

# Has variable access to health care during the COVID-19 pandemic impacted the severity of paediatric diabetic ketoacidosis?

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## Abstract

Previous studies have indicated that paediatric patients with type 1 diabetes mellitus are presenting with more severe diabetic ketoacidosis (DKA) during the COVID-19 pandemic. This study was performed to determine the effect that access to health care had on DKA severity and outcomes in children and young people (CYP) with new-onset diabetes mellitus.

This is a retrospective cohort analysis comparing pre-pandemic and pandemic patients admitted to a 30-bed paediatric intensive care unit (PICU) in the United States with DKA. A database query identified patients and clinical data were extracted and analysed. Additionally, phone interviews focusing on challenges with health care access during the COVID-19 pandemic were performed with the parents of CYP admitted during the pandemic.

A total of 50 pre-pandemic and 43 pandemic patients met inclusion criteria and were included in the analysis. Pandemic patients had more severe acidosis (pH 7.10 versus 7.17), a longer duration of insulin infusion (19 versus 15 hours) and increased PICU length of stay (1 versus 0.75 days, all  $p < 0.05$ ) than pre-pandemic patients. Patients whose families felt the pandemic affected their child's ability to see a physician had a longer PICU length of stay (1.5 versus 0.9 days,  $p = 0.004$ ) and a trend towards a lower pH (7.01 versus 7.13,  $p = 0.106$ ). Patients with a social vulnerability index  $\geq 0.75$  were less likely to see a physician before coming to the hospital ( $p = 0.017$ ).

In conclusion, CYP with new-onset type 1 diabetes who were admitted with DKA during the COVID-19 pandemic had more severe acidosis and a longer PICU stay. Variable access to health care during the COVID-19 pandemic may be contributing to this. Copyright © 2022 John Wiley & Sons.

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## Key words

diabetic ketoacidosis; COVID-19; insulin

## Introduction

Paediatric diabetic ketoacidosis (DKA) is a potentially severe, life-threatening presentation of diabetes that can require immediate treatment in the emergency department (ED). Although it is largely preventable with early recognition and treatment of diabetes, it carries an estimated mortality rate of 0.2–2%.<sup>1–10</sup> Some studies have suggested that when DKA is diagnosed in new-onset type 1 diabetes, it could serve as a measure of delayed access to health care.<sup>11–13</sup> During the COVID-19 pandemic, both an increased incidence of paediatric DKA and more severe DKA on presentation to the ED have been described.<sup>14–17</sup> It is unclear if this is related to the previously

documented decline in the number of children and young people (CYP) visiting the ED during the COVID-19 pandemic, as parents do not want to expose their CYP to COVID-19 in the ED.<sup>18</sup> Since prior COVID-19 pandemic paediatric DKA studies have been primarily focused on describing the severity on presentation, our study aim was to not only compare the severity of DKA pre- and intra-pandemic and the complications and outcomes, but also to elucidate whether access to health care played a role in the severity of DKA.

## Materials and methods

The Institutional Review Board approved this study and the requirement for informed consent was

waived. The study design was a single-centre retrospective cohort study that compared patients with new-onset type 1 diabetes mellitus and DKA admitted prior to the COVID-19 pandemic with those admitted during the COVID-19 pandemic. All patients were admitted to a 30-bed paediatric intensive care unit (PICU) at a free-standing children's hospital in the United States of America.

The pre-pandemic patients were admitted during a two-year period prior to the pandemic and the pandemic patients were admitted from 1 March 2020 through to 31 March 2021. The inclusion criteria were any patients admitted to the PICU for the treatment of new-onset type 1 paediatric DKA that was treated with an insulin infusion. Known CYP with DKA were excluded, as well as those with diabetes admitted and treated for acute pancreatitis or for hyperosmolar hyperglycaemic state (HHS). HHS was defined as having a plasma glucose >600mg/dL, serum osmolality >330mOsm/kg H<sub>2</sub>O and absence of significant ketosis and acidosis.<sup>19</sup> There was no change in our PICU admission criteria for DKA nor in our treatment algorithm during the two periods. All patients were treated with the two-bag system according to our intravenous (IV) fluid titration protocol as we have previously described.<sup>20</sup> Our primary outcome measures were severity of ED hyperglycaemia and acidosis. The secondary outcome measures included: time to resolution of acidosis; duration of insulin infusion; PICU length of stay (LOS); use of hypertonic saline; and mortality.

Data were extracted from the Virtual Pediatric Systems LLC database<sup>21</sup> and the electronic health record. The following data were collected from pre-pandemic and pandemic patients: age; height; weight; Pediatric Risk of Mortality version 3 (PRISM III)–12 score;<sup>22</sup> duration of symptoms; diagnoses; PICU LOS; ED laboratory values; initial fluid bolus dose; insulin infusion doses and duration of infusion; time to resolution of metabolic acidosis; suspected

cerebral oedema; and mortality. The PRISM III score is derived from age-stratified physiologic variables, pupillary reactions, Glasgow coma scores, ventilation status from the first 24 hours of admission and blood gas values, complete blood count, coagulation and chemistry studies taken during the first 12 hours after admission. Both low- and high-risk diagnoses are also incorporated in the score. ED glucose values were plasma samples from laboratory testing rather than bedside point of care testing. Use of hypertonic saline was used as a proxy for cerebral oedema, as our PICU rarely obtains brain computer tomography to diagnose cerebral oedema with DKA. Mannitol is not used in our ED or PICU for therapy of cerebral oedema in DKA. The social vulnerability index (SVI) was recorded on pandemic patients as percentile ranking for their county of residence among California counties.<sup>23–26</sup> The SVI was obtained by entering the patient's address on admission into the Centers For Disease Control and Prevention SVI calculator.<sup>23</sup> The main difference between the SVI and social or area deprivation index is that SVI includes race in addition to education, income/employment, household characteristics and housing.<sup>27</sup>

A telephone survey was performed with the parents of CYP admitted during the pandemic. The survey consisted of five questions that focused on delay of care due to limited access caused by the pandemic and potential delay due to fear of exposing their child to COVID-19 in a medical setting (Table 3). The survey question answers were scored on a standard Likert scale from 1 (not at all) to 5 (a lot) and examined on both ordinal and dichotomous scales (yes [neutral/not sure, a little, or a lot], and no [not at all, or not much]).

#### Statistical analysis

Data were analysed using Statistical Package for the Social Sciences, PASW Statistics for Windows, Version 18.0 (SPSS, Chicago, IL). Continuous

variables were compared by Mann-Whitney U test and categorical by Chi-square analysis. For the relationship between SVI and whether a family sought a medical provider for their child prior to coming to the ED, we conducted receiver operating characteristic (ROC) analyses with SVI as test variable and identified the best threshold (maximised sum of sensitivity and specificity) to classify parent response to survey question 5. Spearman's correlation coefficient was used to measure the monotonic relationship between outcomes and age, SVI, and symptom duration. Multivariate analysis was performed using the generalised linear model (GLM) procedure to examine primary outcome of pH (severity) on pandemic patients with a model that included age, duration of symptoms and SVI. Linear distribution for pH was specified in the GLM procedure with assumption of normality checked by Shapiro-Wilk's test ( $p=0.203$ ). For all analyses,  $p$ -values  $\leq 0.05$  were considered statistically significant.

#### Results

A total of 50 patients with new-onset type 1 diabetes and DKA were admitted to the PICU during a two-year pre-pandemic period and 43 patients during the COVID-19 pandemic. There was no difference in the median age, weight, PRISM III score, initial blood glucose, blood urea nitrogen or creatinine levels between the two cohorts. Pandemic patients had more severe acidosis than pre-pandemic patients (pH 7.10 vs 7.17,  $p=0.044$ ). (Table 1.) Pandemic patients also had a longer duration of insulin infusion (19 vs 15 hours), longer duration of metabolic acidosis (15 vs 12 hours) and increased PICU LOS (1 vs 0.75 days); all  $p<0.001$ . (Table 2.) There was no difference in the incidence of cerebral oedema or mortality. Only two patients were diagnosed with a COVID-19 infection and they appeared similar to the larger group.

The majority of families interviewed (66%) did not believe that

COVID-19 had much impact on the ability to receive care for their child and only 37% stated that they were concerned that their child might catch COVID-19 in the hospital. CYP whose families felt the pandemic affected their child's ability to see a physician had a longer PICU LOS (1.5 vs 0.9 days,  $p=0.004$ ) and a trend towards more severe acidosis indicated by lower median pH (7.01 vs 7.13,  $p=0.106$ ). There was no difference in the severity of acidosis and whether the patient was seen by a physician prior to the ED. (Table 3.)

ROC analyses found that an SVI value of 0.75 was the best cut-off threshold for question 5 about whether the patient saw a medical provider prior to coming to the ED, with a moderate AUC of 0.611. A significantly greater percentage of children whose families did not seek care compared to those who did seek care prior to the ED were in the more vulnerable SVI category defined by  $SVI \geq 0.75$  (94% vs 59%,  $p=0.017$ ). (Figure 1.) A monotonic relationship was found between severity of acidosis and duration of symptoms ( $r_s = 0.317$ ,  $p < 0.05$ ); Table 4. However, the adjusted analysis did not show a significant relationship between severity of acidosis in pandemic patients and their age, duration of symptoms, or SVI (data not shown).

## Discussion

The primary finding in this study is that during the COVID-19 pandemic, paediatric patients with new-onset type 1 diabetes presented to the hospital with more severe acidosis. Consequently, they required longer durations of an insulin infusion to correct DKA and therefore stayed in the PICU longer. This occurred in the absence of any changes to the DKA management algorithm for our PICU. This is the first study to demonstrate both more severe DKA on presentation to the hospital and adverse outcomes, such as increased time on an insulin infusion and increased LOS.

Although our hypothesis was that CYP were presenting with more severe DKA because of potential delay in

Parameter	Pre COVID-19 (n=50)	Post COVID-19 (n=43)	P-value
Age (months)	127 [84, 170]	144 [110, 144]	0.416
Weight (kg)	36.7 [23.4, 50.7]	35.6 [24.8, 67.2]	0.603
Gender (male)	21 (42.0)	16 (37.2)	0.638
Duration of symptoms (days)	14.0 [4.4, 21.0]	7.0 [3.0, 14.0]	0.186
Social vulnerability index (SVI)	–	0.845 [0.696, 0.923]	–
PRISM III score	7.0 [4.0, 10.0]	8.0 [4.0, 9.0]	0.921
ED blood glucose (mg/dL)	539 [408, 734]	553 [467, 674]	0.641
HCO <sub>3</sub> <sup>-</sup> (mmol/L)	9.0 [6.0, 12.0]	7.5 [4.0, 10.0]	0.085
pH	7.17 [7.06, 7.23]	7.10 [7.01, 7.20]	<b>0.044</b>
Blood urea nitrogen (mg/dL)	12.0 [11.0, 17.0]	13.5 [10.0, 23.0]	0.816
Creatinine (mg/dL)	1.10 [0.90, 1.26]	1.12 [0.71, 1.40]	0.724
Data expressed as median [IQR] or number (%). The laboratory levels are all on presentation to the emergency department (ED) prior to any therapy. Continuous variables compared by Mann-Whitney U test, and gender by Chi-square analysis. SVI ranges from 0–1, with 1 being most vulnerable.			

**Table 1.** Patient characteristics and laboratory values (n=93)

Parameter	Pre COVID-19 (n=50)	Post COVID-19 (n=43)	P-value
ED IV fluid boluses (ml/kg)	20 [10.0, 20.0]	22 [17.5, 24.0]	0.051
Insulin started in ED	29 (58.0)	23 (53.4)	0.662
PICU LOS (days)	0.75 [0.62, 0.94]	1.00 [0.81, 1.40]	<b>&lt;0.001</b>
Resolution of acidosis* (hrs)	12 [4.0, 12.0]	15 [11.5, 19.0]	<b>&lt;0.001</b>
Insulin infusion duration (hrs)	15 [12.0, 19.0]	19 [17.0, 24.0]	<b>&lt;0.001</b>
Total insulin dose (u/kg)**	1.24 [0.90, 1.70]	1.75 [1.38, 2.04]	<b>&lt;0.001</b>
Cerebral oedema therapy	5 (10.0)	3 (7.0)	0.604
Mortality	0	1 (2.3)	0.462
Data expressed as median [IQR] or number (%). *Time to pH $\geq 7.3$ . **Includes all insulin given in the emergency department (ED) and the paediatric intensive care unit (PICU). Cerebral oedema therapy relates to patients who were given 3% hypertonic saline for presumed cerebral oedema. Continuous variables compared by Mann-Whitney U test and categorical by Chi-square analysis.			

**Table 2.** Diabetic ketoacidosis treatment and outcomes (n=93)

care, we were unable to conclusively demonstrate an association through our interviews with families. This may be because the number of patients in this study was too small to demonstrate a statistically significant association, as our p-value was 0.106 for the relationship between whether the pandemic affected the ability for the child to be seen and severity of acidosis. A recent study from Germany proposed that access to health care might be a factor in DKA severity during the pandemic, but did not interview the families of their patients.<sup>16</sup> We did find that CYP whose families felt that the pandemic affected the ability to have their child seen had a longer PICU LOS. Although there may be multiple factors that account for a longer PICU LOS for DKA, it is still noteworthy that patients had a difference in outcome in this regard.

Another recent study from the United Kingdom found that delayed presentations of CYP with type 1 diabetes during the COVID-19 pandemic were associated with fear of COVID and inability to obtain face-to-face appointments. They confirmed these delays through surveys of all diabetes units caring for CYP in England, Wales, Scotland and those submitting data to the National Paediatric Diabetes Audit (NPDA). Additionally, that study found increased severity in DKA during this COVID-19 pandemic period.<sup>17</sup> The main differences between our study and the UK study is that the latter was a larger study that relied on the health care providers' recall as to the number of presentations delayed due to COVID-19 and their perceptions of the reasons for their delay. We interviewed the parents of the

CYP in order to decipher the potential factors leading to delay of care from the parents' perspective. Additionally, the UK study did not look at how variable access to health care contributed to delays in care, nor did the authors analyse specific patient data to try and delineate whether the delays were associated with increased severity of DKA.

We were surprised that the majority of families did not feel that there was any delay in care. This is further supported by 58% actually seeing a provider either in an urgent care, primary care, or telehealth before presenting to the ED. It is difficult to interpret the answer to this question, as the majority of these patients' symptoms were so advanced when they were seen in an outpatient setting that they were directly referred over to the ED after diabetes was

	Question response category N/Y (no.)*	pH Median [IQR]	PICU length of stay (days) Median [IQR]	Time to acidosis resolved Median [IQR]	Time on insulin infusion Median [IQR]	Total insulin (u/kg) Median [IQR]
Q1. Do you believe the COVID pandemic affected your ability to see a physician about your child's symptoms?	Yes (13) No (25) <i>p-value:</i>	7.01 [6.94, 7.15] 7.13 [7.05, 7.20] <i>p=0.106</i>	1.5 [1.1, 1.7] 0.9 [0.8, 1.2] <b><i>p=0.004</i></b>	16.0 [14.0, 17.0] 15.0 [10.0, 19.0] <i>p=0.405</i>	20.0 [17.0, 31.0] 19.0 [17.0, 21.0] <i>p=0.179</i>	1.9 [1.6, 2.4] 1.7 [1.3, 2.0] <i>p=0.309</i>
Q2. Do you believe there was any delay in getting a medical appointment or getting your child seen by a physician due to the COVID pandemic?	Yes (10) No (28) <i>p-value:</i>	7.1 [6.9, 7.2] 7.1 [7.0, 7.2] <i>p=0.486</i>	1.0 [0.9, 1.7] 1.0 [0.8, 1.4] <i>p=0.529</i>	15.5 [11.0, 23.0] 15.0 [11.5, 18.5] <i>p=0.378</i>	22.0 [19.0, 43.0] 18.0 [16.0, 21.5] <b><i>p=0.024</i></b>	1.9 [1.4, 2.4] 1.7 [1.4, 2.0] <i>p=0.595</i>
Q3. Were you concerned that your child had COVID when you brought them to the hospital? Did you believe their symptoms may have been due to COVID?	Yes (9) No (29) <i>p-value:</i>	7.1 [7.0, 7.1] 7.1 [7.0, 7.2] <i>p=0.336</i>	1.5 [0.9, 1.7] 0.9 [0.8, 1.3] <i>p=0.154</i>	15.0 [12.0, 16.0] 15.0 [11.0, 19.0] <i>p=1.00</i>	19.0 [17.0, 28.0] 19.0 [17.0, 22.0] <i>p=0.679</i>	1.7 [1.4, 1.9] 1.8 [1.4, 2.1] <i>p=0.891</i>
Q4. Were you concerned that your child would get COVID in the hospital?	Yes (14) No (24) <i>p-value:</i>	7.1 [7.0, 7.2] 7.1 [6.9, 7.2] <i>p=0.173</i>	1.0 [0.8, 1.5] 1.1 [0.8, 1.4] <i>p=0.904</i>	15.5 [14.0, 22.0] 14.5 [11.0, 18.5] <i>p=0.476</i>	19.5 [17.0, 24.0] 19.0 [17.0, 24.5] <i>p=0.715</i>	1.8 [1.3, 2.1] 1.8 [1.4, 2.1] <i>p=0.739</i>
Q5. Did you seek care from a medical provider for your child prior to bringing them to the hospital when they were diagnosed?	Yes (22) No (16) <i>p-value:</i>	7.1 [7.0, 7.2] 7.0 [7.0, 7.2] <i>p=0.208</i>	0.9 [0.8, 1.5] 1.1 [0.8, 1.5] <i>p=0.679</i>	15.0 [10.0, 19.0] 15.5 [12.0, 19.0] <i>p=0.733</i>	19.0 [17.0, 21.0] 19.5 [16.5, 25.5] <i>p=0.929</i>	1.7 [1.4, 2.0] 1.8 [1.5, 2.3] <i>p=0.615</i>

\*Yes = neutral/not sure, a little, or a lot; No = not at all or not much. Yes/no response compared by Mann-Whitney U test.

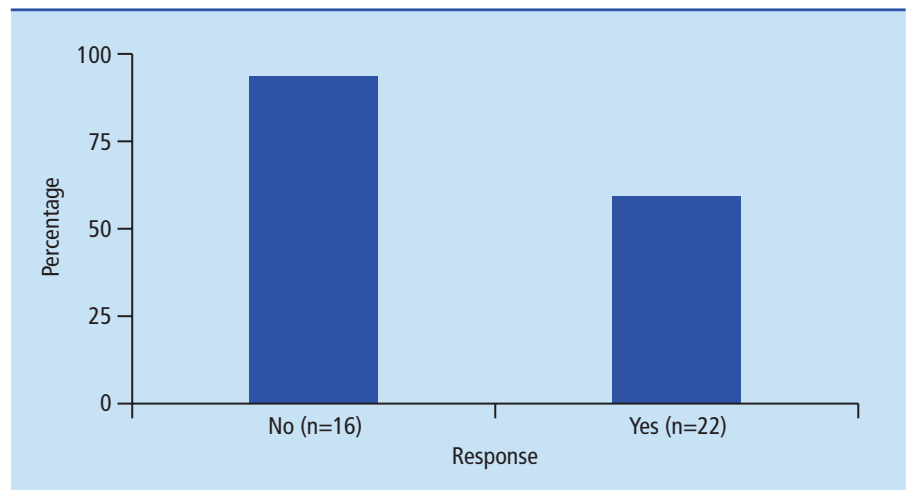
**Table 3.** In post COVID-19 patients who completed the survey, concerns regarding COVID exposure in the emergency room during the pandemic described in relation to outcomes in patients with newly diagnosed type 1 diabetes (n=38)

confirmed. Interestingly, most families that came directly to the ED did not believe the pandemic affected or delayed their child's care. This suggests that people either continue to think about the ED as a first point of care rather than primary care clinics, or that they did not pick up on earlier symptoms and only sought care when their child's condition had deteriorated significantly.

In addition to interviewing families, we utilised the SVI to help determine whether challenges with access to health care were associated with more severe DKA. We did not find an association between SVI and the primary outcome measures, but this may be because the patients in our catchment area are largely from lower socioeconomic backgrounds with a high median SVI of 0.845. We did find that children who lived in areas with the highest SVIs were more likely to come directly to the ED. This general association of SVI and ED visits was recently reported to the United States Congress, but more COVID-19 pandemic data are needed to further clarify its impact on children with chronic diseases, such as diabetes.<sup>28</sup>

Although we did not find any difference in mortality or the number of patients treated for cerebral oedema, our only patient who died was seen during the busiest part of the pandemic and was evaluated both in urgent care and by paramedics at home. This young person was felt to have COVID-19 and anxiety and was not initially brought to the hospital. She later presented to the ED in extremis, had a cardiac arrest and died from multiple organ dysfunction syndrome in the PICU. Clearly, the COVID-19 pandemic delayed the diagnosis and impacted the outcome in this tragic case.

There are limitations to this study. This is a small single-centre study and larger public health population studies are needed to further evaluate how access to health care during the COVID-19 pandemic may be affecting severity of paediatric DKA, as this is now the fifth study that has demonstrated that CYP are presenting with



**Figure 1.** A comparison of who sought medical care prior to coming to the emergency department expressed as the percentage of parents with social vulnerability index  $\geq 0.75$  out of total parent interviews ( $n=38$ )

rs	pH	PICU length of stay	Time to acidosis resolved	Time on insulin infusion	Total insulin
Age	0.147	0.012	0.181	0.226	0.162
SVI	-0.109	0.269	0.238	0.214	0.189
Symptom duration	<b>0.317*</b>	-0.148	-0.253	-0.160	-0.128

rs = Spearman's correlation coefficient. \* $p < 0.05$  (significant correlation). SVI ranges from 0–1 with 1 being most vulnerable.

**Table 4.** In post COVID-19 patients, age in months, social vulnerability index (SVI), and symptom duration (days) examined in relation to outcomes in newly diagnosed type 1 diabetes ( $n=43$ )

more severe acidosis. This study was also performed in the United States and the results may not be applicable to other countries that have different health care models. Although we were able to interview 88% of our families, it is possible that we may have found an association if we had reached all of the parents of our CYP. Additionally, we interviewed some families many months after the child was seen and after some of the initial panic of the pandemic had 'calmed down' a bit. It is possible this affected the families' recollection of how they felt months earlier. Finally, we obtained very few brain computer tomography scans to document cerebral oedema. Rather, we used the administration of hypertonic saline as a proxy to suspected

cerebral oedema. Although this approach is supported in recent literature, it is possible that we missed or over-diagnosed cases of cerebral oedema.<sup>29</sup>

In conclusion, children with new-onset type 1 diabetes admitted to the PICU for DKA during the COVID-19 pandemic presented with more severe acidosis which took longer to resolve, required a longer duration of insulin infusion, and had an increased PICU LOS. The presence of a COVID-19 infection did not affect the overall outcome. CYP whose family felt that the pandemic affected their ability to have their child seen had a longer PICU LOS and patients who lived in areas with a higher SVI were less likely to seek

care before coming to the hospital. Since CYP are presenting with more severe acidosis during this pandemic, it may be helpful to have standardised processes in place in the ED to rapidly identify and triage the severity of paediatric DKA during these busy times, especially in areas of high social vulnerability. Larger multi-centre studies are still needed to elucidate all the factors involved in the increasing severity of DKA being seen in the ED during the COVID-19 pandemic.

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### Declaration of interests

There are no conflicts of interest declared. Tricia Morphey serves as a biostatistical consultant to Memorial Healthcare Services through Morphey Consulting, LLC. Mrs Morphey has no conflict of interest.

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### KEY POINTS

- Children and young people with new-onset type 1 diabetes mellitus are presenting with more severe diabetic ketoacidosis (DKA) during the COVID-19 pandemic
- They require a longer duration of insulin infusion to correct DKA and a have longer PICU length of stay than their pre-pandemic counterparts
- Those with a higher social vulnerability index are less likely to see a physician before coming to the hospital with DKA
- Those whose families feel that the COVID-19 pandemic affected their child's ability to see a physician have a longer PICU length of stay and a trend towards a lower pH on presentation to the emergency department

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