

| pISSN 2586-6052 | eISSN 2586-6060

Impact of the COVID-19 pandemic on diabetic ketoacidosis management in the pediatric intensive care unit

Fevzi Kahveci¹, Buse Önen Ocak², Emrah Gün¹, Anar Gurbanov¹, Hacer Uçmak¹, Ayşen Durak Aslan², Ayşegül Ceran³, Hasan Özen¹, Burak Balaban¹, Edin Botan¹, Zeynep Şıklar³, Merih Berberoğlu³, Tanıl Kendirli¹

¹ Division of Pediatric Intensive Care, Department of Pediatrics, Ankara University Faculty of Medicine, Ankara, Türkiye ² Department of Pediatrics, Ankara University Faculty of Medicine, Ankara, Türkiye ³ Division of Pediatric Endocrinology, Department of Pediatrics, Ankara University Faculty of Medicine, Ankara, Türkiye

Background: Diabetic ketoacidosis (DKA) is a common endocrine emergency in pediatric patients. Early presentation to health facilities, diagnosis, and good management in the pediatric intensive care unit (PICU) are crucial for better outcomes in children with DKA.

Methods: This was a single-center, retrospective cohort study conducted between February 2015 and January 2022. Patients with DKA were divided into two groups according to pandemic status and diabetes diagnosis.

Results: The study enrolled 59 patients, and their mean age was 11±5 years. Forty (68%) had newly diagnosed type 1 diabetes mellitus (T1DM), and 61% received follow-up in the pre-pandemic period. Blood glucose, blood ketone, potassium, phosphorus, and creatinine levels were significantly higher in the new-onset T1DM group compared with the previously diagnosed group (P=0.01, P=0.02, P<0.001, P=0.01, and P=0.08, respectively). In patients with newly diagnosed T1DM, length of PICU stays were longer than in those with previously diagnosed T1DM (28.5±8.9 vs. 17.3±6.7 hours, P<0.001). The pandemic group was compared with pre-pandemic group, there was a statistically significant difference in laboratory parameters of pH, HCO₃, and lactate and also Pediatric Risk of Mortality (PRISM) III score. All patients survived, and there were no neurologic sequelae. **Conclusions:** Patients admitted during the pandemic period were admitted with more severe DKA and had higher PRISM III scores. During the pandemic period, there was an increase in the incidence of DKA in the participating center compared to that before the pandemic.

Key Words: children; COVID-19; diabetic ketoacidosis; pediatric intensive care

Original Article

Received: January 5, 2023 Revised: April 26, 2023 Accepted: May 14, 2023

Corresponding author Fevzi Kahveci

Division of Pediatric Intensive Care, Department of Pediatrics, Ankara University Faculty of Medicine, Ankara 06100, Türkiye Tel: +90-532-0631836 Email: fevziikahvecii@gmail.com

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is an immune-mediated disease that begins as autoimmune damage to pancreatic β cells, resulting in exogenous insulin dependence to maintain adequate energy production due to decreased endogenous insulin production [1,2]. Diabetic ketoacidosis (DKA) is a common cause of emergency endocrine problems, with a mortality rate of 0.3%–0.5% in developed countries; mortality rates are much higher in developing countries [3]. Mortality in patients with DKA was around 10% in the 1980s; with the development of

Copyright © 2023 The Korean Society of Critical Care Medicine

This is an Open Access article distributed under the terms of Creative Attributions Non-Commercial License (https://creativecommons.org/ li-censes/by-nc/4.0/) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.



protocols for diagnosis and treatment, mortality has decreased significantly [4].

Risk factors for DKA include racial/ethnic minority status, young age, male sex, low income, low parental education level, and lack of health insurance [5,6]. DKA presents clinically in two ways, either at the time of diagnosis of T1DM (onset of disease) or in patients who have been diagnosed with T1DM but do not comply with treatment and diet or whose disease cannot be adequately controlled [2,7]. During treatment of DKA, hypoglycemia, hypokalemia, hypocalcemia, hypomagnesemia, severe hypophosphatemia, hyperchloremic metabolic acidosis, and brain edema may develop. Therefore, care should be taken in patient follow-up and treatment management.

In late 2019, the first known infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the related coronavirus disease 2019 (COVID-19), causing a pandemic. This study aimed to evaluate and characterize the clinical profile of the patient population diagnosed with DKA in the pediatric intensive care unit (PICU) during pre-pandemic and pandemic periods as well as treatment protocols and outcomes.

MATERIALS AND METHODS

The local Institutional Ethics Committee of Ankara University Faculty of Medicine approved this study (No. 106-353-22). The research was conducted according to the ethical principles of the World Medical Association Declaration of Helsinki.

This was a descriptive, retrospective, single-center study conducted between February 2015 and January 2022 in patients who were diagnosed with DKA and followed up in the PICU. In the participating center, patients with moderate and severe DKA are followed in the PICU until resolution of ketoacidosis. Patients with DKA were divided into two groups according to pandemic status (group 1) and diabetes diagnosis status (group 2). Both groups were examined in two subcategories (pandemic status: pre-pandemic (2015-2020 March) vs. pandemic (2020 March-2022); and diabetes diagnosis status: previously diagnosed vs. newly diagnosed). Sixty-eight patients aged 1 month to 18 years were retrospectively investigated. Nine patients were excluded from the study due to a lack of medical data, leaving 59 patients for analysis. Patients with DKA were admitted to the tertiary-level referral PICU with a fellowship program. For diagnosis of ketoacidosis, hyperglycemia (blood glucose >200 mg/dl), acidosis (venous pH <7.3 and/or plasma bicarbonate <15 mmol/L), and ketonemia

KEY MESSAGES

- Patients admitted during the pandemic period had more severe diabetic ketoacidosis (DKA) and higher Pediatric Risk of Mortality (PRISM) III scores.
- Public health presentations were not effective during the coronavirus disease 2019 (COVID-19) period.
- Awareness-raising campaigns are necessary to prevent DKA through early symptom recognition and early treatment.

and ketonuria were required [5]. In the hospital, both pediatric critical care medicine and pediatric endocrinology teams used the standard DKA treatment protocol shown in Table 1 [8].

Factors evaluated at admission or during hospitalization included patient age; sex; body mass index (BMI); current DKA diagnosis; family history; symptoms and duration of symptoms at admission; center; comorbidity; duration of insulin infusion therapy; length of PICU stay; pediatric endocrinology ward length of stay; blood gas levels (pH, pCO₂, HCO₃, base excess, lactate); levels of blood glucose, blood ketone, glycated hemoglobin (HbA1c), sodium, potassium, blood urea nitrogen-creatinine, alanine aminotransferase, aspartate aminotransferase, and C-reactive protein; complete blood count; Glasgow Coma Score (GCS); Pediatric Risk of Mortality (PRISM) III score; and recurrent intensive care admissions. COVID-19 polymerase chain reaction (PCR) results were obtained from hospital records. The PRISM III is a scoring system used to predict mortality in a pediatric group [9].

Statistical Analysis

The data were analyzed using IBM SPSS ver. 23.0 (IBM Corp.). Mean, standard deviation, median, frequency distribution, and percentage values were determined as descriptive statistics of the variables. Mean values were used in parametric tests, and median values were used in nonparametric tests. Pearson's chi-square test and Fisher's exact test were used to analyze categorical variables. The data were tested for normal distribution using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test). The independent samples t-test was used to analyze differences in normally distributed variables between two independent groups. The Mann-Whitney U-test was used to analyze differences between the median values of non-normally distributed variables. P-values <0.05 were considered statistically significant.



Table 1. General characteristics of DKA management in the participating PICU

1. Fluid management	
	n mild to moderately dehydrated patients. In severely dehydrated patients, use normal saline in bolus (10 ml/kg). If in shock ime loading should not exceed 500 ml.
Calculation of the total fluid in	ntake according to the dehydration of the patients:
Total fluid: deficit+mainten	ance
Calculation of the amount	of the deficit:
30–50 ml/kg in case of n	nild dehydration
60–90 ml/kg in case of n	noderate dehydration
100 ml/kg in case of seve	ere dehydration
Hourly fluid volume=(deficit/4	8)+hourly maintenance
If he is not in shock, the first	loaded fluid is subtracted from the total fluid when calculating the hourly fluid amount.)
2. Glycemic control	
nsulin therapy:	
Standard insulin after norm	nal saline hydration
	ith a different intravenous access 0.1 UI/kg/hr. Insulin liquid prepared by adding 50 units of regular insulin into 50 ml of iven speed. A dose of 0.05 UI /kg/hr may be preferred in children under the age of three.
Target: decrease glycemia 7 can be increased to 0.15 l	5 mg/dl/hr, if glycemia comes down lower than 50 mg/dl/hr or there is not pH correction in 2–4 hours, insulin infusion rai J/kg/hr.
Glucose administration:	
Start continuous glucose ir	fusion after reaching <250 mg/dl initiate with 5% glucose and raise glucose infusion concentration
If the patient experiences a acidosis is corrected.	rapid fall in blood glucose, increase the glucose concentration, do not reduce or discontinue the insulin infusion until the
3. Electrolytes management	
Va target: 135–150 mEq/L	
K target 3.5–5 mEq/L	
PO₄ target >3 mEq/L	
Jnless there is renal insufficie	ncy, 40 mmol/L KCL is added to all fluids except bolus fluid.
or half KC+KPO ₄). If the patie	nt is hyperkalemia, potassium replacement until urine output should be delayed.
4. Laboratory	
mmediate assessment:	
Blood glucose-blood and u nitrogen and creatinine	rine ketones-blood gases-serum electrolytes (sodium, potassium, chloride, calcium, phosphate, magnesium)-blood ureic
Hourly: blood glucose	
Every 2 hourly: blood gas	ses
Every 4 hourly: blood ket	ones, calcium, magnesium-ketones and glucose in urine-blood ureic nitrogen and creatinine.
(The frequency of monitorin negative, discontinue keto	ng the parameters can be changed according to the severity of the DKA. If $pH > 7.3$, discontinue blood gas. If ketone is one test.)

RESULTS

Study Flow Diagram

A total of 59 patients was included in the study. The mean age of the patients was 11±5 years, and 37 (62.5%) were female. Forty of 59 (68%) had no previous diagnosis of diabetes, and 66% were admitted from the pediatric emergency department; the remainder was transferred from different hospitals by the national transport team. Thirty-six (61%) patients were admitted during the pre-pandemic period. The characteristics of the patients were examined in two categories; previously diagnosed vs. newly diagnosed and pre-pandemic vs. pandemic periods.

Patient Demographic Data

The SARS-CoV-2 PCR was positive in only one of the patients with DKA admitted during the pandemic. No complications were observed in any patients during the follow-up period.

<mark>∧CC</mark>∿

Antibiotic and antiviral treatments were administered to 17 of 59 patients, and the most commonly used antibiotic was ampicillin-sulbactam (10/17), used to treat pneumonia. In patients whose symptoms (cough, fever, or wheezing) were clinically and radiologically compatible with pneumonia (opacity, infiltration), if there was also acute phase reactant elevation, antibiotic treatment was started until the respiratory tract PCR result was obtained because the patient was hospitalized in the intensive care unit. Four patients received ceftriaxone treatment for urinary tract infection. Piperacillin tazobactam treatment was given to one patient for pancreatitis. Treatment plans were based on laboratory and culture results in patients with a diagnosis of urinary tract infection or pancreatitis.

Patients with newly diagnosed T1DM were treated with more hours of insulin infusions than those with previously diagnosed T1DM (20.7 ± 5.1 vs. 17.8 ± 14 hours, P=0.244) and

those followed (28.5 ± 8.9 vs. 17.3 ± 6.7 hours, P<0.001) in the PICU. The total hospital length of stay was longer in the newly diagnosed group because of the need to regulate treatment and educate families about the new diagnoses (P<0.05). There were no complications during the PICU stay; neither mechanical ventilation nor inotropes were required.

Comparison between Characteristic Features of the Patients Followed with DKA According to Diabetes Diagnosis

Patient demographic features, admission findings, and first laboratory data are given in Table 2. The most common hospital admission symptoms were polydipsia (45.8%), polyuria (45.8%), vomiting (39%), and abdominal pain (11.9%), (P<0.001). When the laboratory parameters were evaluated, blood glucose, blood ketone, potassium, phosphorus, and creatinine were statistically significant (P=0.01, P=0.02, P<0.001, P=0.01, and

Table 2. Examination of the characteristic features of patients followed for DKA according to diabetes diagnosis

Parameter	Total patient	Diabetes diagnosis status		Dualus
Parameter		Previously diagnosed (n=19)	Newly diagnosed (n=40)	P-value
Female	37 (62.7)	12 (20.3)	25 (42.4)	0.96 ^{a)}
Age (yr)	11±5	14.3±2.5	11.4±3.1	< 0.001 ^{b)}
Diabetes diagnosis age (yr)	8.98±4.3	8.3±3.7	9.2±4.6	0.47 ^{c)}
Height (cm)	149±26.4	161.5±15	152±15	< 0.001 ^{b)}
BMI (kg/m²)	16.8±4.6	20.0±3.7	16.5±5.2	0.003 ^{b)}
Height z-score	0.38 (-6.6 to 4.0)	0.14 (-3.2 to 1.6)	0.54 (-6.6 to 4.0)	0.21 ^{b)}
BMI z-score	-0.28 (-4.3 to 3.1)	0.03 (-2.5 to 2.2)	-0.66 (-4.3 to 3.1)	0.15 ^{b)}
Symptom duration (day)	7.0±10.3	2.5±3.4	14.0±11.0	< 0.001 °)
PICU length of stay (hr)	25.0±9.7	17.3±6.7	28.5±8.9	< 0.001 ^{c)}
Hospital stay (day)	9.0±4.0	5.0±2.8	9.0±3.4	< 0.001 ^{b)}
GCS	15.0±2.4	13.5±2.6	15.0±2.5	0.39 ^{b)}
PRISM III score	8.0±2.1	8.0±2.3	8.0±2.1	0.80 ^{b)}
Pandemic status (pre-pandemic), yes	41 (69.5)	12 (20.3)	29 (49.2)	0.46 ^{a)}
Total saline bolus (ml/kg)	10.0±7.2	10.0±4.2	10.0±6.2	0.23 ^{b)}
Using crystalline insulin (hr)	20.0±8.8	17.8±14	20.7±5.1	0.24 ^{c)}
Polydipsia, yes	27 (45.8)	3 (5.1)	24 (40.7)	$< 0.001^{a}$
Polyuria, yes	27 (45.8)	3 (5.1)	24 (40.7)	$< 0.001^{a}$
Vomiting, yes	23 (38.9)	13 (22.0)	10 (16.9)	$< 0.001^{a}$
Stomachache, yes	7 (11.9)	6 (10.2)	1 (1.7)	0.002 ^{a)}
Blood glucose (mg/dl)	466±129	517±102	431±132	0.01 ^{c)}
Sodium (mmol/L)	134.3±4.2	134.0±4.6	134±4	0.92 ^{c)}
Potassium (mmol/L)	4.2±0.8	4.7±0.7	4.0±0.8	< 0.001 ^{c)}
Phosphorus (mg/dl)	3.7±1.5	4.9±1.9	3.5±1.2	0.01 ^{b)}
Creatine (mg/dl)	0.8±0.3	0.9±0.3	0.7±0.3	0.08 ^{c)}
Blood ketone (mmol/L)	6.2±1.1	6.0±1.2	6.9±1.0	0.02 ^{b)}

Values are presented as number (%), mean±standard deviation, or median (range).

DKA: diabetic ketoacidosis; BMI: body mass index; PICU: pediatric intensive care unit; GCS: Glasgow coma score; PRISM: Pediatric Risk of Mortality.

a) Chi-square test; b) Mann-Whitney U-test; c) Independent samples t-test.



P=0.08, respectively) between patients with newly and previously diagnosed T1DM.

Patients with newly diagnosed T1DM presented to the hospital, on average, 14 days after symptom onset, while those with previously diagnosed T1DM were admitted to the hospital within an average of 2.5 days. Symptom duration was much longer in newly diagnosed patients due to their low awareness of symptoms (P<0.001). When the patient population was examined in terms of previous and new diagnoses, age, height, and BMI were lower than in the previously diagnosed group (P<0.01, P<0.001, and P=0.09, respectively). When the comorbidities of the patients admitted with diagnosis of DKA were evaluated, the most common comorbidities were hypothyroidism (13%), obesity (1.6%), hypertension (3.2%), celiac disease (1.6%), and medullary nephrocalcinosis (1.6%). Cerebral edema was suspected in three of the patients with low GCS and severe acidosis. These three patients were examined using computed cranial tomography. Cerebral edema was detected in one of them and a 3% NaCl infusion was given. No complications were observed in the follow-up.

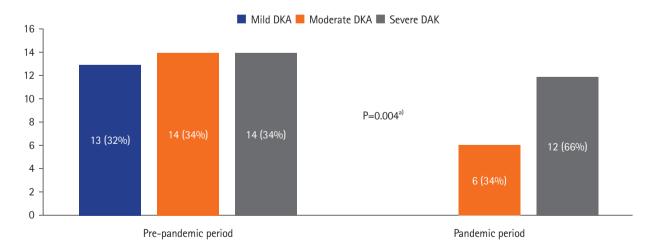
Comparison between Characteristics of Patients Followed with DKA According to the Pandemic Period

When patients were evaluated according to the pre-pandemic and pandemic periods, severe DKA was more common during the pandemic period. Patients admitted during the pandemic period had higher PRISM III scores (10 ± 2 vs. 8 ± 2) and lower pH values (7.0 ± 0.1 vs. 7.1 ± 0.1). The differences in PRISM III and pH values were statistically significant (P=0.021 and P=0.008, respectively). The severity of disease at the time of admission to the PICU before and during the pandemic period of patients admitted to the hospital is shown in Figure 1.

The pandemic group was compared with pre-pandemic group, there was a significant difference in laboratory parameters of pH, HCO₃, and lactate and also of PRISM III score (P=0.008, P=0.017, P=0.008, and P=.021, respectively). Late admission of patients to the hospital because of the negative effects of the pandemic resulted in worse blood gas parameters. Table 3 illustrates the evaluation of patients before and after the pandemic.

DISCUSSION

DKA treatment has been extensively studied and described in the literature. Few studies have compared clinical features and results between patients who presented with DKA with a diagnosis of T1DM and patients without a previous diagnosis of T1DM, and examination of the effects of the COVID-19 pandemic on such patients is rare. In the present study, patients with newly diagnosed T1DM presented to the hospital, on average, 14 days after symptom onset, and those with previously diagnosed T1DM were admitted to the hospital within an average of 2.5 days. Patients admitted during the pandemic period had higher PRISM III scores and lower pH values. Patients with newly diagnosed T1DM received longer insulin infusions and were followed longer in the PICU. For the study, patients were divided into two groups and four subgroups. This comparison was preferred because pandemic subgroups and pre-pandem-



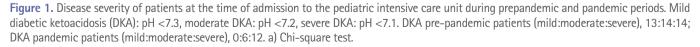




Table 3. Examination of the characteristics of patients followed for DKA according to time period

Parameter	Total patients	Pandemic status		
		Pre-pandemic (n=41)	Pandemic (n=18)	P-value
Newly diagnosed	40 (100)	29 (72.5)	11 (27.5)	0.33 ^{a)}
Female	37 (62.7)	25 (42.2)	12 (20.3)	0.67 ^{a)}
Age (yr)	11±5	11±5	12±5	0.45 ^{b)}
Diabetes diagnosis age (yr)	9±4	9±4	9±4	0.74 ^{b)}
Height (cm)	149±27	143±26	148±27	0.51 ^{b)}
BMI (kg/m ²)	16.8±4.6	17.9±4.3	18.2±5.4	0.94 ^{b)}
Height z-score	0.39 (-6.6 to 4.0)	0.1 (-6.1 to 4.0)	0.5 (-6.6 to 3.9)	0.66 ^{c)}
BMI z-score	-0.4±1.7	-0.3±1.6	-0.8±1.9	0.36 ^{b)}
Body weight (kg)	40±19	38±19	42±20	0.53 ^{b)}
Symptom duration (day)	7.0±10.3	7.0±9.9	6.0±11.4	0.54 ^{c)}
PICU length of stay (hr)	25.0±9.7	25.5±10.1	23.6±8.9	0.51 ^{b)}
Hospital stay (day)	9±4	9±4	8±4	0.18 ^{c)}
GCS	15.0±2.4	13.5±2.5	12.8±2.3	0.22 ^{b)}
PRISM III score	8.7±2.1	8.0±2.0	10.0±2.0	0.02 ^{c)}
Total saline bolus (ml/kg)	10±7	10±8	10±6	0.79 ^{c)}
Blood glucose (mg/dl)	466±129	452±139	491±103	0.35 ^{b)}
HbA1c (%)	11.8±3.3	11.8±3.4	11.8±3.0	0.91 ^{b)}
рН	7.10±0.13	7.13±0.13	7.03±0.10	0.01 ^{c)}
pCO ₂	21.3±11.3	21.5±12.7	17.2±5.4	0.09 ^{b)}
HCO ₃	7.0±3.8	8.4±4	4.2±2.4	0.01 ^{c)}
Lactate	2.0±1.4	2.4±1.7	1.9±1.3	0.01 ^{b)}
Leukocyte (×10 ⁹ /L)	14,584±8,017	16,672±9,445	12,970±7,087	0.003 ^{b)}
Neutrophil (×10 ⁹ /L)	10,047±7,823	12,300±8,853	8,211±6,915	0.02 ^{b)}

Values are presented as number (%), mean±standard deviation, or median (range).

DKA: diabetic ketoacidosis; BMI: body mass index; PICU: pediatric intensive care unit; GCS: Glasgow coma score; PRISM: Pediatric Risk of Mortality.

a) Chi-square test; b) Independent samples t-test; c) Mann-Whitney U-test.

ic subgroups were not proportional.

Nausea, vomiting, and abdominal pain are indicators of ketosis and represent metabolic decompensation of diabetes. In this study, similar to the study by Lopes et al. [10], the most common hospital admission symptoms were polydipsia, polyuria, vomiting, and abdominal pain. The duration of symptoms, similar to the study of Lopes et al. [10], was 2.5 days on average for patients with a previous diagnosis and an average of 14 days in patients who were diagnosed with diabetes while under intensive care hospitalization. The researchers think that this is because of the earlier recognition of metabolic decomposition in patients with previously diagnosed T1DM, owing to awareness. They also believe this was related to faster decompensation of patients using insulin. Similar to the study of Lopes et al. [10], mean age, BMI, and tendency to enter hypokalemia were similar in patients with newly diagnosed T1DM in the present study.

The present study also found that, similar to the study of

Baloch et al. [11], the pandemic-onset group presented with more severe DKA. The admission pH of patients hospitalized in the unit was seven during the pandemic, and the mean pH was 7.1 in the pre-pandemic period. The PRISM III score can assist physicians in the early prediction of adverse clinical outcomes in patients with DKA and may help improve outcomes in the management of DKA. In the study of Baloch et al. [11] of 114 patients, inotropic use, mechanical ventilation support, and mortality were observed in patients with PRISM III scores higher than 8. Regarding PRISM III scores of patients in the present study, the average was 8 points in the pre-pandemic period and 10 points in the pandemic-onset period, a significant difference. However, none of the patients required inotropes and were not intubated.

According to the literature, the COVID-19 pandemic may have affected the incidence of DKA admissions and newly diagnosed diabetes. In a meta-analysis by Alfayez et al. [12] examining the relationship between DKA frequency and the



pandemic, the risk of DKA increased, especially the risk of severe DKA. There appears to be a bidirectional interaction between DKA and infection by SARS-CoV-2. Whether SARS-CoV-2 directly infects pancreatic β -cells and potentially contributes to the development of DKA is not clear. However, some reports on this issue have stated that the infection caused by SARS-CoV-2 can cause severe metabolic decompensation and DKA in patients. Also, based on observations that other coronaviruses bound to angiotensin-converting enzyme 2 receptors expressed by pancreatic beta cells, there is speculation that infection by SARS-CoV-2 may directly damage pancreatic beta cells, triggering the development of ketoacidosis [13-16].

The most feared complication of DKA is cerebral edema. Although its incidence is between 0.5% and 0.9%, it causes a high mortality rate of 21%-24% [17,18]. Patients who develop moderate-to-severe DKA may have poorer performance on measures of short-term memory, long-term memory, and general IQ [19]. Durward et al. [20] demonstrated the role of glucose-corrected serum sodium as a potential early marker of cerebral edema in a retrospective cohort study of 53 patients with severe DKA. In the present study, cerebral edema was suspected in three patients with low GCS and severe acidosis. These patients were examined using computed cranial tomography. Cerebral edema was detected in one of these patients and a 3% NaCl infusion was given. No complications were observed during follow-up. The corrected sodium value in study patients was 140±3.9 mEq/L, and no significant relationship was found between corrected sodium and cerebral edema. The researchers attributed this to the presence of cerebral edema in only one patient in the study cohort. Similar to the present study, research comparing 117 children hospitalized for DKA in a hospital in Pakistan showed that patients with a new diagnosis of T1DM stayed longer in the PICU due to treatment regulation and family education [21].

Ther present study analyzed 45 patients with DKA admitted to the participating center during the five years preceding the pandemic. After the onset of the pandemic, 23 such patients were admitted. During the pandemic, there was an increase in the number of patients diagnosed with DKA admitted to the PICU of the hospital. In conclusion, there has been an increase in the incidence of DKA in the center. Although the reason for this is not known, it may be because public health presentations about DKA and its symptoms were not effective during the COVID-19 period, families were worried about presenting to the hospital, admissions were late, and physicians were more reluctant to perform blood sugar and urinalysis because of the greater focus on COVID-19.

Interruption of health services for chronic diseases during the pandemic period reduced patient access to health services. In addition, families delayed visits to health institutions when their children got sick, resulting in more severe PICU presentation during the pandemic period. According to the literature, if parents suspected diabetes in their children, patients were admitted to the hospital with mild DKA. Although distance education and consultation opportunities such as telemedicine were provided, deficiencies in the management of chronic diseases during the pandemic period and the delay in new diagnosis of diabetes caused patients to present to hospitals with more severe disease.

In their study of 615 patients with newly diagnosed T1DM (401 admitted before the pandemic and 214 admitted during), Chambers et al. [22] found that patients who presented during the pandemic period had more severe DKA and longer hospital stays. In the present study, there was no statistically significant difference between the hospitalization times of patients with DKA regardless of period, contrary to what was expected. This could be related to the smaller sample size and the more heterogeneous patient group. This situation also might be affected by faster and more intense treatment arrangements and training of patients to meet the new hospitalization demands due to the decrease in bed capacity for isolation measures during the pandemic.

The strength of this study is that 59 patients were managed with the same DKA protocol, allowing comparison of patient outcomes. Limitations of the study were that it was a single-center, retrospective study and had a small number of patients compared with previous studies.

Early recognition and management of diabetes can prevent costly hospitalizations. However, diagnosis of diabetes and DKA may be delayed due to the negative effects of the COVID-19 pandemic on the healthcare system and difficulties in providing health services. The authors believe that awareness-raising campaigns (reminder brochures, social media reminders, and education) are necessary to prevent DKA through early symptom recognition and early treatment.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

FUNDING

None.

ACKNOWLEDGMENTS

None.

ORCID

Fevzi Kahveci Buse Önen Ocak Emrah Gün Anar Gurbanov Hacer Uçmak Ayşen Durak Aslan Ayşegül Ceran Hasan Özen Burak Balaban Edin Botan Zeynep Şıklar Merih Berberoğlu Tanıl Kendirli https://orcid.org/0000-0002-5176-1040 https://orcid.org/0000-0001-5631-500X https://orcid.org/0000-0001-7337-0190 https://orcid.org/0000-0003-1383-5130 https://orcid.org/0000-0003-2927-2360 https://orcid.org/0000-0002-7699-5652 https://orcid.org/0000-0002-3869-1340 https://orcid.org/0000-0002-2349-1602 https://orcid.org/0000-0001-6636-2678 https://orcid.org/0000-0003-4586-1595 https://orcid.org/0000-0003-0921-2694 https://orcid.org/0000-0003-3102-0242 https://orcid.org/0000-0001-9458-2803

AUTHOR CONTRIBUTIONS

Conceptualization: FK, AG, AC, HO, EB. Methodology: FK, EG, ADA, AC, BB, EB. Validation: FK. Formal analysis: FK, EG, AG, HU, BB, ZS, MB. Data curation: FK, BOO, EG, HU, ADA, AC, HO, EB, ZS, TK. Project administration: ZS, MB, TK. Writing-original draft: FK. Writing-review & editing: ZS, TK.

REFERENCES

- 1. von Saint Andre-von Arnim A, Farris R, Roberts JS, Yanay O, Brogan TV, Zimmerman JJ. Common endocrine issues in the pediatric intensive care unit. Crit Care Clin 2013;29:335-58.
- 2. Sherry NA, Levitsky LL. Management of diabetic ketoacidosis in children and adolescents. Paediatr Drugs 2008;10:209-15.
- 3. Ganesh R, Suresh N, Ramesh J. Diabetic ketoacidosis in children. Natl Med J India 2006;19:155-8.
- Jayashree M, Singhi S. Diabetic ketoacidosis: predictors of outcome in a pediatric intensive care unit of a developing country. Pediatr Crit Care Med 2004;5:427-33.
- **5.** Wolfsdorf JI, Allgrove J, Craig ME, Edge J, Glaser N, Jain V, et al. ISPAD Clinical Practice Consensus Guidelines 2014: diabetic

ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes 2014;15 Suppl 20:154-79.

- 6. Castellanos L, Tuffaha M, Koren D, Levitsky LL. Management of diabetic ketoacidosis in children and adolescents with type 1 diabetes mellitus. Paediatr Drugs 2020;22:357-67.
- Del Pozo P, Aránguiz D, Córdova G, Scheu C, Valle P, Cerda J, et al. Clinical profile of children with diabetic ketoacidosis in fifteen years of management in a Critical Care Unit. Rev Chil Pediatr 2018;89:491-8.
- Çocuk Endokrinoloji ve Diyabet Derneği. Child diabetes group diabetic ketoacidosis (DKA) treatment and follow-up guide [Internet]. Çocuk Endokrinoloji ve Diyabet Derneği; 2016 [cited 2023 May 10]. Available from : https://www.cocukendokrindiyabet.org/uploads/dokumanlar/9UtrSqWB3LMvcHyPLJw9.pdf
- **9.** Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. Crit Care Med 1996;24:743-52.
- Lopes CL, Pinheiro PP, Barberena LS, Eckert GU. Diabetic ketoacidosis in a pediatric intensive care unit. J Pediatr (Rio J) 2017;93:179-84.
- Baloch SH, Ibrahim PM, Lohano PD, Gowa MA, Mahar S, Memon R. Pediatric risk of mortality III score in predicting mortality among diabetic ketoacidosis patients in a pediatric intensive care unit. Cureus 2021;13:e19734.
- 12. Alfayez OM, Aldmasi KS, Alruwais NH, Bin Awad NM, Al Yami MS, Almohammed OA, et al. Incidence of diabetic ketoacidosis among pediatrics with type 1 diabetes prior to and during COVID-19 pandemic: a meta-analysis of observational studies. Front Endocrinol (Lausanne) 2022;13:856958.
- 13. Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. Lancet Diabetes Endocrinol 2020;8:782-92.
- Chee YJ, Ng SJH, Yeoh E. Diabetic ketoacidosis precipitated by Covid-19 in a patient with newly diagnosed diabetes mellitus. Diabetes Res Clin Pract 2020;164:108166.
- Li J, Wang X, Chen J, Zuo X, Zhang H, Deng A. COVID-19 infection may cause ketosis and ketoacidosis. Diabetes Obes Metab 2020;22:1935-41.
- Rubino F, Amiel SA, Zimmet P, Alberti G, Bornstein S, Eckel RH, et al. New-onset diabetes in Covid-19. N Engl J Med 2020;383:789-90.
- 17. Glaser N, Barnett P, McCaslin I, Nelson D, Trainor J, Louie J, et al. Risk factors for cerebral edema in children with diabetic ketoacidosis. N Engl J Med 2001;344:264-9.
- 18. Lawrence SE, Cummings EA, Gaboury I, Daneman D. Population-based study of incidence and risk factors for cerebral ede-



ma in pediatric diabetic ketoacidosis. J Pediatr 2005;146:688-92.

- 19. Ghetti S, Kuppermann N, Rewers A, Myers SR, Schunk JE, Stoner MJ, et al. Cognitive function following diabetic ketoacidosis in children with new-onset or previously diagnosed type 1 diabetes. Diabetes Care 2020;43:2768-75.
- **20.** Durward A, Ferguson LP, Taylor D, Murdoch IA, Tibby SM. The temporal relationship between glucose-corrected serum sodium and neurological status in severe diabetic ketoacidosis. Arch Dis Child 2011;96:50-7.
- **21.** Lone SW, Siddiqui EU, Muhammed F, Atta I, Ibrahim MN, Raza J. Frequency, clinical characteristics and outcome of diabetic ketoacidosis in children with type-1 diabetes at a tertiary care hospital. J Pak Med Assoc 2010;60:725-9.
- 22. Chambers MA, Mecham C, Arreola EV, Sinha M. Increase in the number of pediatric new-onset diabetes and diabetic ketoacidosis cases during the COVID-19 pandemic. Endocr Pract 2022;28:479-85.