Sharp Rise in New-Onset Pediatric Diabetes During the COVID-19 Pandemic

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ABSTRACT

Introduction: Recent studies report a significant impact of the COVID-19 pandemic on the incidence, severity, and management of diabetes.

Objective: To determine the incidence of new onset pediatric diabetes prepandemic versus during the pandemic and to analyze the presentation based on age, severity, HbA1c, body mass index, and COVID testing.

Methods: We conducted a retrospective review of all pediatric patients admitted with newly diagnosed type 1 and type 2 diabetes mellitus admitted to the American Family Children's Hospital (Madison, Wisconsin) from 2018 through 2021. Data included age at diagnosis, body mass index, hemoglobin A1c percent and pH at presentation, presence of autoimmune pancreatic antibodies, and COVID-19 polymerase chain reaction (PCR) results at admission in pre-COVID (January 2018-February 2020) versus during COVID (March 2020-December 2021). Statistical analysis was performed using SAS software with the incidences analyzed using univariate and multivariate Poisson regression analyses.

Results: During the pandemic, the incidence of both type 1 and type 2 diabetes mellitus increased significantly (69% and 225%, $P<0.001$, respectively), and a higher number of patients had diabetic ketoacidosis. Type 1 diabetes patients with a body mass index greater than the 95th percentile increased from 11.1% to 16.9% (OR 0.62; 95% CI, 0.29-1.29; $P=0.19$). Almost all patients were COVID-19 PCR negative at the time of diagnosis.

Conclusions: A dramatic increase in number and severity of newly diagnosed pediatric diabetes cases was seen during the pandemic. The increase was not explained by factors such as changes in referral patterns or insurance coverage. Further work is needed to understand the impact of societal factors and the direct diabetogenic effect of SARS-CoV-2.

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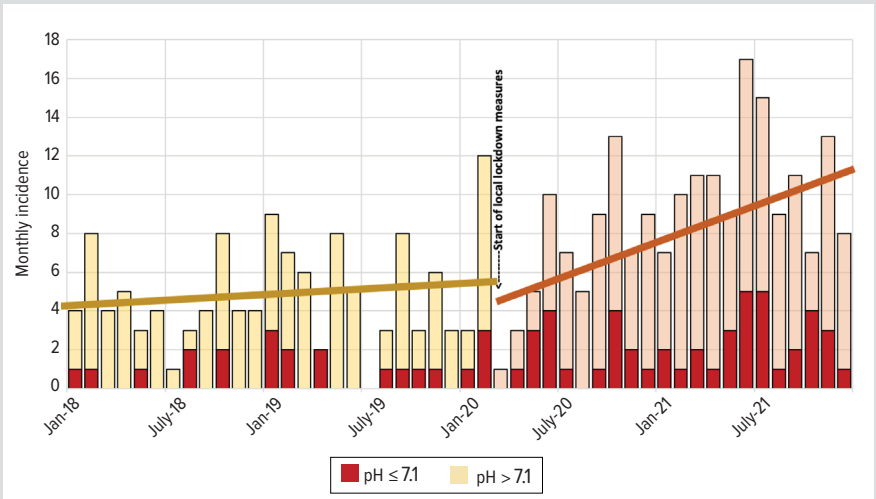
INTRODUCTION

Since the start of the COVID-19 pandemic, our institution has seen acute increases in both the number and severity of new-onset diabetes diagnoses among pediatric patients. Our study aims to better characterize this observation by comparing the presentation of newly diagnosed diabetes admitted to the American Family Children's Hospital in Dane County, Wisconsin, before and during the coronavirus pandemic.

The United States remains one of the countries most affected by the COVID-19 pandemic, with over 46 million cases reported and 25% of those cases in children.[1] Although severe illness in children is relatively rare,[2] it is imperative to further analyze the long-term effect of the pandemic on children's health.

The relationship between COVID-19 and diabetes has sparked interest since early in the pandemic. There are reports of an increase in pediatric new onset type 1 diabetes mellitus (T1DM) in areas heavily affected by the pandemic, with concern that a higher number are presenting in severe diabetic ketoacidosis.[3-6] The cause of this increase is not clear. Prior to the COVID-19 pandemic, research in related coronaviruses suggested that SARS-CoV-2-like viruses could increase the risk of diabetes due to its direct impact on beta cell function.[7,8] Reports of increased diabetic ketoacidosis presentations may suggest that effects of the pandemic led to delayed care.[9,10] This is in contrast to previous

Figure. Monthly Incidence Rates for Types 1 and 2 Diabetes Before and During the Pandemic, With Linear Regression Trend Lines of Pre- and During COVID Incidence



Pre-COVID: slope = 0.02 (P = 0.738); during COVID: slope = 0.27 (P = 0.024).

Table. Analysis of Diabetes Incidence Rate in Pre-COVID and COVID Periods

	Pre-COVID	During COVID	Rate Ratio	*P* value
Mean monthly total	4.88	8.95	1.83	<0.001
Mean monthly type 2	0.46	1.50	3/25	0.001
Mean monthly type 1	4.42	7.45	1.69	0.001
Mean monthly with pH ≤ 7.1	0.85	2.14	2.52	<0.001
Mean monthly with pH > 7.1	4.04	6.82	1.69	<0.001

All reported *P* values are 2-sided.

studies reporting a decrease in the rate of diabetic ketoacidosis at the time of diagnosis of T1DM from 38% in the late 1990s to 29% in 2010-2013.[11]

This study examines the number of cases of both type 1 and type 2 diabetes mellitus and severity of presentation prior to and during the pandemic through the end of 2021, thus allowing us to investigate the perceived increase and severity of the new-onset cases of diabetes.

METHODS

This is a retrospective study of pediatric patients admitted with newly diagnosed diabetes (type 1 or 2) to our institution from January 2018 through December 2021, comparing pre-COVID (January 2018-February 2020) to COVID (March 2020-December 2021). Data collected included age, date of admission, serum pH, antibody testing results for T1DM, body mass index (BMI), and hemoglobin A1c. T1DM was defined when any of the autoantibodies (islet cell antibody, 65 kDa glutamic acid decarboxylase, insulinoma-associated protein 2, or zinc transporter 8) were positive or BMI was greater than the 85th percentile, with polyuria and polydipsia. T2DM was defined if all pancreatic antibody testing was negative and BMI was greater than the 85th percentile. At our institution, all children with new-onset T1DM are admitted for initiation of insulin and education. For those with T2DM, only those in diabetic ketoacidosis or a significantly elevated A1c requiring insulin initiation are admitted. Incidence of T1DM and T2DM were analyzed using univariate and multivariate Poisson regression analyses. In order to account for potential confounding effects, age, BMI, and pH values at diagnosis were included as covariates in the multivariate analyses. Collinearity was evaluated by examining variance inflation factors. The comparison of pre-COVID-19 versus during COVID-19 was quantified by calculating the rate ratios of the monthly incidence rates and reported along with the corresponding 2-sided 95% confidence intervals. Monthly incidences (displayed in Figure) were calculated using regression analysis to display trends in pre-COVID and COVID-19 periods. All reported P values are 2-sided, and $P < 0.05$ was used to define statistical significance. Statistical analyses were analyzed using Microsoft Excel and SAS software (SAS Institute Inc., Cary NC), version 9.4. Approval for this study was obtained from the University of Wisconsin Institutional Review Board.

RESULTS

The incidence rate of T1DM increased by 69% ($P < 0.001$) overall from pre-COVID versus COVID, while T2DM increased by 225% ($P < 0.001$). The Figure further illustrates that the incidence rate of new diabetes cases increased dramatically after the pandemic measures were enforced in Wisconsin in March 2020, as indicated by the line of linear regression. The mean monthly rates of severe diabetic ketoacidosis (pH ≤ 7.1) increased from 0.85 pre-COVID to 2.14 during COVID (Table). The percent of T1DM patients with a BMI greater than the 95th percentile increased from 11.1% pre-COVID to 16.9% during COVID (OR 0.62; 95% CI, 0.29-1.29; $P = 0.19$). The majority of T2DM had an elevated BMI above the 95% percentile both pre-COVID and during the pandemic. There were no significant differences in HbA1c observed between the 2 time periods (data not displayed). Most patients were between 6 and 16 years of age at diagnosis, with no significant change in ages compared to previous years.

All patients from March 2020 onwards were tested for COVID-19 via polymerase chain reaction (PCR) at the time of hospital admission, with 9 positive results (5.6% of patients). It is unknown how many patients may have had previously contracted COVID-19, as routine screening for history of COVID-

19 was not consistently recorded at the time of admission, and COVID-19 antibody testing was performed in only a minority of patients.

DISCUSSION

While the rate of new pediatric cases of both T1DM and T2DM has been increasing slowly, we report an unexpectedly sharp rise for both conditions during the COVID-19 pandemic. In addition, a larger percent presented with severe ketoacidosis requiring intensive care. Our findings for T1DM are in line with other reports from European, Australian, and American pediatric populations during the COVID-19 pandemic.[2,4,5,10,12] Our study also reported a rise in new-onset T2DM requiring admission for insulin initiation, without a significant change in the BMI in this cohort. There were no changes in our referral patterns during this study.

The incidence of both T1DM and T2DM has risen steadily over the preceding decades. Between 2002 and 2015, the SEARCH study demonstrated an average annual increase of 1.9% in incidence of T1DM and 4.8% in T2DM in pediatric patients.[13] The increase in T2DM is attributed to the obesity epidemic and associated changes in diet, exercise, and sedentary behaviors. Reasons for the increase in T1DM are less clear, although childhood illnesses such as enterovirus and other environmental factors are often considered.[14] However, the increase we see in our study is dramatically higher compared to previous years before the pandemic.

The association of pediatric diabetes and COVID-19 is supported by a recent report by the Centers for Disease Control and Prevention, which found that following COVID-19 infection from March 1, 2020, through February 26, 2021, persons aged less than 18 years were more likely to receive a new diabetes diagnosis after 30 days since infection. Interestingly, non–SARS-CoV-2 respiratory infection was not associated with an increased risk for diabetes.[15] Our patient cohort had only 9 patients with a positive COVID-19 PCR at the time of diabetes diagnosis. Antibody testing for COVID-19 was not performed, thus we had limited ability to assess for prior infections and preexisting damage.

The mechanism of COVID-19 and increasing cases of pediatric diabetes is unknown. For T1DM and COVID-19, the hypothesis focuses on the direct effects of SARS-CoV-2 infection on pancreatic islet cells via the ACE2 receptor, thus binding and leading to cellular dysfunction and acute hyperglycemia.[16] Indirect effects of the pandemic involved in the pathophysiology of T1DM include isolation, stress, and increased BMI.[17]

For T2DM and COVID-19, the mechanism of action could include a direct impact of the virus on beta cells and other mechanisms, but also indirect effects such as sedentary lifestyle, limited medical access, and stress brought on by the pandemic. Physical education classes were altered or canceled entirely with the transition to online learning. School sports were often canceled or limited in scope. Stay-at-home ordinances may have led to decreased outdoor activities and group activities for some children.[18] In addition, dietary habits for children may have changed due to changes in schedules, increased access to snacks during the online school day at home, and psychosocial stress leading to compensatory eating behaviors.[19]

The increase in severity at presentation with ketoacidosis has been reported previously.[2,9,12,20] Reasons include delays in seeking care related to COVID-19. Several of our patient families reported delaying well-child appointments and evaluation for perceived minor concerns due to fears of exposure to infection. School closures and learning from home also limited the exposure of children to supervising adults, such as teachers and school nurses, who may notice changes in health missed by parents.[21]

Our study was limited due to its single center setting. Whether the SARS-CoV-2 virus itself increases the susceptibility to diabetes by triggering islet cell inflammation or by affecting the time of overt diabetes in patients with existing autoimmunity or the results we are seeing in our study are the downstream effects of the pandemic remain unknown. It will be imperative to carry out multicenter studies over extended time periods to explore the long-term effects of COVID-19 infection. Continued efforts such as the CoviDiab Registry (CoviDiab.e-dendrite.com) are critical in developing evidence-based guidelines and care for our vulnerable patients with comorbidities.

The major COVID variants noted during our study were alpha, beta, and delta, prior to the Omicron variant that presented near the end of 2021. Likewise, vaccinations for pediatric patients became available starting in early 2021 for those ages 16 to 18 years of age, May 2021 for those ages 12 to 15, and November for those ages 5 to 11 years of age, possibly influencing the trends seen towards the end of 2021. However, one of the limitations of our study remains that patient vaccination status and COVID variants were not recorded. It will be interesting to note how both of these factors continue to influence pediatric diabetes trends in the future. Health care systems should monitor this to adjust resources to meet the growing demands of the pediatric diabetes population.

CONCLUSIONS

We report a dramatic increase in number and severity of newly diagnosed pediatric diabetes cases seen during the COVID-19 pandemic. The increase was not explained by factors such as changes in referral patterns or insurance coverage. Further work is needed to understand the impact of societal factors and the direct diabetogenic effect of SARS-CoV-2.

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