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## LETTER



# The COVID-19 pandemic and associated worsening of diabetic ketoacidosis presentation in youth

The coronavirus 2019 (COVID-19) pandemic has had a substantial impact on healthcare systems across the world. Initiatives such as social distancing and limitations of nonessential services, including conversion of in-person wellchild visits to telehealth visits, were put in place to reduce the transmission of the virus.<sup>1,2</sup> These limitations may have also had unforeseen consequences, especially in regard to delay of medical care in children.<sup>3</sup> There is particular concern about youth with diabetic ketoacidosis (DKA) as their clinical manifestation may be subtle despite severe metabolic abnormalities.<sup>4,5</sup> At clinical onset, the finding of DKA has become more common worldwide, including the United States, with several implications including impaired brain growth and lower cognitive scores with only a single episode of DKA.<sup>6,7</sup> Thus, the objective of this study was to compare the proportion of youth with diabetes admitted to the hospital with DKA during the COVID-19 pandemic to the previous year.

This single-centre retrospective study included youth between 9 months and 21 years of age, admitted to our hospital with diagnoses of diabetes mellitus or DKA during two defined time periods. The two time periods were 1 March to 30 June 2019 ('Pre-COVID-19') and 1 March to 30 June 2020 ('COVID-19'), mirroring the first wave of COVID-19 infections in Ohio. The primary outcome of this study was prevalence of DKA, stratified by severity. Based on venous blood gas findings, mild DKA was defined as pH of 7.2-7.29 or bicarbonate (HCO3) of 10-14 mEq/L, moderate DKA was defined as pH of 7.1-7.19 or HCO3 of 5-9 mEq/L, and severe DKA was defined as pH less than 7.1 or HCO3 less than 5 mEq/L.<sup>8</sup> Chi-square and Fisher's exact tests were utilized to examine the relationship between categorical measures. Logistic regression was used to compute odds ratios for presenting in DKA. Ordinal logistic regression was used for DKA severity and Mann-Whitney U tests were used for continuous measures.

Our study identified a total of 128 youth who met inclusion criteria, 64 patients were admitted during the pre-COVID-19 time period and 64 patients were admitted during the COVID-19 time period. Youth presenting more than once per time period or in both time periods were only counted for their first visit. There was a higher prevalence of DKA on presentation during the COVID-19 time period compared to the pre-COVID-19 time period (73% vs 47%). There was a significant worsening of DKA severity in the COVID-19 time period compared to the pre-COVID-19 time period. There was no statistically significant difference in the proportion of youth with new onset diabetes presenting in DKA between the two time periods (64% vs 42%). Of the youth with new onset diabetes who presented in DKA, there was no difference in severity of DKA. There was a significantly higher proportion of youth with established diabetes who presented in DKA during the COVID-19 time period when compared to the pre-COVID-19 time period (84% vs 52%). Additionally, there was a higher odds ratio for presenting in more severe DKA in the established diabetes group (OR 5.60, 95% CI [1.59–19.75]) (Table 1).

This study adds significant information to the growing foundation of evidence provided by previous studies from other nations on youth with primarily type 1 diabetes.<sup>9-11</sup> Given the unique excess mortality and economic burden of the COVID-19 pandemic in the United States, understanding the impact of this pandemic on the paediatric population is vital. Furthermore, this study incorporates all youth with diabetes, including type 1 and type 2, as well as the established and newly diagnosed paediatric population. Incorporating all youth with diabetes may better assist in our understanding of this vulnerable population and aid in directing resources and education.

This retrospective study demonstrated a significantly higher rate and severity of DKA in patients admitted during the COVID-19 time period. Patients with established diabetes were significantly more likely to be admitted in DKA with worsened severity during COVID-19; this did not reach statistical significance in the new-onset group. Although the odds ratio confidence intervals of the new-onset group and established group overlapped, the higher overall rate and severity of DKA may have been driven by youth with previously established diagnosis of diabetes. These patients had uninterrupted access to their diabetes team via clinic visits, telehealth visits, and 24-h phone support during COVID-19. Parents of children with established diabetes may have chosen to not take advantage of these resources and attempted management at home to avoid undue risk of exposure at a clinic, urgent care, or ED. Alternatively, families of youth with new-onset diabetes, who would have never experienced similar symptoms in the past, may have resorted to hospital presentation.

TABLE 1 Comparison of Prevalence and Severity of DKA on Presentation in Youth presenting in DKA

	Pre-COVID-19 (March-June 2019)	COVID-19 (March-June 2020)	Odds Ratio [95% CI]	p value
Total Participants in DKA				
Prevalence of DKA	30/64 (47%)	47/64 (73%)	3.13 [1.49–6.57]	$0.003^{*}$
DKA Severity				
Mild	15/30 (50%)	10/47 (21%)	3.18 [1.32–7.66] <sup>†</sup>	$0.01^*$
Moderate	8/30 (27%)	16/47 (34%)		
Severe	7/30 (23%)	21/47 (45%)		
New Onset Diabetes Mellitus				
Prevalence of DKA	13/31 (42%)	21/33 (64%)	2.42 [0.89-6.63]	$0.09^{*}$
DKA Severity				
Mild	6/13 (46%)	6/21 (29%)	1.93 [0.52–7.16] <sup>†</sup>	0.33*
Moderate	2/13 (15%)	4/21 (19%)		
Severe	5/13 (39%)	11/21 (52%)		
Established Diabetes Mellitus				
Prevalence of DKA	17/33 (52%)	26/31 (84%)	4.89 [1.51–15.86]	$0.008^{*}$
DKA Severity				
Mild	9/17 (53%)	4/26 (15%)	5.60 [1.59–19.75] <sup>†</sup>	$0.007^*$
Moderate	6/17 (35%)	12/26 (46%)		
Severe	2/17 (12%)	10/26 (38%)		

\*p values obtained by Wald Chi-Square test.

†Odds ratio derived from ordinal regression.

Limitations of our study are similar to those of most singlecentre retrospective studies. Our study was limited to a small sample size in a single region in the United States which may not be representative of other regions. Despite these limitations, this study represents a comprehensive first look into the impact of COVID-19 restrictions on complications of diabetes in the paediatric population in a large US paediatric hospital.

Further large-scale study of the paediatric diabetes population in the United States is required to confirm the effects noted in this study. With further study, we can improve the future planning and resource allocation for this vulnerable population as this pandemic continues and in the planning for future possible pandemics.

### **CONFLICT OF INTEREST**

The authors have no conflicts of interest to disclose.

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### REFERENCES

- Lerner AM, Folkers GK, Fauci AS. Preventing the spread of SARS-CoV-2 with masks and other "Low-tech" interventions. *JAMA*. 2020;324:1935-1936.
- Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and metaanalysis. *Lancet (London, England)*. 2020;395:1973-1987.
- Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. *Lancet Child Adolesc Health*. 2020;4:e10-e11.

- Jaswaney R, Cerdeña JP. COVID-19 school closures: implications for pediatric diabetes management - a commentary. *Health Behav Policy Rev.* 2020;7:325-328.
- Cherubini V, Gohil A, Addala A, et al. Unintended consequences of coronavirus disease-2019: remember general pediatrics. J Pediatr. 2020;223:197-198.
- Cariou B, Hadjadj S, Wargny M, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. *Diabetologia*. 2020;63:1500-1515.
- Aye T, Mazaika PK, Mauras N, et al. Impact of early diabetic ketoacidosis on the developing brain. *Diabetes Care*. 2019;42:443-449.
- Wolfsdorf JI, Glaser N, Agus M, et al. ISPAD clinical practice consensus guidelines 2018: diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *Pediatric Diabetes*. 2018;19(Suppl 27):155-177.
- 9. Rabbone I, Schiaffini R, Cherubini V, Maffeis C, Scaramuzza A. Has COVID-19 delayed the diagnosis and worsened the

presentation of type 1 diabetes in children? *Diabetes Care*. 2020:dc201321.

- Kamrath C, Mönkemöller K, Biester T, et al. Ketoacidosis in children and adolescents with newly diagnosed type 1 diabetes during the COVID-19 pandemic in Germany. JAMA. 2020;324:801-804.
- 11. Unsworth R, Wallace S, Oliver NS, et al. New-onset type 1 diabetes in children during COVID-19: multicenter regional findings in the U.K. *Diabetes Care*. 2020;43:e170-e171.

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