in terms of insurance type, with more people on public insurance in the first-surge group (57% vs 38%, $P<.001$). In addition, median HbA1c was higher (9.3% vs 8.4%, $P<.001$) and continuous glucose monitor and insulin pump use were less common ($P=.02$ and <.001, respectively) in the early surge.

All symptoms and adverse outcomes were reported more often in the first surge, including diabetic ketoacidosis (DKA; 32% vs 15%; $P<.001$) and severe hypoglycemia (4% vs 1%, $P=.04$). Hospitalization (52% vs 13%, $P<.001$) and ICU admission (24% vs 9%, $P<.001$) were reported more often in the first-surge group.

Regression Analyses

Table 2 shows the results of logistic regression analyses for hospitalization in the pediatric (≤19 years of age) and adult (>19 years of age) groups, along with the odds of hospitalization during the first vs late surge among COVID-positive people with T1D. Adult patients who tested positive in the first surge were about 5 times more likely to be hospitalized than adults who tested positive for infection in the late surge after adjusting for age, insurance type, sex, race, and HbA1c levels. Pediatric patients also had an increased odds for hospitalization during the first surge, but this increase was not statistically significant.

Table 1. **Characteristics of COVID-19 Cases in Patients With Type 1 Diabetes During First Surge (April 2020–July 2020) vs Late surge (August 2020-January 2021)**

	First surge (n=188)	Late surge (n=410)	*P* value
Age, mean (SD), y	28 (18)	18.8 (11.1)	<.001
Age, median (IQR), y	20 (15-40)	17 (13-20)	<.001
Age category, No. (%), y			<.001
0 to 10	14 (7)	41 (10)	
11 to 19	73 (39)	255 (62)	
20 to 30	39 (21)	73 (18)	
31 to 40	15 (8)	18 (4)	
41 to 50	15 (8)	10 (2)	
51 to 60	14 (7)	4 (1)	
61+	18 (10)	9 (2)	
Female, No. (%)	97 (52)	211 (51)	1
Race/Ethnicity, No. (%)			<.001
Non-Hispanic White	73 (39)	260 (63)	
Non-Hispanic Black	54 (29)	48 (12)	
Hispanic	44 (23)	82 (20)	
Other	17 (9)	20 (5)	
Insurance type, No. (%)			<.001
Public	107 (57)	154 (38)	
Private	77 (41)	246 (60)	
Uninsured	4 (2)	10 (2)	
HbA1c, median (IQR)	9.3 (7.8-11.8)	8.4 (7.3-10.1)	<.001
Duration of T1D, No. (%), y			<.001
New onset	18 (10)	26 (6)	
<1	12 (6)	23 (6)	
1 to 5	41 (22)	151 (37)	
6 to 10	30 (16)	95 (23)	
11 to 20	50 (27)	77 (19)	
>20	37 (20)	38 (9)	
Continuous glucose monitoring use, Yes, No. (%)	79 (42)	215 (52)	.02
Insulin pump use, Yes, No. (%)	56 (30)	199 (49)	<.001
Most prevalent comorbidities, No. (%)			.09
Obesity	33 (18)	27 (7)	<.001
Hypertension/cardiovascular disease	42 (22)	23 (6)	<.001
Asthma	16 (9)	19 (5)	.08
Chronic kidney disease	26 (14)	10 (2)	<.001

Table 1. continued

Continued on page 30

	First surge (n=188)	Late surge (n=410)	*P* value
Highest level of care, No. (%)			<.001
Hospitalized	52 (28)	52 (13)	
Intensive care unit	45 (24)	37 (9)	
Not hospitalized	91 (48)	321 (78)	
Adverse outcome, No. (%)			<.001
Death	5 (3)	0 (0)	
Diabetic ketoacidosis	61 (32)	60 (15)	
Severe hypoglycemia	7 (4)	4 (1)	
Other	7 (4)	22 (5)	
None	110 (59)	324 (79)	
Region, No. (%)			<.001
New England	7 (4)	0 (0)	
Mid-Atlantic	91 (48)	64 (16)	
Midwest	28 (15)	74 (18)	
South	28 (15)	84 (20)	
Southwest	14 (7)	56 (14)	
West	19 (10)	132 (32)	

Table 2. **Logistic Regression for Hospitalization Among Patients With Confirmed COVID-19 and Type 1 Diabetes**

	Adjusted odds ratio (95% CI)[a]
First surge vs late surge (pediatrics, n=376)	1.83 (0.99-3.37)
First surge vs late surge (adults, n=207)	5.01 (2.11-12.63)

[a]Adjusted for age, insurance type, sex, race, and HbA1c level.

Discussion

Our analysis of COVID-19 cases in patients with T1D reported by diabetes providers across the United States found that adverse outcomes were more prevalent early in the pandemic. There may be a number of reasons for this difference in outcomes between patients who presented in the first surge vs a later surge. First, because testing for COVID-19 was extremely limited and reserved for hospitalized patients early in the pandemic, the first-surge patients with confirmed COVID-19 likely represent a skewed population of higher-acuity patients. This may also explain the relative paucity of cases in younger patients reported early in the pandemic. Second, worse outcomes in the early surge may also have been associated with overwhelmed hospitals in New York City at the start of the outbreak. According to Cummings et al, the abrupt surge of critically ill patients hospitalized with severe acute respiratory distress syndrome initially outpaced their capacity to provide prone-positioning ventilation, which has been expanded since then.[15] While there was very little hypertension, cardiovascular disease, or kidney disease reported in the pediatric groups, there was a higher prevalence of obesity in the pediatric group from the mid-Atlantic region. Obesity has been associated with a worse prognosis for COVID-19 illness in children.[16] Finally, there were 5 deaths reported in this study, all of which were reported during the first surge. Older age and increased rates of cardiovascular disease and chronic kidney disease in the first surge cases likely contributed to worse outcomes for adults in mid-Atlantic region relative to the other regions. Minority race and the use of public insurance, risk factors for more severe outcomes in all regions, were also more

common in cases reported from the mid-Atlantic region.

This study has several limitations. First, it is a cross-sectional study that relies upon voluntary provider reports. Second, availability of COVID-19 testing was limited in all regions in spring 2020. Third, different regions of the country experienced subsequent surges at different times within the reported timeframes in this analysis. Fourth, this report time period does not include the impact of the newer COVID-19 variants. Finally, trends in COVID-19 outcomes were affected by the evolution of care that developed throughout 2020.

Conclusion

Adult patients with T1D and COVID-19 who reported during the first surge had about 5 times higher hospitalization odds than those who presented in a later surge.

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