Pediatric Diabetes on the Rise: Trends in Incident Diabetes during the COVID-19 Pandemic

Rachel Modarelli MD¹, Salma Sarah MPH, MBBS², Megan E. Ramaker, PhD³, Mboli Bolobiongo, MBS⁴, Robert Benjamin, MD², Pinar Gumus Balikcioglu, MD, MHSc²,³

1. Department of Pediatrics, Duke University Medical Center, Durham, NC, United States
2. Division of Pediatric Endocrinology and Diabetes, Duke University Medical Center, Durham, NC, United States.
3. Duke Molecular Physiology Institute, Duke University Medical Center, Durham, NC, United States.
4. Duke School of Medicine, Master of Biomedical Sciences, Durham, NC, United States

Corresponding Author:

Pinar Gumus Balikcioglu, MD, MHSc
Duke University Medical Center
Division of Pediatric Endocrinology and Diabetes
Lenox Baker Children’s Hospital
3000 Erwin Road
Durham, NC 27705
Tel: 919-668-4002
Fax: 919-684-8613

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Reprint requests should be addressed to Pinar Gumus Balikcioglu, MD, MHSc

Duke University Medical Center

Division of Pediatric Endocrinology and Diabetes

Lenox Baker Children’s Hospital

3000 Erwin Road

Durham, NC 27705

Tel: 919-668-4002

Fax: 919-684-8613

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ABSTRACT:

Context: The effects of the COVID-19 pandemic on the incident cases of pediatric Type 1 (T1D) and Type 2 diabetes (T2D) are not clear.

Objective: To identify trends in incidence and presentation of pediatric new-onset T1D and T2D during the COVID-19 pandemic.

Methods: A retrospective chart review was conducted. Demographics, anthropometrics, and initial labs from patients ages 0-21 who presented with new-onset diabetes to a pediatric tertiary care center were recorded.

Results: During the pandemic incident cases of pediatric T1D increased from 31 in each of the prior two years to 46; an increase of 48%. Incident cases of pediatric T2D increased by 231% from 2019 to 2020. The number of incident cases of pediatric T2D increased significantly more than the number of incident cases of pediatric T1D (p-value = 0.009). Patients with T2D were more likely to present in DKA, though this was not statistically significant (p-value=0.093). Severe DKA was higher compared to moderate DKA (p-value = 0.036) in incident cases of pediatric T2D. During the pandemic, for the first time, incident cases of T2D accounted for more than half of the all newly diagnosed pediatric diabetes cases (53%).

Conclusions: There were more incident pediatric T1D and T2D cases as well as an increase in DKA severity in T2D at presentation during the COVID-19 pandemic. More importantly, incident T2D cases were higher than the incident T1D during the pandemic. This clearly suggests a disruption and change in the pediatric diabetes trends with profound individual and community health consequences.

Key Words: Pediatric diabetes, type 1 diabetes, type 2 diabetes, COVID-19, diabetic ketoacidosis
Introduction

The COVID-19 pandemic has introduced countless challenges to the medical field and has brought increased attention to children with pre-existing disorders such as diabetes. Over six million children have tested positive for coronavirus disease 2019 (COVID-19) since the onset of the pandemic, a number that is projected to continue increasing (1). While children have lower rates of COVID-19 mortality, the presence of pre-existing conditions such as diabetes can heighten the severity of their clinical presentations. Studies in adults have shown new onset diabetes as well as expression of pre-existing diabetes in a significant proportion of patients with COVID-19, both presenting with more severe infection (2). Another study discussing the effect of the pandemic on adults with diabetes showed increases in diabetes-related stress, higher in young adults with T2D compared to older adults (3). However, there are few studies evaluating the effects of COVID-19 on diabetes-related outcomes in children. Current data are not only limited but contradictory regarding the incidence and severity of presentation in childhood diabetes. Reports range from an increase in diabetic ketoacidosis rates in T1D and T2D in children to no change or even a decrease in the incidence of T1D during the pandemic (4-9).

There are several factors proposed to contribute to an increase in either the incidence or severity of pediatric diabetes. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, infects and replicates in cells of the human endocrine and exocrine pancreas, and is suspected to downregulate the renin angiotensin-aldosterone system leading to eventual destruction of pancreatic beta cells (10-13). Additionally, COVID-19 causes an hyperinflammatory state and may induce ketosis and ketoacidosis (13,14). Other factors include the immense behavioral and environmental changes since the onset of the pandemic. Across the globe, children were enrolled in school virtually, extracurricular activities were limited, and daily routines were adjusted to decrease the potential exposure to COVID-19. Consequences of this included increased
screen time, unhealthy eating habits, decreased physical activity, and worsened sleep hygiene, which all have associations with increased body mass index (15, 16).

The objectives of this retrospective study were to compare the rates of diagnosis of new onset pediatric T1D and T2D cases, and to compare the severity of clinical presentation among patients seen at a single academic medical center during the COVID-19 pandemic with those in the two years preceding the pandemic. These are discussed while considering demographic and anthropometric changes in the overall clinic patient cohort. We hypothesized that the number of incident cases of both T1D and T2D have increased during the pandemic and that the severity of clinical presentation increased.

Materials and Methods

Data Collection

This study was completed using retrospective review of the electronic medical record of all patients admitted to Duke University Hospital or seen outpatient in the Duke Pediatric Endocrinology and Diabetes Clinics with a new diagnosis of diabetes over a three-year time period from April 1, 2018 until March 31, 2021. Time periods were separated as follows: April 1, 2018- March 31, 2019, April 1, 2019- March 31, 2020, and April 1, 2020- March 31, 2021. The final time period represents the COVID-19 pandemic. Duke University Hospital is a 190-bed pediatric tertiary acute care hospital with 25 specialties. Our Diabetes Program, recognized by the American Diabetes Association for diabetes self-management education, offers the latest advances in T1D and T2D diabetes care, and provides clinical care to approximately 700 youth with T1D and 300 youth with T2D annually. All patients with new onset T1D are admitted to the hospital, whereas patients with new onset T2D are
admitted only for management of severe hyperglycemia, ketosis, and/or challenging psychosocial circumstances.

The search protocol included any patient ages 0 to 21 at the time of initial diagnosis using ICD-10 diagnosis codes for T1D (E10*), T2D (E11*), and hyperglycemia (R73.9, R73.09). Each patient's demographic and anthropometric data were collected at the time of initial diagnosis. We collected vital signs on presentation to the hospital or clinic, as well as hemoglobin A1c (HbA1c), venous pH, serum bicarbonate, beta hydroxybutyrate (βOHB), c-peptide, sodium, initial point of care glucose, and anion gap. To assess renal and liver involvement, serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, and BUN levels were extracted. Given the effects of COVID-19 on inflammatory and autoimmune processes we also collected white blood cell count, hemoglobin, platelet count, thyroid stimulating hormone (TSH), free thyroxine (FT4) and celiac panel including immunoglobulin A and tissue transglutaminase (TTG) antibodies at presentation. COVID test results were recorded at the time of presentation if tested, using Coronavirus (COVID-19) SARS-CoV-2 PCR or point of care Coronavirus (COVID-19) SARS-CoV-2 Rapid Test.

This protocol was approved and deemed exempt by the Duke University Health System Institutional Review Board.

Definitions

This study's criteria for new onset diabetes aligns with guidelines of the American Diabetes Association, requiring the patient to have either a HbA1c greater than or equal to 6.5%, a fasting plasma glucose of 126 mg/dl or higher, or a random glucose of 200 mg/dl or higher with symptoms of diabetes (17). The diagnosis of T1D was based on presence of positive autoantibodies against GAD65, islet antigen 2 (IA2), insulin, or zinc transporter 8 and a requirement for insulin. T2D was
diagnosed in patients without autoantibodies and BMI percentile of at least 85% within six months of diagnosis. Those without autoantibody testing were categorized based on the impression of the pediatric endocrinologist with consideration of their initial presentation, weight trends, and insulin requirements.

Diabetic ketoacidosis (DKA) was defined as a serum pH equal to or less than 7.3 or bicarbonate less than or equal to 15 mmol/L, with ketonemia or ketonuria, and glucose of 200 mg/dl or greater. DKA was further categorized as severe (pH <7.1), moderate (pH 7.1-7.19), or mild (pH 7.2-7.3) (18). Plasma osmolarity was calculated by using the following formula (Posm =2 [Na]+glucose (mg/dL)/18+BUN (mg/dL)/2.8) unless it was measured directly (19). For calculations uncorrected Na levels were used. Celiac screening was considered positive if the tissue transglutaminase (TTG) antibodies were equal to or greater than 20 units.

Statistical Analysis

Microsoft Excel (2016) was used to calculate descriptive statistics (eg. Mean, standard deviations) and perform statistical analysis of continuous variables (eg. ANOVA). Statistical analysis of categorical variables (eg. sex, race, ethnicity) was performed by Chi-squared test or Fisher’s exact test using R studio version 3.5.2. Cochran Armitage trend tests (one-tailed, p-value cut=0.05) were performed to assess for increases in diabetes severity and T1D vs T2D proportion across the three years using R (version 1.4.1106) and the DescTools package (20, 21).
Results

Demographics:

In total, 207 patients were diagnosed with incident diabetes from April 2018 through March 2021, 108 with T1D and 86 with T2D (Table 1, 2). 13 patients with incident diabetes did not meet the criteria for either type and were excluded from analysis. The race and ethnicity distributions for T1D and T2D patients were consistent without any statistical differences among the three years. 63% of patients with T1D were white, 27% black or African American, and 11% Hispanic or Latino on average across three years (Table 1). Among patients with T2D, 13% were white, 71% black or African American and 19% were Hispanic or Latino on average across three years (Table 2).

Changes in incident cases:

The number of patients diagnosed with T1D between April 1, 2020 and March 31, 2021 (n=46) was 48% higher than the average number of patients with T1D (n=31) from the previous two years (Figure 1). There was also an increase in T2D, with 17 patients in 2018 and 16 in 2019, to 53 patients during the pandemic, a 231% increase from the year prior (Figure 1). The number of incident pediatric T2D cases increased significantly more than the number of incident pediatric T1D cases from 2018-2020 (p-value = 0.009). The average age at initial diagnosis was 10 years for T1D and 13.5 years for T2D and did not differ significantly over the three years (Table 1). There were more females than males diagnosed with T1D with the exception of 2020-2021, where 65% of patients were males, compared to 45% in prior years; however, this did not reach statistical significance (p-value=0.12) No patients tested positive for COVID-19.
Anthropometric trends and clinical severity at presentation:

T1D

The BMI percentiles steadily increased in patients diagnosed with T1D, from 47.48 percentile to 64.83 percentile during the year 2021, nearing statistical significance (p=0.064, Figure 2). There were no changes in HbA1c at presentation (Table 3). Over the three years, 50% (n=54) of patients presented in DKA, with 45% in 2018, 55% in 2019, and 50% in 2020. The number of T1D patients presenting with mild DKA in 2020 rose significantly compared to T1D patients without mild DKA over the three years (p-value = 0.027). Regarding secondary organ involvement, there were no statistical differences in the liver or kidney function tests (Table 4).

T2D

Anthropometric data for patients diagnosed with T2D did not differ significantly over the three-year period. BMI percentile averaged 98.0 in 2018 and 2019, and 96.8 in 2020. At presentation HbA1c averaged 9.0 % in 2018, 9.6 % in 2019, and 10.3% in 2020 (p=0.223) (Table 5). There were no changes in liver or kidney function (Table 6).

The rate of patients presenting in DKA increased overall, from 12% (n=2) in 2018 and 6% (n=1) in 2019, to 23% in 2020 (n=12), an increase of 91.7% from 2018 to 2020 (Figure 3). Patients with T2D were more likely to present in DKA, though this was not statistically significant (p-value=0.093). When data was stratified by the severity of DKA, no patient presented in severe DKA until 2020 (n=1), moderate DKA remained stable each year, and mild DKA increased from 6% (n=1) in 2018 to 13% (n=7) in 2020, an increase of 116% (Figure 3). The number of T2D patients with severe DKA rose significantly more than the number of T2D patients with moderate DKA over the three years (p-value = 0.036). When comparing the race and ethnicity of the patients presenting in DKA, 100% of patients...
in 2018 and 2019 identified as black or African American, and in 2020, 92% (n=11) were black or African American and 8% (n=1) were Hispanic, showing the predominance of minority populations.

Discussion

There were more incident pediatric T1D and T2D cases as well as an increase in DKA at presentation during the initial year of the COVID-19 pandemic. Interestingly, incident T2D cases increased from 2018 to 2020 significantly more than T1D cases (p-value= 0.009). Furthermore, there was a higher number of incident T2D (n = 53) than incident T1D cases (n = 48) during the pandemic. This clearly suggests a disruption and change in the childhood diabetes trends during the COVID-19 pandemic with profound individual and community health consequences.

According to SEARCH, a population-based registry of diabetes, the incidence of diabetes in childhood and adolescence increased from 2002 to 2015 (22). T1D incidence increased at an annual percent change of 1.9%, while the incidence of T2D increased at a rate of 4.8% per year (22). However, the striking increases we have identified are far beyond the previously expected trajectories. A model using SEARCH data as well as the U.S Census projections estimated an increase of T1D by 23% and of T2D by 49% by the year 2050 (23-25). Our data showed a 48% increase in T1DM and a 231% increase in T2D incident cases within just a year, a marked increase from the expected trends.

We also identified a significant increase in mild DKA at presentation for incident T1D and severe DKA in incident T2D cases consistent with the emerging literature (4,7-9). Data shared from the multisite registry Type 1 Diabetes Exchange reported a higher proportion of patients with T1D presenting in DKA when compared to previous years (5). Likewise, in Poland, DKA presentation at the time of T1D diagnosis increased from 40.38% to 52.94% from 2019 to 2020, with a statistically significant number of DKA cases presenting in severe DKA (p=0.0262) (26). What is even more remarkable are the significant increases in severe DKA as the initial presentation of T2D in our pediatric population.
In accord with our study, findings at Children’s Hospital LA reveal that their DKA prevalence rates increased from under 10% prior to the pandemic to 20% in 2020 (p=0.029), and two patients diagnosed with T2D presented in severe DKA in 2020 compared to none prior (4). Likewise, another study from Children’s National Hospital revealed an increase in DKA rates from 4% pre-pandemic to 23.4% during the first 12 months of the COVID-19 pandemic. In our study, the rate of DKA in T2D increased by 91.7%, with 2020 showing the only case of severe DKA and an increase by 116% in mild DKA. Importantly, these increases in DKA also mean that more patients are presenting as inpatient and require more extensive treatment. This confirms our hypothesis that patients are presenting with more severe illness during the pandemic.

There is reason to suspect that the COVID-19 virus downregulates ACE2 upon binding, leading to eventual destruction of pancreatic β-cells (10-13). Additionally, COVID-19 causes a hyperinflammatory state and may induce ketosis and ketoacidosis (13, 14). Given that none of the patients tested positive for COVID, the hypothesis that SARS-CoV2 infection may destroy β-cells may not apply to outcome of this study.

Other potential explanations include patient delay in seeking care due to the pandemic lockdown or decreased clinic availability, and the immense behavioral and environmental changes since the onset of the pandemic. Around the world, children were enrolled in school virtually, extracurricular activities were limited, and daily routines were adjusted to decrease the potential exposure to COVID-19. Potential consequences include increased screen time, unhealthy eating habits, decreased physical activity, and worsened sleep hygiene, all of which have associations with increased BMI (15, 16). A recent meta-analysis showed an increase in BMI in school age children and an increase in obesity prevalence from 10.5% to 12.6% in high school and college students during the pandemic (27). Another study completed by the Children’s Hospital of Philadelphia demonstrated an increased obesity prevalence from 13.7% to 15.4% in 2020 (28). There were no
significant changes in body mass index in children and adolescents with T2D. Given that these patients had pre-existing severe obesity, this might not be surprising. While it did not reach statistical significance, there was a trend for an increase in BMI in patients diagnosed with type 1 diabetes (p-value=0.064). Consistent with our results, a study in Saudi Arabia demonstrated that while the BMI was still within the normal range, the average BMI was significantly higher in 2020 compared to the year prior (29). Whether the increase in BMI may play a role in the rise in incident cases of T1D requires careful consideration. Independent of the COVID19 pandemic, previous studies have reported that an elevated BMI is associated with a higher risk of developing T1D (30). For every 1-kg/m2 increase in BMI, there was a 6.3% increased relative risk in developing T1D (30).

It is proposed that dietary changes with an increase in adiposity can provide one link between rising BMI and incidence of T1D, causing pancreatic β-cell fragility and decline in β-cell mass (31). Also, it is important to consider other possible etiologies of increasing T1D incidence such as the hygiene hypothesis, which connects our improved health hygiene to weaker innate defense mechanisms and increased susceptibility to autoimmune diseases including T1D (31).

While there were no significant differences in the race or ethnicity of the patients presenting during the pandemic, it is important to highlight that the patients diagnosed with T2D who presented in DKA were all of minority race and ethnicity, specifically Black or African American (92%) or Hispanic or Latino (8%). One study in the US demonstrated that non-Hispanic Black and Hispanic youth had worse metabolic control at the time of diagnosis of T2D, and non-Hispanic Blacks had three times the rate of DKA at presentation when compared to other racial or ethnic minorities (32).

Given the effects of COVID-19 on inflammatory and autoimmune processes, we collected data on white blood cell and platelet count (33,34), thyroid stimulating hormone (TSH), free thyroxine (FT4)
and celiac panel including immunoglobulin A and tissue transglutaminase (TTG) antibodies at presentation. We did not observe any differences in white blood cell or platelet counts over the three years. Due to the autoimmune nature of T1D, children and adolescents are at elevated risk of developing additional autoimmune disorders, such as celiac or thyroid disease. Studies report that positive thyroid antibodies are present in 12% to 23% of T1D patients and celiac disease prevalence ranges from 1% to 16% (35). Consistent with the literature, over the three years, 14.8% (n=16) of our patients with T1D had positive celiac screening, with 12.9% (n=4) in 2018, 12.9% (n=4) in 2019, and 16.7% (n=8) in 2020. Though not statistically significant, our data shows a 24.9% increase in positive celiac screening during the pandemic (p-value=0.282). None of the patients with T2D had positive celiac screening. There were no significant changes in thyroid dysfunction both in T1D and T2D. It will be interesting to monitor the rates of autoimmune disorders in patients with T1D and T2D in the upcoming years.

For disease severity at presentation, we investigated secondary organ involvement including liver and kidney functions. Liver function was assessed through measurement of AST and ALT and kidney function through measurement of creatinine and BUN. The hemoglobin was also recorded to assess for signs of hemoconcentration, which can be seen in the setting of DKA due to hypovolemia. There were no statistically significant differences in liver or kidney function over the three years. Remarkably, the average ALT and AST for T1D were 20 U/L and 18.5 U/L, while the average AST and ALT for T2D were 48.6 U/L and 34.7 U/L respectively. This supports the concept that patients with T2D are at higher risk of steatosis and developing nonalcoholic fatty liver disease (36). Hemoglobin values remained consistent over the three-year period.
Limitations of this study warrant consideration. It is important to note that no patients tested positive for COVID-19, thus we cannot state that the trends observed were due to direct effects of COVID-19 infection. However, we did not measure SARS-CoV-2 antibodies and therefore do not know if any of the patients presenting after March 2020 had a prior COVID-19 infection that could have contributed to pancreatic damage (37). There was no COVID-19 testing completed in the outpatient setting. Nevertheless, the findings suggest that social and economic factors exacerbated by COVID-19, contributed to the rising incidence of T1D and T2D in children. Because this data came from a single tertiary medical center, it may not be generalizable to a larger population. Lack of high-risk racial and ethnic minority groups such as American Indian, Pacific Islanders and Asian Americans in our T2D cohort should be highlighted. This points to the necessity of gathering data from multiple different sites globally. Lastly, we cannot derive the incidence data due to lack of an appropriate denominator.

In conclusion, pediatric diabetes cases increased during the pandemic year and there was a significant increase in incident pediatric T2D cases compared to incident pediatric T1D cases from 2018 to 2020. Furthermore, there were more pediatric patients with mild DKA in T1D and severe DKA in T2D cases at presentation during the first year of the COVID-19 pandemic compared to prior years. Strikingly, for the first time, incident T2D cases accounted for a majority (53%) of all newly diagnosed pediatric diabetes cases in 2020. Given that T2D has a more aggressive course in youth than in adults, with early and rapid deterioration of β-cell function, and rapid progression to insulin dependence [38-42], this raises great concern for long-term complications and comorbidities leading to profound individual and community health consequences. Thus, the social and economic factors associated with but not truly caused by COVID-19, should be targeted for achieving health equity and preventing lifelong health consequences.
Data Availability Statement: Some or all data generated or analyzed during this study are included in this published article or in the data repositories listed in References.
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Tables and Figures:

Table 1. Type 1 Diabetes Demographic Data. Age is represented in years indicated by group mean +/- standard deviation. Race, ethnicity, and insurance are indicated by number of participants (N) and percent (%) of group total.

|                | 2018-2019 N=31 | 2019-2020 N=31 | 2020-2021 N=46 | P value |
|----------------|----------------|----------------|----------------|---------|
| Age, years (mean ± SD) | 9.87± 3.49 | 10.39± 4.89 | 10.46± 3.67 | 0.806   |
| Gender         |               |               |               |         |
| Male           | 14 (45%)      | 14 (45%)      | 30 (65%)      | 0.12    |
| Female         | 17 (55%)      | 17 (55%)      | 16 (35%)      | 0.12    |
| Race, N (%)    |               |               |               |         |
| White          | 20 (65%)      | 18 (58%)      | 30 (65%)      | 0.80    |
| Black or African American | 8 (26%) | 10 (33%) | 10 (22%) | 0.59    |
| More than one race | 1 (3%) | 0 (0%) | 0 (0%) | 0.57    |
| American Indian or Alaska Native | 0 (0%) | 1 (3%) | 0 (0%) | 0.57    |
| No Response    | 2 (6%)        | 2 (6%)        | 6 (13%)       | 0.53    |
| Ethnicity, N (%) |           |               |               |         |
| Hispanic or Latino | 3 (10%) | 3 (10%) | 6 (13%) | 0.86    |
| Non-Hispanic or Latino | 27 (87%) | 27 (87%) | 39 (85%) | 1       |
| No response    | 1 (3%)        | 1 (3%)        | 1 (2%)        | 1       |
| Insurance, N (%) |            |               |               |         |
| Public         | 9 (29%)       | 15 (48%)      | 19 (41%)      | 0.29    |
| Private        | 21 (68%)      | 16 (52%)      | 24 (52%)      | 0.33    |
| Uninsured      | 1 (3%)        | 0 (0%)        | 3 (7%)        | 0.39    |

Table 2. Type 2 Diabetes Demographic Data. Age is represented in years indicated by group mean +/- standard deviation. Race, ethnicity, and insurance are indicated by number of participants (N) and percent (%) of group total.

|                | 2018-2019 N=17 | 2019-2020 N=16 | 2020-2021 N=53 | P value |
|----------------|----------------|----------------|----------------|---------|
| Age, years (mean ± SD) | 14.00± 2.35 | 12.94± 2.64 | 13.81± 2.35 | 0.376   |
| Gender         |               |               |               |         |
| Male           | 7 (41%)       | 7 (44%)       | 25 (47%)      | 0.90    |
| Female         | 10 (59%)      | 9 (56%)       | 28 (53%)      | 0.90    |
| Race, N (%)    |               |               |               |         |
| White          | 2 (12%)       | 3 (19%)       | 4 (8%)        | 0.42    |
| Black or African American | 12 (70%) | 13 (81%) | 33 (62%) | 0.40    |
| More than one race | 0 (0%) | 0 (0%) | 0 (0%) | 1       |
| American Indian or Alaska Native | 0 (0%) | 0 (0%) | 2 (4%) | 1       |
| No Response    | 3 (18%)       | 0 (0%)        | 14 (26%)      | 0.55    |
| Ethnicity, N (%) |            |               |               |         |
| Hispanic or Latino | 3 (18%) | 0 (0%) | 11 (20%) | 0.13    |
| Non-Hispanic or Latino | 14 (82%) | 16 (100%) | 39 (74%) | 0.55    |
| No response    | 0 (0%)        | 0 (0%)        | 3 (6%)        | 1       |
| Insurance, N (%) |            |               |               |         |
Table 3. Type 1 Diabetes Initial Labs. P-values indicated from ANOVA tests to identify significant changes throughout the three years.

|                      | 2018-2019 | 2019-2020 | 2020-2021 | P-value |
|----------------------|-----------|-----------|-----------|---------|
|                      | Mean±SD   | Mean±SD   | Mean±SD   |         |
| HbA1c (%)            | 12.28±2.52| 12.68±2.06| 12.09±2.54| 0.565   |
| Initial glucose (mg/dl) | 462.61±151.14 | 522.84±172.35 | 497.61±257.95 | 0.522   |
| pH, Venous           | 7.22±0.18 | 7.23±0.16 | 7.25±0.17 | 0.808   |
| Bicarbonate, Venous (mmol/L) | 16.36±8.53 | 15.51±8.08 | 17.09±8.05 | 0.719   |
| βOHB (mmol/L)        | 5.68±2.53 | 4.79±2.72 | 4.89±2.82 | 0.544   |
| Anion Gap (mmol/L)   | 17.71±6.27| 18.31±5.47| 17.72±6.28| 0.900   |
| Initial C-peptide (ng/ml) | 0.49±0.44 | 0.53±0.32 | 0.71±1.01 | 0.396   |
| Plasma Osmolarity (mOsm/kg) | 298.86±11.50 | 299.08±11.64 | 298.42±12.96 | 0.971   |

Table 4. Type 1 Diabetes secondary organ involvement and autoimmune labs. P-values indicated from ANOVA tests to identify significant changes throughout the three years.

|                      | 2018-2019 | 2019-2020 | 2020-2021 | P-value |
|----------------------|-----------|-----------|-----------|---------|
|                      | Mean±SD   | Mean±SD   | Mean±SD   |         |
| ALT (U/L)            | 19.69±6.45| 16.65±3.89| 23.46±23.03| 0.310   |
| AST (U/L)            | 17.38±4.79| 17.26±6.23| 20.75±7.97 | 0.162   |
| BUN (mg/dl)          | 15.87±11.5| 13.55±5.57| 13.02±4.67 | 0.251   |
| Creatinine (mg/dl)   | 0.87±0.63 | 0.83±0.31 | 0.83±0.35 | 0.904   |
| WBC (x10^9/L)        | 11.92±8.1 | 10.48±10.2| 10.20±6.39 | 0.589   |
| Platelet (x10^9/L)   | 335.00±78.66| 322.55±10.65| 310.38±91.77 | 0.569   |
| Hgb (g/dl)           | 14.66±1.06| 14.51±1.32| 14.81±1.54 | 0.663   |
| FT4(ng/dl)           | 0.97±0.23 | 0.93±0.23 | 0.94±0.2  | 0.779   |
| TSH (µIU/mL)         | 2.56±2.80 | 1.96±1.46 | 2.21±1.31 | 0.482   |
| IgA (mg/dl)          | 169.46±103.4| 167.34±100.6| 176.21±100.4 | 0.929   |
| TTG (Units)          | 8.32±10.96| 12.69±25.17| 17.41±36.53| 0.412   |
Table 5. Type 2 Diabetes initial labs. P-values indicated from ANOVA tests to identify significant changes throughout the three years.

|                      | 2018-2019 | 2019-2020 | 2020-2021 | P-value |
|----------------------|-----------|-----------|-----------|---------|
|                      | Mean±SD   | Mean±SD   | Mean±SD   |         |
| HbA1c (%)            | 9.04±2.62 | 9.56±2.67 | 10.31±2.85| 0.223   |
| Initial glucose (mg/dl) | 248.06±146.8 | 276.13±145.16 | 358.64±293.71 | 0.209   |
| pH, Venous           | 7.27±0.11 | 7.27±0.11 | 7.26±0.13 | 0.986   |
| Bicarbonate, Venous (mmol/L) | 21.36±6.98  | 23.00±4.81  | 20.82±7.03 | 0.662   |
| βOHB (mmol/L)        | 2.84±3.51 | 2.39±1.67 | 3.60±0.769| 0.769   |
| Anion Gap (mmol/L)   | 11.82±4.42| 12.10±4.58 | 15.00±0.254| 0.254   |
| Initial C-peptide (ng/ml) | 3.68±2.82  | 3.10±2.24  | 2.84±0.674| 0.674   |
| Plasma Osmolarity (mOsm/kg) | 292.51±6.31 | 294.09±9.89 | 299.08±0.425| 0.425   |

Table 6. Type 2 Diabetes initial secondary organ involvement and autoimmune Labs. P-values indicated from ANOVA tests to identify significant changes throughout the three years.

|                      | 2018-2019 | 2019-2020 | 2020-2021 | P-value |
|----------------------|-----------|-----------|-----------|---------|
|                      | Mean±SD   | Mean±SD   | Mean±SD   |         |
| ALT (U/L)            | 41.77±45.36 | 53.10±99.38 | 50.89±53.89 | 0.881   |
| AST (U/L)            | 32.38±33.63 | 33.33±46.48 | 38.49±32.44 | 0.831   |
| BUN (mg/dl)          | 9.61±3.36 | 10.67±3.89 | 10.11±5.90 | 0.881   |
| Creatinine (mg/dl)   | 0.72±0.22 | 0.80±0.34 | 0.90±0.72 | 0.600   |
| WBC (x10^9/L)        | 10.00±9.46 | 9.46±3.65 | 10.22±4.67 | 0.913   |
| Platelet (x10^9/L)   | 345.28±73.35 | 322.43±49.77 | 296.42±69.9 | 0.171   |
| Hgb (g/dl)           | 14.01±1.72 | 14.39±1.20 | 14.41±1.83 | 0.858   |
| FT4 (ng/dl)          | 2.21±3.74 | 1.03±0.18 | 0.94±0.18 | 0.087   |
| TSH (µIU/mL)         | 1.37±0.79 | 7.91±15.90 | 2.28±1.15 | 0.022   |
| IgA (mg/dl)          | 170.8±65.09 | 143.0±21.21 | 199.60±93.1 | 0.586   |
| TTG (Units)          | 3.80±1.64 | 3.50±0.71 | 3.60±2.08 | 0.975   |
**Figure 1.** Incident Cases of Pediatric Type 1 diabetes and Type 2 Diabetes rose significantly during the COVID 19 pandemic compared to prior two years. Exact number of cases are indicated on the top of each bar.

**Figure 2.** BMI percentiles, T1D and T2D. Average BMI percentile showed an increasing trend in patients with new onset T1D from 2018 to 2021. * = Anova p-value < 0.1

**Figure 3.** DKA Severity in Type 2 Diabetic patients increased during the COVID-19 pandemic (2020-2021) compared to prior years.
Figure 2

- 2018-2019: 47.48
- 2019-2020: 61.71
- 2020-2021: 64.83

- 2018-2019: 98.05
- 2019-2020: 98.18
- 2020-2021: 96.83
