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EPIDEMIOLOGY

Increase in newly diagnosed type 1 diabetes in youth during the COVID-19 pandemic in the United States: A multi-center analysis

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Abstract

Background: An increase in newly diagnosed type 1 diabetes (T1D) has been posited during the COVID-19 pandemic, but data are conflicting. We aimed to determine trends in newly diagnosed T1D and severity of presentation at diagnosis for pediatric and adolescent patients during COVID-19 (2020) as compared to the previous year (2019) in a multi-center analysis across the United States.

Methods: This retrospective study from seven centers in the T1D Exchange Quality Improvement Collaborative (T1DX-QI) included data on new onset T1D diagnosis and proportion in DKA at diagnosis from January 1 to December 31, 2020, compared to the prior year. Chi-square tests were used to compare differences in patient characteristics during the pandemic period compared to the prior year.

Results: Across seven sites, there were 1399 newly diagnosed T1D patients in 2020, compared to 1277 in 2019 ($p = 0.007$). A greater proportion of newly diagnosed patients presented in DKA in 2020 compared to 2019 (599/1399(42.8%) vs. 493/1277(38.6%),

These data were presented as a poster presentation at ISPAD's 47th Annual Conference in October 2021.

$p = 0.02$), with a higher proportion presenting with severe DKA ($p = 0.01$) as characterized by a pH <7.1 and/or bicarbonate of <5 mmol/L. Monthly data trends demonstrated a higher number of new T1D diagnoses over the spring and summer months (March to September) of 2020 compared to 2019 ($p < 0.001$).

Conclusions: We found an increase in newly diagnosed T1D and a greater proportion presenting in DKA at diagnosis during the COVID-19 pandemic compared to the prior year. Future longitudinal studies are needed to confirm these findings with population level data and determine the long-term impact of COVID-19 on diabetes trends.

KEYWORDS
COVID-19, diabetic ketoacidosis, new onset, newly diagnosed, type 1 diabetes

1 | INTRODUCTION

Throughout the COVID-19 pandemic, diabetes mellitus has been associated with a worse prognosis of COVID-19 infection, with acute complications and increased mortality.[1,2] Furthermore, patients with COVID-19 have experienced severe hyperglycemia necessitating treatment with insulin, sometimes resulting in a new diagnosis of diabetes.[3,4]

Historically, viruses have been associated with acute-onset diabetes, including SARS coronavirus 1 pneumonia, but the relationship between the current COVID-19 pandemic and newly diagnosed type 1 diabetes (T1D) remains uncertain, particularly in the pediatric population.[3,4]

As lockdowns ensued around the world during the first wave of the COVID-19 pandemic, early reports suggested that individuals were avoiding hospitals and medical care, leading to increased severity of illness at presentation.[5,6] Data from Germany, Italy, and the United States demonstrated an increase in diabetic ketoacidosis (DKA) incidence at the presentation of newly diagnosed T1D in children and adolescents, suggesting delays in seeking medical care.[7–9] Further, the T1D Exchange showed that in patients with existing T1D, the most common adverse outcome associated with concurrent COVID-19 infection was DKA, and this was more prevalent in non Hispanic (NH) and Hispanic individuals than N.H. Whites.[10–12]

An increase in newly diagnosed T1D has been posited during the COVID-19 pandemic. However, published reports have shown conflicting findings, with some reports suggesting an increase in newly diagnosed T1D in children and adolescents,[13–15] and others showing no change in expected or actual numbers of newly diagnosed T1D.[16,17] Our objective for this study was to describe trends in newly diagnosed T1D, as well as the severity of presentation at diagnosis during COVID-19 compared to the prior year using data from seven large U.S. clinical centers.

2 | RESEARCH DESIGN AND METHODS

This retrospective, multi-center study was conducted as part of the T1DX-QI project, a collaborative quality improvement platform engaging over 40 diabetes clinics in the United States evaluating the current state of diabetes care and sharing data and best practices to improve care delivery in type 1 diabetes.[18–20] Seven member sites contributed aggregate longitudinal data for this cross-sectional analysis assessing trends in newly diagnosed T1D. These sites were SUNY Upstate Medical University, New York; Barbara Davis Center for Pediatric Diabetes, Colorado; Cincinnati Children's Hospital Medical Center, Ohio; NYU Pediatric Diabetes Center, New York; Rady Children's Hospital, San Diego, California; Mott Children's Hospital, University of Michigan, Michigan and Johns Hopkins Children's Center, Maryland.

Our study population of interest were patients aged 0–26 years who were diagnosed with T1D in 2019 and 2020. Diagnosis and DKA data were collected from January 1 to December 31, 2020, and compared to January 1 to December 31, 2019. The number of newly diagnosed T1D patients was calculated, their associated DKA data, and total outpatient T1D patients, followed at each center. Data was de-identified and submitted in aggregate by month for the years 2019 and 2020 using an online data platform Smartsheet [www.smartsheet.com]. IRB approval was obtained by a central review board (Western Institutional Review Board) as an exempt study, and each site obtained local IRB approval as needed, with a waiver of consent. The main outcome of interest was the absolute number, and percentage of newly diagnosed patients seen in 2019 and 2020, which was calculated by dividing the number of new onset patients by the total number of independent patients seen as outpatients at all centers combined for each respective calendar year. Month-by-month new onset trends were calculated as a percentage of T1D patients seen via in-person/telemedicine visit by each month. Month-by-month DKA in new onset trends were calculated as a percentage of newly diagnosed T1D patients seen by each month. The capture rate for T1D Exchange data is almost 100%. All patients with at least one in person or telemedicine visit in the study time frame were included in the analysis for the respective clinics.

Independent variables included: Patient age at diagnosis, gender, race/ethnicity, insurance type, and type 1 diabetes autoantibody data, DKA and DKA severity at presentation. Patients diagnosed with Type 2 diabetes were excluded.

International Society for Pediatric and Adolescent Diabetes 2018 guidelines were used to define DKA severity: mild DKA was categorized at presentation with pH <7.3 and/or bicarbonate <15 mmol/L, moderate DKA (pH <7.2, and/or bicarbonate <10 mmol/L), and severe DKA (pH <7.1, and/or bicarbonate <5 mmol/L).[21]

2.1 | Statistical analysis

Descriptive statistics were used to summarize data. Because centers reported categorical age data, the midpoint coding method was used to calculate mean and standard deviation. Chi-square tests were used to compare differences in patient characteristics during the pandemic period compared to the pre-pandemic comparison group. All analysis was performed using R version 2.4.1.

3 | RESULTS

3.1 | Newly diagnosed T1D trends

Seven sites contributed longitudinal data for this cross-sectional analysis assessing trends in newly diagnosed T1D. There was a total of 17,749 and 17,597 T1D patients seen as outpatients at these centers in 2019 and 2020, respectively. As shown in Table 1, there were 1277 newly diagnosed patients in 2019 (7.2 per 100 total T1D patients) as compared to 1399 newly diagnosed patients (8 per 100 total T1D patients) in 2020 ($p = 0.007$). The mean age of patients diagnosed with T1D was not different, although there were fewer NH White youth diagnosed in 2020 ($p < 0.001$). Newly diagnosed patients were less likely to have private insurance in 2020 ($p = 0.001$).

3.2 | Severity of DKA

Of the newly diagnosed patients, a greater proportion presented in DKA in 2020 compared to 2019 (599 [42.8%] vs. 493 [38.6%], $p = 0.02$), and more patients presented with severe DKA ($p = 0.003$) as characterized by a pH <7.1 and/or bicarbonate of <5 mmol/L.

TABLE 1 Characteristics of patients with newly diagnosed T1D patients in 2019 versus 2020 (*N*[%])

Characteristics	Year 2019	Year 2020	*p*-Value
Total T1D patients	17,749	17,597	
Newly diagnosed T1D patients	1277 (7.2 per 100 patients)	1399 (8 per 100 patients)	0.007
Sex (female)	622 (48.7)	648 (46.3)	0.2
Mean age (SD)	10.63 (5.5)	10.19 (5.8)	0.5
Age category[a]			
0–5 Years	225 (17.6)	220 (15.7)	0.3
6–10 Years	413 (32.3)	440 (31.5)	0.6
11–19 Years	588 (46)	688 (49.2)	0.1
20+ years	44 (3.4)	48 (3.4)	1
Race/ethnicity			
NH White	830 (65)	810 (57.9)	<0.001
NH Black	146 (11.4)	156 (11.2)	0.8
Hispanic	121 (9.5)	140 (10)	0.6
Asian	15 (1.2)	15 (1.1)	0.9
Others	109 (8.5)	114 (8.1)	0.7
Not reported[b]	56 (4.4)	164 (11.7)	<0.001
Insurance type[c]			
Public	456 (35.7)	543 (38.8)	0.1
Private	691 (54.1)	670 (47.9)	0.001
Others	127 (9.9)	107 (7.6)	0.04
DKA on presentation	493 (38.6)	599 (42.8)	0.02
DKA severity[d]			
Mild	150 (11.7)	147 (10.5)	0.03
Moderate	133 (10.4)	146 (10.4)	0.4
Severe	145 (11.4)	215 (15.4)	0.003

Note: Mild DKA: ph <7.3 and/or bicarbonate <15 mmol/L; moderate DKA: pH <7.2, and/or bicarbonate <10 mmol/L; severe DKA pH <7.1, and/or bicarbonate <5 mmol/L.

[a]Patients in age category groups do not add up to the total because of under reporting.

[b]There is under reporting for race/ethnicity, which are categorized as not reported.

[c]There is under reporting for insurance type.

[d]Patients in DKA severity categories do not add up to the total number of patients who presented in DKA, due to under reporting.

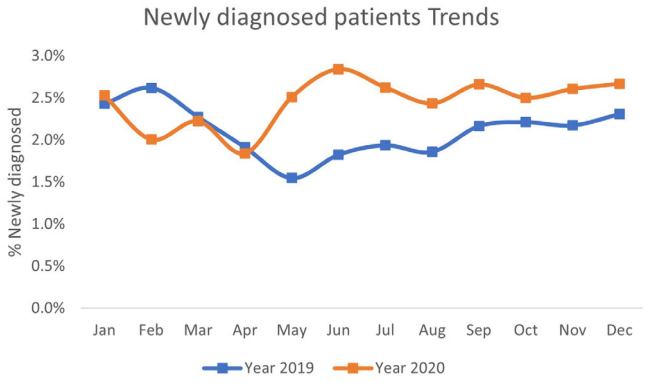

FIGURE 1 % of newly diagnosed T1D patients in 2019 versus 2020 (p-value = 0.007)

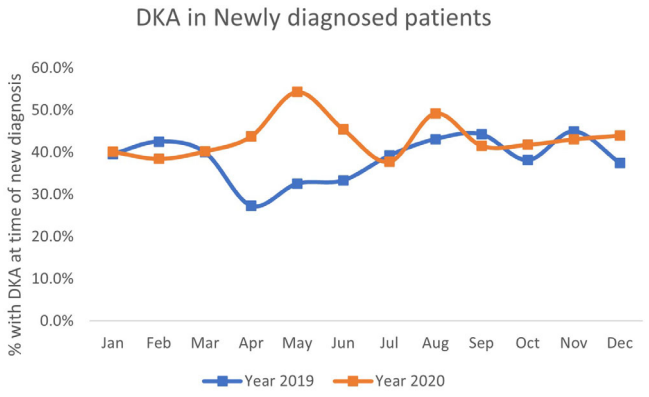

FIGURE 2 % of newly diagnosed T1D patients with DKA in 2019 versus 2020 (p-value = 0.02)

Hemoglobin A1c levels at the time of diagnosis were not available. Differences by age, race/ethnicity, insurance type in the newly diagnosed T1D patients presenting with and without DKA could not be analyzed from the aggregate data.

3.3 | Temporal trends in newly diagnosed T1D and DKA

Figures 1 and 2 display the monthly trends showing that more patients were diagnosed with T1D during the spring and summer months (March to September) of 2020 compared to 2019 ($p < 0.001$), with more patients presenting in DKA during the same period in 2020 ($p = 0.006$; Table S1) The percent of newly diagnosed T1D by race/ethnicity categories did not change significantly across both years. The monthly trends at each contributing site were independently analyzed and are provided in the Supplement. Analysis of clinic-to-clinic variations in incidence of new onset T1D showed that 6 out of the 7 contributing sites had an increase in incidence during this period (3 of 6 had a statistically significant increase), while one site had a statistically significant decrease in incidence. (Figures S1–S7).

4 | DISCUSSION

Our analysis presents the largest multi-center study of longitudinal trends of newly diagnosed T1D in the United States during the COVID-19 pandemic. These sites represented U.S. hospitals in the Northeast, Midwest, and West. In 2020, there was a significant increase in newly diagnosed T1D patients compared to the prior year. There was also an increase in patients with newly diagnosed T1D presenting in DKA during COVID-19 compared to the same period for the previous year, possibly representing delayed care due to lockdowns and deferred primary care.[7–9]

Initial reports suggested an increase in newly diagnosed T1D during the first wave of the COVID-19 pandemic (March 23–June 4, 2020), but this data was limited to 30 children in five inpatient units in one region of the United Kingdom.[13] In another analysis of newly diagnosed T1D across Germany during the first wave of the pandemic (March 1 to June 30, 2020), there was no increase in T1D diagnosis in this time frame compared to the prior 8 years.[16,17] While these previous studies are limited by small sample sizes and include data from only the first wave of the pandemic, our analysis offers a first look at the longitudinal data spanning multiple institutions across the United States, multiple waves of the pandemic, and a diverse patient population.

Similar to reports from other countries, an increase in the proportion of newly diagnosed T1D patients presenting in DKA was noted in this multicenter cohort, increasing from 38.6% to 42.8% from 2019 to 2020.[8] These rates are higher than recent worldwide data (29.9% rate of DKA at initial presentation of T1D), but are consistent with DKA rates in the United States which have been reported to be as high as 58% at the time of T1D diagnosis.[22–25] The increase in DKA at diagnosis during the COVID-19 pandemic could be attributed to delays in seeking medical care, especially in the early months of the pandemic from March to June of 2020, when "stay-at-home" orders were in effect in many parts of the United States. Although we were not able to analyze differences in DKA rates by race/ethnicity in aggregate data, other studies have shown that youth presenting in DKA at diagnosis were more likely to be minority race/ethnicity, have public insurance, and lower household income than youth without DKA at diagnosis.[26] Furthermore, a T1D exchange study of patients with known T1D during the COVID-19 pandemic showed that non-Hispanic black and Hispanic individuals were more likely to present in DKA with concurrent COVID-19 infection compared to non-Hispanic white individuals. Since the COVID-19 pandemic has disproportionately affected minority and low-income populations,[27,28] it is likely that these communities affected by social determinants of health bear a larger burden of DKA at diagnosis of T1D, and larger studies utilizing patient-level data should investigate this further. Given the high frequency of patients with new onset T1D presenting in DKA, it is important to increase public awareness of the symptoms of diabetes so that it can be identified early and treated.[22]

There was a decrease in non-Hispanic white youth with newly diagnosed T1D in 2020 compared to 2019. This is similar to recent SEARCH data suggesting that the incidence of T1D is increasing in Hispanic youth more significantly than non-Hispanic white youth and

that minority populations will likely represent a larger burden of diabetes in the future.[24]

Seasonal variation in the diagnosis of type 1 diabetes has previously been described, with more children being diagnosed between the months of December and February.[29] While 2019 data followed these typical trends, there were fewer newly diagnosed T1D in our cohort in January through April of 2020, suggesting that the COVID-19 pandemic upended typical temporal trends in T1D diagnosis. It is possible that some of the newly diagnosed patients would have been diagnosed sooner and have avoided DKA if not for "stay-at-home" orders, limited access and hesitance to seek preventive care during the initial wave of the pandemic. Further, there were regional differences in COVID-19 waves and pandemic lockdowns, which likely accounts for the site-to-site variation in incidence of new onset T1D.[30] Historically, some viruses have been associated with a diagnosis of diabetes, namely enteroviruses and SARS coronavirus 1 pneumonia.[4,31–34] Reports from both the United States and the United Kingdom suggest changes in other virus (Influenza, Rotavirus, Norovirus) activity during the pandemic, which could possibly account for differences in seasonality observed in our analysis.[35,36] Recent data from the Center for Disease Control suggests that there may be an increase in cases of diabetes (both type 1 and type 2 diabetes) after COVID-19 infection.[15] Future prospective long-term studies of youth with confirmed COVID-19 infections will need to be done to determine if future incidence of T1D changes due to the viral exposure of 2020 and 2021.

The main strengths of this study include large population size, data from time of diagnosis, and multiple sites. However, there are several limitations to this study. While this was a large multi-center study, no sites represented the Southeast and Southwest, limiting the generalizability of our findings. A major limitation of the study was the use of the outpatient T1D clinic population as the denominator, as it does not represent a population based sample and could be subject to referrals into the practice and/or transfers out of the practice which were not measured. Since data were submitted in aggregate and not patient-level data, there were limitations on the analysis we could perform. Differences in age, race/ethnicity, or insurance type in the subset of patients with newly diagnosed T1D patients presenting in DKA could not be assessed. Further, data on the presence of COVID-19 at diagnosis was not collected as COVID-19 PCR testing was initially limited and antibody testing was not routinely done.

5 | CONCLUSIONS

In summary, there was an increase in newly diagnosed T1D and a greater proportion of newly diagnosed T1D presenting in DKA at diagnosis during the COVID-19 pandemic compared to the prior year. Ongoing longitudinal studies are needed to understand the impact of COVID-19 on trends in diabetes diagnoses in the coming years.

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The T1D Exchange QI Collaborative is a quality improvement and learning health system of over 40 U.S. Endocrinology Centers. The centers collaboratively share data and improvement ideas to advance diabetes care.

CONFLICT OF INTEREST

Dr. Wolf reports financial support from Boehringer Ingelheim and Dexcom, not relevant to this manuscript. Dr. Ebekozien reports being on the Medtronic Diabetes Health Equity Advisory Board and financial support from Medtronic, Dexcom, and Eli Lilly through his organization. Dr. Lee is on the Medical Advisory Board of GoodRx. The other authors received no external funding.

AUTHOR CONTRIBUTIONS

Osagie Ebekozien conceived of the study. All authors collected the data. Nudrat Noor analyzed the data. Risa M. Wolf wrote the manuscript. All authors reviewed, edited, and approved the final version of the manuscript. Osagie Ebekozien, Nudrat Noor had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/pedi.13328.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

IRB approval was obtained by a central review board (Western Institutional Review Board) as an exempt study, and each site obtained local IRB approval as needed, with a waiver of consent.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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