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Research Article

Increased Risk for Diabetic Ketoacidosis Admissions in Youth with Type 1 Diabetes During the First Wave of COVID-19 in The United States: A 5-Year Analysis

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ABSTRACT

Background: During COVID-19, an increase in pediatric diabetes diagnoses and incidence of diabetic ketoacidosis (DKA) has been theorized. This study sought to evaluate trends in hospital visits for type 1 diabetes (T1D) and type 2 diabetes (T2D) at a U.S. academic children's hospital from March to June 2020 compared to 2016-2019, coincident with the first wave of COVID-19.

Methods: Diabetes and DKA admissions data from March 11th to June 30th 2020, were compared with the same timeframe in 2016-2019.

Results: 313 hospital visits were analyzed, 62 admissions in 2020 compared to 251 admissions from 2016-2019. In 2020, a greater proportion of admissions were due to DKA (56% vs 42%, p=0.04), with a 1.7-fold increased risk of being in DKA compared to prior years (OR= 1.77, 95% CI 1.01-3.11, p= 0.045). A greater proportion of patients with known T1D were admitted in DKA in 2020 (p=0.01), without difference in DKA severity (p=0.2). There was no significant difference in admissions or severity of new-onset T1D, or new or known T2D in 2020.

Conclusions: Hospitalizations in known T1D during the first wave of COVID-19 were more likely DKA related, possibly due to delayed care. There was no increase in new onset T1D or T2D during the first wave of COVID-19. Future longitudinal data throughout the pandemic may highlight new trends.

KEYWORDS

Pediatric diabetes, Type 1 diabetes, Type 2 diabetes, COVID-19, Admissions.

Ethics approval: This study was approved by the institution's IRB in accordance with the Declaration of Helsinki. Waiver of consent was obtained along with waivers of parental assent and parental permission, given the minimal risk to participants. This was a non-treatment, non-intervention study, and no patient identifiable data was collected as part of the study. As a retrospective chart review of hospital admissions, contacting each family admitted over the last 5 years was not possible or practical.

List of Abbreviations: Type 1 diabetes (T1D), Type 2 diabetes (T2D), Diabetic ketoacidosis (DKA), Cystic Fibrosis related diabetes (CFRD).

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Introduction

The novel coronavirus, COVID-19 started spreading in December 2019, with the World Health Organization declaring a worldwide pandemic on March 11, 2020. The first COVID-19 related stay at home order in the United States (U.S.) went into effect on March 10th, 2020. Hospital data from Italy and the UK suggested that as COVID-19 daily deaths increased, the number of non-COVID-19 emergency department visits and admissions decreased, suggesting that families were avoiding hospital visits due to fear of exposure to COVID-19 [1,2].

While the pediatric population has been relatively spared from the serious health consequences of COVID-19, children have been affected in other ways. The availability of healthcare services was limited, families were more reluctant to seek medical care in offices or at the hospital, and while the increase of tele-medicine visits improved access to medical personnel, it made diagnosis of certain diseases or conditions more difficult. Early case series from Italy and Israel illustrated the difficulty of accurate and timely diagnosis of acute illness in children, which is reflected in severity of illness at presentation and potential complications [3,4].

There have been published reports and lay press of trends in diabetes admissions and possible increases in new onset diabetes and severity of diabetic ketoacidosis (DKA) [5]. Recent data from the UK reported an increase in new onset diabetes, [6] and data from Germany, the UK and the T1D exchange found an increase in incidence of DKA at presentation of new onset diabetes in the pediatric population during the COVID-19 pandemic [6-8].

To date, there is limited U.S. data on diabetes related admissions in youth. This study sought to evaluate trends in hospital visits for type 1 (T1D) and type 2 diabetes (T2D) at a tertiary referral children's hospital from March to June 2020 compared to March to June 2016-2019.

Methods

Diabetes-related hospital admission data for the period of March 11th to June 30th, 2020, were compared to March to June 2016-2019 at the Johns Hopkins Children's Center. This period was coincident with the first wave of COVID-19 in Maryland, and a stay-at-home order in effect on March 10th, 2020. This study was approved by the institution's IRB in accordance with the Declaration of Helsinki.

We collected information on patient age at admission, gender, race/ethnicity, diabetes type (T1D, T2D, Cystic Fibrosis related diabetes (CFRD)), pH, bicarbonate, and COVID-19 PCR testing results (for 2020). The maximum age of admission to the Children's Center for diabetes was 21 years. Patients with steroid induced diabetes, mitochondrial diabetes, post-transplant diabetes, medication induced hyperglycemia and pancreatitis related diabetes were excluded. DKA was defined per ISPAD 2018 guidelines as pH less than 7.3 and/or bicarbonate less than 15mmol/L: severe DKA if pH less than 7.1 and/or bicarbonate less than 5mmol/L [9].

The frequency and proportions of new onset T1D, T2D, and DKA admissions observed from March 11th to June 30th 2020, were compared with March 11th to June 30th, 2016-2019 using Fisher exact test. ANOVA was used to test for differences in any year. Analyses were performed using Stata 15, with a p-value <0.05 considered significant.

Results

A total of 313 hospital visits was analyzed, 62 admissions in 2020 and 251 admissions from 2016-2019. As shown in Table 1, of diabetes-related admissions, a greater proportion in 2020 were DKA admissions compared to prior years (56% (35/62) vs 42% (106/251), p=0.04), with a 1.7-fold increased risk of being in DKA in 2020 (OR= 1.77, 95% CI 1.01-3.11, p= 0.045). Of patients with known T1D, a greater proportion in 2020 was admitted in DKA compared to the prior four years (90% (18/20) vs 67% (49/73), p=0.01); with no difference in severity of DKA (35% (7/20) vs 29% (14/49), p=0.2). Patient-reported causes of DKA in 2020 included: 16/18 missed insulin doses and 2/18 insulin pump malfunction. All tested negative for COVID-19 PCR.

There was no difference in new onset T1D admissions, or severity of new onset T1D presentation in 2020 compared to prior years**.** There was also no significant change in the number of new onset or known T2D (on insulin or starting insulin) patients admitted in 2020 compared to prior years, and no difference in the proportion presenting in DKA. There was one CFRD admission in 2020 (n=1/62), compared to 22 total from 2016-2019 (22/251).

Conclusions

This study analyzed trends in all pediatric diabetes admissions during the first wave of the COVID-19 pandemic, and is among the first reports of data from the U.S. A greater proportion of diabetes related admissions were for DKA, and youth with known T1D were more likely to be admitted for DKA during the first wave of COVID-19, and less likely to be for other reasons such as elective surgery, possibly due to delayed care during the initial months of the pandemic. The precipitating factor for a majority of the known T1D DKA admissions was missed insulin doses, which may have been due to difficulty refilling prescriptions, or dose omission for children who typically receive supervised insulin dosing in schools.

There was no significant increase in the number of patients presenting with new onset T1D, nor was there an increase in new onset T1D in DKA in 2020. These results differ from those reported from Germany, where researchers noted an increase in patients with new onset T1D presenting in DKA and severe DKA, [7] and the UK, where researchers proposed an increase in new onset T1D compared to previous years, theorized to be due to the COVID-19 pandemic [6]. However, the UK data was based on a limited sample size of 33 patients without comparing to prior years, and thus may not be representative of a true increase in new onset T1D. Lay media also reported an increase in new T1D during the first wave of the pandemic; however worldwide data have not yet fully substantiated this claim. In Italy, researchers noted fewer new

Table 1: Characteristics of patients and diabetes admissions in March to June 2020 compared to the prior 4 years (2016-2019).

	2020	2019	2018	2017	2016	p-value	2016-2019	p-value
	n=62	n=75	n=65	n=61	n=50	all years	n=251	2020 compared to 2016-2019
Clinical characteristic								
Age	12.9 +/- 3.9						12.5 +/- 4.7	0.5
Sex, male, n (%)	42 (49%)	29 (39%)	30 (45%)	24 (39%)	19(38%)	0.6	102 (40%)	
Ethnicity, n (%)								
NHW	27 (44%)	31 (41%)	27 (42%)	28 (46%)	28 (56%)	0.4	114 (45%)	
Black	28 (45%)	37 (49%)	33 (51%)	27 (44%)	20 (40%)		118 (47%)	
Hispanic	3 (5%)	5 (7%)	2 (3%)	4 (7%)	2 (4%)		13 (5%)	
Asian/Other	4 (6%)	2 (3%)	3 (5%)	2 (3%)	0		7 (3%)	
Total DKA	35/62 (56%)	36/75 (48%)	26/65 (40%)	20/61 (33%)	24/50 (48%)	0.08	106/251 (42%)	**0.04**
New onset T1D	21/62 (33%)	18 (24%)	21 (32%)	21 (34%)	26 (52%)	0.2	86/251 (34%)	0.3
DKA	15/21 (71%)	13/18 (72%)	14/21 (67%)	9/21 (43%)	14/26 (54%)	0.2	50/86 (58%)	0.3
Severe DKA (pH<7.1, bicarb<5)	6/21 (29%)	5/18 (28%)	7/21 (33%)	4/21 (19%)	3/26 (12%)	0.6	19/50 (38)%	1
Known T1D	20/62 (32%)	31/75 (41%)	14/65 (22%)	18/61 (30%)	10/50 (20%)	**0.01**	73/251 (29%)	0.05
DKA	18/20 (90%)	21/31 (68%)	11/14 (79%)	8/18 (44%)	9/10 (90%)	**0.01**	49/73 (67%)	0.05
Severe DKA (pH<7.1, bicarb<5)	7/20 (35%)	8/31 (26%)	2/14 (14%)	0	4/10 (40%)	0.2	14/49 (29%)	0.6
New onset T2D	7/62 (11%)	7/75 (9%)	11/65 (17%)	8/61 (13%)	7/50 (14%)	0.5	33/251 (13%)	1
DKA	1 (14%)	1 (14%)	0	2 (25%)	1 (14%)	0.5	4/33 (12%)	1
Known T2D	2/62 (3%)	2/75 (3%)	4/65 (6%)	4/61 (6%)	1/50 (2%)	0.6	11/251 (4%)	0.4
DKA	1 (50%)	1 (50%)	1 (25%)	0	0	0.6	2/11 (18%)	0.4
T2D New insulin start	5/62 (8%)	0	1/65 (2%)	2/61 (3%)	1/50 (2%)	0.4	4/251 (2%)	0.4
CFRD	1/62 (2%)	5/75 (7%)	6/65 (9%)	7/61 (11%)	4/50 (8%)		22/251 (9%)	
Other diabetes admissions	6/62 (10%)	12/75 (16%)	8/65 (12%)	1 (2%)	1 (2%)		22/251 (9%)	

NHW- nonHispanic White, DKA = diabetic ketoacidosis, T1D - type 1 diabetes, T2D- type 2 diabetes, CFRD - cystic fibrosis related diabetes
Other diabetes admissions include patients admitted for psychiatric concerns and other reasons not related to diabetes
P-values calculated by Fisher's exact test

onset T1D during the first wave, but an increase in severity of DKA in 2020 compared to 2019 [10]. Larger, longitudinal studies that account for multiple waves of the pandemic are needed to identify the impact of COVID-19 on new onset diabetes.

There was no significant change noted in pediatric T2D admissions during the first wave of the COVID-19 pandemic. However, we did see an increase in the number of patients with known T2D admitted for insulin initiation, though this increase was not statistically significant given the small sample size. There is currently a paucity of data regarding T2D in the pediatric population during the pandemic, and the impact that virtual school, decreased activity levels, and worsening food insecurity has on obesity and developing T2D. Further, pediatric T2D primarily affects minority youth, who have also been disproportionately affected during the pandemic. Data collected in India among adults over 49 days of the lockdown show an increase in BMI among 40% of the cohort studied, increasing their ADA calculated risk of developing T2D. (11) There has been concern about worsening pediatric obesity during the pandemic [12,13], and it is plausible that similar weight-data may be seen in the US in the pediatric population. Further longitudinal studies are needed to fully understand the impact of the effect of the stay-at-home order on pediatric T2D, as the impact likely has not been realized in this analysis of the first wave.

While this study is limited by the small sample from a single institution, the patient demographics are diverse and representative of many locations around the U.S, in comparison to some of the concurrent reports from Europe. Although this study compares 2020 to the prior 4 years to limit the effect of random annual variation in diabetes admissions, results may still be affected by secular trends and time of year. Because of multiple comparisons made within this study, its findings should be replicated. Larger multicenter studies accounting for the different waves of COVID-19 across the United States are recommended.

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