Title: Differences in COVID-19 outcomes among patients with type 1 diabetes: first versus late surges

Short title: COVID-19 in T1D first vs. late surges

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Abstract

Background

Outcomes of the novel coronavirus SARS-CoV-2 (COVID-19) have improved throughout the pandemic. However, whether outcomes of COVID-19 in the type 1 diabetes (T1D) population improved over time is unknown. Therefore, we aim to investigate differences in COVID-19 outcomes for patients with T1D in the US.

Method

We analyzed data collected via a registry of patients with T1D and COVID-19 from 56 sites between April 2020 and January 2021. First, we grouped cases into First Surge (04/09/2020 - 07/31/2020, n=188) and Late Surge (08/01/2020 - 01/31/2021, n=410). Then, we 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% versus 15%, p<0.001), severe hypoglycemia (4% versus 1%, p=0.04) and hospitalization (52% versus 22%, p<0.001). The First surge cases were older (28 +/- 18.8 years versus 18.8 +/- 11.1 years, p<0.001), had higher hemoglobin A1c (HbA1c) levels (Median (IQR): 9.3 (4.0) versus 8.4(2.8), <0.001) and use public insurance (n(%): 107 (57) versus 154 (38), p <0.001). There were five times increased odds of hospitalization for adults (OR 5.01 (2.11,12.63) in the first surge compared to the late surge.

Conclusion

COVID-19 cases among patients with T1D reported during the first surge had a higher proportion of adverse outcomes than those presented in a later surge.

Background

The World Health Organization declared the novel coronavirus SARS-CoV-2 (COVID-19) a pandemic on March 11, 2020 thereafter the Centers for Disease Control identified patients with diabetes as high risk for severe illness. (1-7).

The case fatality rate for COVID-19 have significantly improved in the last 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 have 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..

Methods

This study was coordinated by the T1D Exchange and approved as non-human subject research by the Western Institutional Review Board (WIRB). All participating centers also obtained local Institutional Review Board (IRB) approval. No identifiable patient information was collected as part of this non-interventional, 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 which 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 one 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 percentage of patients. Summary statistics, including frequency and percentage for categorical variables, were calculated for all patient-related and clinical characteristics. The date of August 1, 2021, as the end of the first surge, was selected based on a review of national COVID19 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, gender, race, insurance and HbA1c.

All tests were two-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: A Language and Environment for Statistical Computing, R Core Team, R Foundation for Statistical Computing, Vienna, Austria, 2020, https://www.R-project.org).

Results

The characteristics of COVID-19 cases in patients with T1D that were reported earlyin the pandemic, before 08/01/2020 (First), versus those reported on and after 08/01/2020 (Later), are shown in Table 1.

The cases reported during the first surge as compared to the later surges were older (mean age 28 +/- 18.8 years vs. 18.8 +/- 11.1 years, $p<0.001$) and had a longer duration of diabetes ($p<0.001$). The First surge group also had more patients with > 20 years' diabetes duration (20% vs. 9%, $p<0.001$). Obesity, hypertension, and chronic kidney disease were also more commonly reported in first surge cases (all $p<0.001$).

There was a significant difference in race and ethnicity reported in the first surge versus the later surge cases, with fewer patients identifying as Non-Hispanic White in the first surge group

(39% vs, 63%, p<0.001) and more patients identifying as Non-Hispanic Black in the First surge group (29% vs. 12%, p<0.001). There was also a significant difference in insurance type, with more people on public insurance in the First surge group (57% vs. 38%, p <0.001). In addition, median HbA1c was higher (9.3% vs. 8.4%, p<0.001), and continuous glucose monitor (CGM) and insulin pump use were less common (p=0.02 and <0.001, respectively) in the early surge. All symptoms and adverse outcomes were reported more often in the First surge, including DKA (32% vs. 15%, p<0.001) and severe hypoglycemia (4% vs. 1%, p=0.04). Hospitalization (52% versus 22%, p<0.001) and ICU admission (24% versus 9%, p<0.001) were reported more often in the first surge cases.

Regression analyses

Table 2 shows the logistic regression analyses for hospitalization in the pediatric (</=19 years of age) and adult (> 19 years of age) groups.

Table 2 shows the odds of hospitalization during the first vs. late surge among COVID positive people with type 1 diabetes. Adult patients who tested positive in the first surge were about five times more likely to be hospitalized than adult tested positive for infection in the late surge after adjusting for age, insurance type, gender, race, and HbA1c levels. Pediatric patients also exhibited an increased odds for hospitalization during the first surge, however this increase was not statistically significant.

Discussion

Our analysis of COVID-19 cases in patients with T1D reported by diabetes providers across the US found that adverse outcomes were more prevalent early in the pandemic.. There may be a number of reasons for this difference in outcomes between early and late surge. Firstly, because testing for COVID-19 was extremely limited and reserved for hospitalized patients early in the pandemic, the early surge subjects 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. Secondly, worse outcomes in the early surge

may also have been associated with overwhelmed hospitals in NYC 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. In addition, obesity has been associated with a worse prognosis for COVID-19 illness in children (16). Finally, there were five deaths reported in this study, all of which were reported during the firstsurge. Older age and increased rates of cardiovascular disease and chronic kidney disease in the first surge cases likely contributed to more severe outcomes for adult cases in that 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 in this analysis. Fourth, this report time period doesn't include the impact of the newer COVID19 variants. Finally, trends in COVID-19 outcomes were affected by the evolution of care that developed throughout 2020.

Conclusion

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

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Tables

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). N (%) or median [IQR].

	First Surge (n=188)	Late Surge (n=410)	P-value
Mean Age (SD)	28 (18)	18.8 (11.1)	<0.001
Median Age (IQR)	20 (25.2)	17 (7.0)	<0.001
Age Category			<0.001
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)	
Gender			
Female	97 (52)	211 (51)	1
Race/Ethnicity			<0.001
NH White	73 (39)	260 (63)	
NH Black	54 (29)	48 (12)	
Hispanic	44 (23)	82 (20)	
Other	17 (9)	20 (5)	

Insurance Type			<0.001
Public	107 (57)	154 (38)	
Private	77 (41)	246 (60)	
Uninsured	4 (2)	10 (2)	
HbA1c Median (IQR)	9.3 (4)	8.4 (2.8)	<0.001
Duration of T1D			<0.001
New onset	18 (10)	26 (6)	
Less than 1 year	12 (6)	23 (6)	
1- 5 years	41 (22)	151 (37)	
6 - 10 years	30 (16)	95 (23)	
11 - 20 years	50 (27)	77 (19)	
More than 20 years	37 (20)	38 (9)	
CGM Use			0.02
Yes	79 (42)	215 (52)	
Insulin Pump Use			<0.001
Yes	56 (30)	199 (49)	
Most Prevalent Comorbidities			0.09
Obesity	33 (18)	27 (7)	<0.001
Hypertension/CVD	42 (22)	23 (6)	<0.001
Asthma	16 (9)	19 (5)	0.08
CKD	26 (14)	10 (2)	<0.001
Highest level of care			<0.001
Hospitalized	52 (28)	52 (13)	
ICU	45 (24)	37 (9)	
Non-Hospitalized	91 (48)	321 (78)	
Adverse Outcome			<0.001
Death	5 (3)	0 (0)	
DKA	61 (32)	60 (15)	
Severe Hypoglycemia	7 (4)	4 (1)	
Other	7 (4)	22 (5)	
None	110 (59)	324 (79)	

Region			<**0.001**
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)	

Abbreviations: IQR, interquartile range; CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis.

Table 2: Logistic regression for hospitalization among patients with confirmed COVID-19 and type 1 diabetes.

	Adjusted Odds Ratio
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)

Adjusted for age, insurance type, gender, race and HbA1c level