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Reevaluating bicarbonate therapy in pediatric DKA: A propensity score-matched analysis of neurological and respiratory outcomes

Milan Patel [a], Ahmed M. Afifi, MD [b,*], Rhonda L. Hercher, MD [b], Mohamad Moussa, MD [b]

[a] The University of Toledo College of Medicine and Life Sciences, USA
[b] Department of Emergency Medicine, The University of Toledo, Toledo, OH, USA

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is a serious and potentially life-threatening complication of diabetes mellitus, responsible for up to 40 % of diabetes-related morbidity and mortality. Despite its use in severe cases of pediatric DKA, bicarbonate therapy remains controversial due to potential associations with adverse outcomes such as cerebral edema.

Objectives: Prior studies evaluating bicarbonate therapy in pediatric DKA have been limited by confounding variables, small sample sizes, and short follow-up periods. This study aims to evaluate the association between bicarbonate therapy and adverse outcomes using a large clinical dataset, extended follow-up, and propensity score (PS) matching to control for baseline differences.

Methods: We conducted a retrospective cohort study using TriNetX, a global research network of deidentified electronic health records. Pediatric DKA patients (<12 years) were stratified by bicarbonate therapy status and matched using PS to reduce confounders. Risk analysis was conducted to assess clinical outcomes.

Results: After PS matching, each cohort included 211 patients. No significant difference in cerebral edema was observed between groups (RD = 0.002; 95 % CI: −0.039 to 0.044; $p = 0.911$). However, bicarbonate use was associated with higher risks of coma (RD = 0.047; $p = 0.001$), pulmonary edema (RD = 0.048; p = 0.001), and acute respiratory failure (RD = 0.071; $p = 0.008$).

Conclusion: Although bicarbonate therapy was not linked to increased cerebral edema, it was associated with significant respiratory and neurologic complications. These findings suggest that clinicians should use bicarbonate cautiously and that current treatment guidelines may warrant reevaluation.

1. Introduction

Diabetic Ketoacidosis (DKA) is a life-threatening complication of diabetes characterized by an accumulation of ketone acids in the blood, resulting from insulin deficiency and counter-regulatory hormone excess [1,2]. Patients with DKA typically present with polydipsia, polyuria, and fruity acetone-scented breath due to the acidotic physiological state [3-5]. If left untreated, DKA can rapidly progress to loss of consciousness and death [6,7].

Notably, DKA remains the leading cause of morbidity and mortality in children with type 1 diabetes mellitus, occurring at the time of diagnosis in approximately 30 to 40 % of cases in the United States [8,9]. Bicarbonate therapy in DKA is generally reserved for patients with more severe presentations, particularly those who are critically ill or exhibit profound acidemia. Current clinical guidelines for managing severe DKA emphasize a stepwise approach: first addressing airway, breathing, and circulation (ABCs), followed by intravenous fluid resuscitation, and then administering insulin once the patient is stabilized [10,11]. Importantly, these guidelines contraindicate the routine use of sodium bicarbonate due to its association with adverse outcomes [12].

A significant concern regarding bicarbonate therapy in pediatric DKA is the increased risk of cerebral edema. A multicenter study found that children with DKA treated with bicarbonate had an increased relative risk of developing cerebral edema compared to those who did not receive bicarbonate [13]. Another study also found that bicarbonate therapy may potentially be harmful in pediatric patients due to increased cerebral edema [14]. Furthermore, a systematic review of multiple studies concluded that bicarbonate use in pediatric DKA is not justified, as it fails to provide sustained clinical benefits [15].

Despite these findings, prior research on bicarbonate therapy in DKA often lacks sufficient adjustment for confounding factors such as patient

* Corresponding author at: Department of Emergency Medicine, The University of Toledo, Dowling Hall 2488, Mail Stop 1088, 3000 Arlington Avenue, Toledo, OH 43614, USA.
E-mail address: ahmed.abdelwahab@utoledo.edu (A.M. Afifi).

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demographics, comorbidities, diagnosis, and lab values. A retrospective review by Yaneva et al. reported that a significant proportion of pediatric DKA patients who developed cerebral edema had received sodium bicarbonate therapy [16]. However, this study did not control baseline differences such as comorbidities, demographics, or biochemical profiles, limiting the reliability of its conclusions. To address these limitations, our study employs propensity score matching to balance baseline characteristics and obtain more accurate estimates of risk differences associated with bicarbonate therapy in pediatric DKA patients. We aim to provide a clearer understanding of the complications associated with bicarbonate use, particularly its association with neurological and respiratory complications in this vulnerable population.

2. Methods

2.1. Setting

This study utilized TriNetX®, a global network of deidentified electronic health record (EHR) data from over 100 healthcare organizations. This data, including diagnoses, procedures, medications and laboratory results, is available through a real-time, browser-based platform. This is a retrospective observational cohort study using EHR data from pediatric patients aged 0 to 12 years. The in-hospital data reviewed for this study includes clinical events that occurred within a 20-year window prior to January 30, 2025, 21:06:49 UTC—the date on which the data was accessed. Due to platform limitations, we were unable to access the dose or administration rate of sodium bicarbonate. All queries used for this study's database analysis were based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) for diagnosis and RxNORM for medications.

2.2. Ethics statement

TriNetX is compliant with General Data Protection Regulation and the Health Insurance Portability and Accountability Act. All the data presented on the platform are deidentified per the standard definition in section 164.514(a) of the Health Insurance Portability and Accountability Act Privacy Rule. Given that no protected health information was used, the University of Toledo College of Medicine and Life Sciences Institutional Review Board (IRB) determined that IRB approval was not required.

2.3. Cohort

The population was divided into two cohorts, Cohort A and Cohort B, of pediatric patients aged 0 to 12 years old diagnosed with any of the following ICD-10 codes: E11.1, E10.1 and E13.1. Cohort A consisted of patients who were treated with sodium bicarbonate (RXNORM:36676), while Cohort B was comprised of patients who did not receive sodium bicarbonate. We excluded patients with missing demographics or outcomes recorded prior to the index event.

2.4. Pre-specified outcomes

This study assessed the complications and outcomes that occurred in the time window that started on first day of the time index and ended 30 days after. The complications assessed in our study were identified were extracted using ICD 10 codes. The outcomes were grouped into neurological (cerebral edema [G93.6], coma [R40.2]), respiratory complications (acute respiratory failure [J96.0], pulmonary edema [J81.0], and metabolic complications (hypokalemia [E87.6], hyperkalemia [E87.5]). Mortality was captured using the "Deceased" status.

2.5. Propensity score matching parameters

Propensity score matching was utilized using the TriNetX platform. The following characteristics were matched for: demographics (White, Unknown Race, and Black or African American), diagnosis (volume depletion, metabolic disorders, factors influencing health status and contact with health services, diseases of the circulatory system, diseases of the digestive system, acute kidney failure, chronic kidney disease) and laboratory values in serum, plasma, or blood (bicarbonate, glucose, magnesium, chloride, potassium, phosphate, creatinine, and urea nitrogen).

2.6. Statistical analysis

To limit confounding variables, propensity score (PS) matching was performed for both cohorts prior to analysis of outcomes to match baseline characteristics. PS matching was performed using the following variables: age, sex, race, diagnosis, and laboratory values. Before and after PS matching patient characteristics can be found in Table 1. Following PS matching, risk analysis was performed to obtain the risk difference (RD) between the risk of each outcome in Cohort A ($n = 211$) and Cohort B ($n = 211$). Patients were excluded from individual outcome results if they had an outcome prior to the time window. The analysis excluded patients with outcomes prior to the time window of 0–30 days. In all the analyses, a 95 % confidence interval (95 % CI) was considered evidence of statistical significance. Statistical significance was defined as P-value <0.05. Statistical tests and plots were generated using R; descriptive summaries were exported from TriNetX [17].

3. Results

TriNetX identified a total of 9181 pediatric patients with DKA from 103 healthcare organizations. Of these patients, 226 patients comprised Cohort 1 (patients treated with sodium bicarbonate), while 8955 patients comprised Cohort 2 (patients not treated with sodium bicarbonate).

After PS matching, both Cohort 1 and Cohort 2 consisted of 211 patients each. Descriptive statistics for demographics, comorbidities, and laboratory values before and after PS matching—including percentages, means ± standard deviations, and associated p-values—are summarized in Table 1.

3.1. Clinical outcomes post-propensity score matching

After excluding patients with outcomes present prior to the study time window, we compared the incidence of several adverse clinical outcomes between the two matched cohorts. Risk differences, risk ratio, odds ratio, log-rank p, and hazard ratios are summarized in Table 2. Risk differences (RDs), 95 % confidence intervals (CIs), and p-values are plotted as a forest plot in Fig. 1.

- Cerebral Edema: Of the remaining 200 patients in Cohort 1, 10 developed cerebral edema, compared to 10 of 210 in Cohort 2. The difference was not statistically significant (RD = 0.002; 95 % CI [−0.039, 0.044]; $p = 0.911$). This finding contrasts with earlier studies that reported a heightened risk of cerebral edema with bicarbonate therapy but were limited by small sample sizes and very short follow-up window. In contrast, our analysis includes a substantially larger matched cohort and a 30-day outcome window, allowing for a more comprehensive assessment of delayed complications. These results suggest that, when controlling for baseline characteristics, bicarbonate therapy may not independently increase the risk of cerebral edema as previously thought.

Table 1
Baseline characteristics of pediatric DKA patients before and after propensity score matching, including demographics, diagnoses, and laboratory values. Values are presented as means ± SD or percentages, with associated p-values and standardized differences.

Cohort 1 ($N = 226$) and cohort 2 ($N = 8950$) characteristics before propensity score matching

Demographics

Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	2106–3	White		123	54.40 %	0.252	0.077
2				5212	58.20 %		
1	UNK	Unknown Race		48	21.20 %	0.01	0.162
2				1343	15.00 %		
1	2054–5	Black or African American		34	15.00 %	0.679	0.028
2				1438	16.10 %		

Diagnosis

Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	E86	Volume depletion		71	31.40 %	<0.001	0.793
2				308	3.40 %		
1	E70-E88	Metabolic disorders		108	47.80 %	<0.001	1.083
2				505	5.60 %		
1	Z00-Z99	Factors influencing health status and contact with health services		145	64.20 %	<0.001	0.771
2				2533	28.30 %		
1	I00-I99	Diseases of the circulatory system		55	24.30 %	<0.001	0.693
2				192	2.10 %		
1	K00-K95	Diseases of the digestive system		100	44.20 %	<0.001	0.699
2				1273	14.20 %		
1	N17-N19	Acute kidney failure and chronic kidney disease		40	17.70 %	<0.001	0.628
2				43	0.50 %		

Laboratory

Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	9021	Bicarbonate [Moles/volume] in Serum, Plasma or Blood	19.3 +/− 6.8	144	63.70 %	0.156	0.115
2			20.1 +/− 5.6	1196	13.40 %		
1		0–0 mmol/L		144	63.70 %	<0.001	1.209
2				1196	13.40 %		
1	9025	Glucose [Mass/volume] in Serum, Plasma or Blood	165.5 +/− 141.2	144	63.70 %	0.269	0.096
2			178.8 +/− 136.7	1335	14.90 %		
1		0–0 mg/dL		144	63.70 %	<0.001	1.153
2				1335	14.90 %		
1	9026	Magnesium [Mass/volume] in Serum, Plasma or Blood	1.9 +/− 0.3	94	41.60 %	0.827	0.025
2			1.9 +/− 0.3	407	4.50 %		
1		0–0 mg/dL		94	41.60 %	<0.001	0.979
2				407	4.50 %		
1	9023	Chloride [Moles/volume] in Serum, Plasma or Blood	105.9 +/− 6.5	144	63.70 %	<0.001	0.467
2			102.9 +/− 6.1	1200	13.40 %		
1		0–0 mmol/L		144	63.70 %	<0.001	1.207
2				1200	13.40 %		
1	9028	Potassium [Moles/volume] in Serum, Plasma or Blood	3.9 +/− 0.8	149	65.90 %	<0.001	0.354
2			4.2 +/− 0.7	1241	13.90 %		
1		0–0 mmol/L		150	66.40 %	<0.001	1.269
2				1241	13.90 %		
1	9027	Phosphate [Mass/volume] in Serum, Plasma or Blood	4.3 +/− 1.5	109	48.20 %	0.899	0.012
2			4.3 +/− 1.2	532	5.90 %		
1		0–0 mg/dL		109	48.20 %	<0.001	1.082
2				532	5.90 %		
1	9024	Creatinine	0.5 +/− 0.4	136	60.20 %	<0.001	0.387

Cohort 1 (N = 211) and cohort 2 ($N = 211$) characteristics after propensity score matching

Demographics

Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	2106–3	White		112	53.10 %	0.922	0.009
2				111	52.60 %		
1	UNK	Unknown Race		45	21.30 %	0.725	0.034
2				48	22.70 %		
1	2054–5	Black or African American		33	15.60 %	0.601	0.051
2				37	17.50 %		

Diagnosis

Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	E86	Volume depletion		58	27.50 %	0.746	0.032
2				61	28.90 %		
1	E70-E88	Metabolic disorders		93	44.10 %	1	<0.001
2				93	44.10 %		
1	Z00-Z99	Factors influencing health status and contact with health services		130	61.60 %	0.92	0.01
2				131	62.10 %		
1	I00-I99	Diseases of the circulatory system		44	20.90 %	0.54	0.06
2				39	18.50 %		
1	K00-K95	Diseases of the digestive system		86	40.80 %	0.376	0.086
2				95	45.00 %		
1	N17-N19	Acute kidney failure and chronic kidney disease		27	12.80 %	0.547	0.059
2				23	10.90 %		

Laboratory

Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
1	9021	Bicarbonate [Moles/volume] in Serum, Plasma or Blood	19.2 +/− 6.9	130	61.60 %	0.026	0.276
2			20.9 +/− 5.4	132	62.60 %		
1		0–0 mmol/L		130	61.60 %	0.841	0.02
2				132	62.60 %		
1	9025	Glucose [Mass/volume] in Serum, Plasma or Blood	170.3 +/− 147.6	129	61.10 %	0.552	0.075
2			160.9 +/− 99.0	125	59.20 %		
1		0–0 mg/dL		129	61.10 %	0.691	0.039
2				125	59.20 %		
1	9026	Magnesium [Mass/volume] in Serum, Plasma or Blood	1.9 +/− 0.4	80	37.90 %	0.619	0.079
2			2.0 +/− 0.3	78	37.00 %		
1		0–0 mg/dL		80	37.90 %	0.841	0.02
2				78	37.00 %		
1	9023	Chloride [Moles/volume] in Serum, Plasma or Blood	105.6 +/− 6.5	129	61.10 %	0.004	0.359
2			103.5 +/− 5.0	132	62.60 %		
1		0–0 mmol/L		129	61.10 %	0.764	0.029
2				132	62.60 %		
1	9028	Potassium [Moles/volume] in Serum, Plasma or Blood	3.9 +/− 0.8	134	63.50 %	0.007	0.331
2			4.1 +/− 0.7	137	64.90 %		
1		0–0 mmol/L		135	64.00 %	0.839	0.02
2				137	64.90 %		
1	9027	Phosphate [Mass/volume] in Serum, Plasma or Blood	4.3 +/− 1.6	95	45.00 %	0.496	0.099
2			4.4 +/− 1.1	94	44.50 %		
1		0–0 mg/dL		95	45.00 %	0.922	0.01
2				94	44.50 %		
1	9024	Creatinine	0.5 +/− 0.4	121	57.30 %	0.006	0.355

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Table 1 (*continued*)

Laboratory								Laboratory							
Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.	Cohort			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
2		[Mass/volume] in Serum, Plasma or Blood	0.4 +/− 0.2	1181	13.20 %			2		[Mass/volume] in Serum, Plasma or Blood	0.4 +/− 0.2	120	56.90 %		
1		0–0 mg/dL		136	60.20 %	<0.001	1.116	1		0–0 mg/dL		121	57.30 %	0.922	0.01
2				1181	13.20 %			2				120	56.90 %		
1		Urea nitrogen	12.6 +/− 7.6	127	56.20 %			1		Urea nitrogen	12.3 +/− 7.3	112	53.10 %		
2	9030	[Mass/volume] in Serum, Plasma or Blood	12.4 +/− 5.3	1140	12.70 %	0.607	0.041	2	9030	[Mass/volume] in Serum, Plasma or Blood	12.0 +/− 4.5	111	52.60 %	0.672	0.057
1		0–0 mg/dL		127	56.20 %	<0.001	1.028	1		0–0 mg/dL		112	53.10 %	0.922	0.009
2				1140	12.70 %			2				111	52.60 %		

- Coma: Ten patients in Cohort 1 experienced coma compared to none in Cohort 2 (RD = 0.047; 95 % CI [0.019, 0.076]; $p = 0.001$), indicating a significantly increased risk. Given the severity of this neurological complication and its exclusive occurrence in the bicarbonate-treated group, clinicians should reconsider the risk-benefit balance of bicarbonate use, even in cases of severe acidosis.
- Acute Respiratory Failure: Twenty-five patients in Cohort 1 developed acute respiratory failure versus 10 in Cohort 2 (RD = 0.071; 95 % CI [0.019, 0.123]; $p = 0.008$), also showing a significant increase in risk. The tripling of respiratory failure risk in the bicarbonate group highlights the importance of fluid and ventilation management and suggests potential harm associated with bicarbonate-induced fluid shifts.
- Hypokalemia: Among patients without prior hypokalemia, 24 of 180 in Cohort 1 and 15 of 201 in Cohort 2 developed this complication (RD = 0.059; 95 % CI [−0.003, 0.120]; $p = 0.059$). Although not statistically significant, this borderline result remains clinically relevant, as bicarbonate can promote intracellular potassium shifts that increase the risk for life-threatening cardiac arrhythmias [18].
- Hyperkalemia: Thirteen of 201 patients in Cohort 1 and 10 of 200 in Cohort 2 developed hyperkalemia. No significant difference was observed (RD = 0.015; 95 % CI [−0.031, 0.060]; $p = 0.527$).
- Mortality: Ten patients in each cohort died, after excluding 10 with prior death outcomes from Cohort 1. The mortality risk was equal between the groups (RD = 0.000; 95 % CI [−0.040, 0.041]; $p = 0.911$), suggesting no measurable difference in short-term mortality following bicarbonate therapy.
- Pulmonary Edema: Ten of 208 patients in Cohort 1 developed acute pulmonary edema compared to none in Cohort 2 (RD = 0.048; 95 % CI [0.019, 0.077]; $p = 0.001$), representing a significant increase in risk for the bicarbonate-treated group. This significant association underscores the possibility that bicarbonate therapy may contribute to fluid overload and respiratory compromise, supporting the need for careful monitoring of fluid balance when bicarbonate is used.

4. Discussion

Previous literature suggests that sodium bicarbonate therapy in severe pediatric DKA may increase the relative risk of cerebral edema [14,19]. However, our study found no significant difference in cerebral edema risk between bicarbonate-treated and non-treated patients after propensity score matching. This contrasts with earlier findings and may be explained by limitations in prior study designs. For example, in a study done by Assal et al., they found that bicarbonate did not significantly alter the clinical course of nine patients, though a slower decline in CSF osmolality was observed [20]. However, their follow-up lasted only four hours, lacking insight into long-term complications associated with the therapy. In contrast, our 30-day outcome window allowed for a more comprehensive assessment of delayed effects such as cerebral edema.

Similarly, Edge et al.'s UK case–control study identified acidosis severity and electrolyte imbalances as predictors of cerebral edema, but their analysis did not include matching for demographics or comorbidities—potentially confounding factors that may influence outcomes [21]. Our use of propensity score matching controlled these variables, offering a more accurate risk assessment. Additionally, the study by Lawrence et al. linked lower initial bicarbonate levels to increased cerebral edema risk, but their sample size included only 13 pediatric cases, limiting statistical power [8]. Our study, with a much larger matched cohort, strengthens the reliability of our findings and helps clarify the true relationship between bicarbonate use and cerebral edema in pediatric DKA.

Notably, our analysis found no significant risk difference in mortality between bicarbonate-treated and non-treated pediatric patients following propensity score matching. This finding is meaningful, as the research examining the mortality outcomes in this population is limited [13]. A randomized controlled trial by Lawrence R. Morris et al. reported no improvement in morbidity or mortality with sodium bicarbonate administration; however, the study's small sample size may have limited

Table 2
Comparison of adverse outcomes between pediatric patients with and without sodium bicarbonate administration during diabetic ketoacidosis (DKA) treatment.

Outcomes	ICD-10 Code	Ped-With Risk (%)	Ped-Without Risk (%)	Risk Difference (95 % CI)	Risk Ratio (95 % CI)	Odds Ratio (95 % CI)	Log-Rank P	Hazard Ratio (95 % CI)
Cerebral edema	G93.6	5.0 (10/200)	4.8 (10/210)	0.002 (−0.039, 0.044)	1.050 (0.477, 2.469)	1.053 (0.429, 2.586)	0.209	N/A
Coma	R40.2	4.7 (10/211)	0 (0/210)	0.047 (0.019, 0.076)	N/A	N/A	0.318	N/A
Acute respiratory failure	J96.0	11.8 (25/211)	4.7 (10/211)	0.071 (0.019, 0.123)	2.500 (1.231, 5.075)	2.702 (1.263, 5.777)	0	10.905 (2.549, 46.658)
Hypokalemia	E87.6	13.3 (24/180)	7.4 (15/201)	0.059 (−0.003, 0.120)	1.787 (0.968, 3.298)	1.908 (0.967, 3.763)	0.057	1.833 (0.962, 3.495)
Hyperkalemia	E87.5	6.5 (13/201)	5.0 (10/200)	0.015 (−0.031, 0.060)	1.294 (0.581, 2.881)	1.314 (0.562, 3.070)	0.026	3.296 (1.075, 10.109)
Mortality	N/A	4.8 (10/210)	4.7 (10/211)	0.000 (−0.040, 0.041)	1.005 (0.427, 2.364)	1.005 (0.409, 2.467)	0.01	9.206 (1.166, 72.668)
Acute pulmonary edema	J81.0	4.8 (10/208)	0 (0/211)	0.048 (0.019, 0.077)	N/A	N/A	0.314	N/A

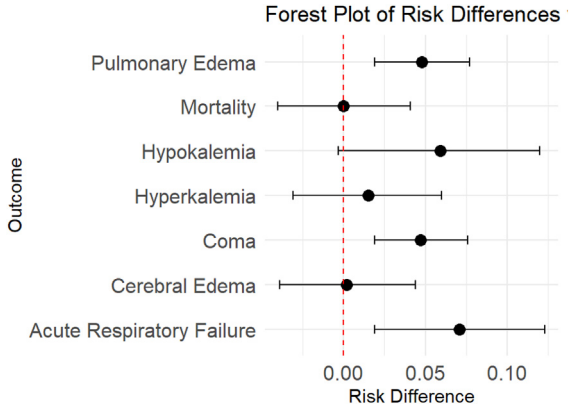

Fig. 1. Forest plot of risk differences with 95 % confidence intervals for major adverse outcomes in pediatric DKA patients treated with and without sodium bicarbonate.

its statistical power [22]. In contrast, our study's larger matched cohort offers a more robust assessment of this outcome. Unlike earlier studies that relied on small cohorts or brief observation periods, this study is the first to evaluate the risk of bicarbonate therapy on both neurological and respiratory complications over a 30-day follow-up window in a large, matched pediatric cohort with DKA. These findings can be used to update current guidelines.

Despite no observed increase in cerebral edema or mortality, our findings indicate that sodium bicarbonate therapy is associated with a higher risk of coma, acute respiratory failure, and pulmonary edema. Notably, coma occurred exclusively in the bicarbonate-treated cohort (10/211 vs. 0/211), a finding that cannot be overlooked. This outcome mandates reevaluation of risk thresholds and early neurologic monitoring during DKA management in children receiving bicarbonate therapy. Similarly, acute respiratory failure (25/211 vs. 10/211) and pulmonary edema (10/208 vs. 0/211) were significantly more common in the bicarbonate group. These adverse neurological and respiratory outcomes may stem from bicarbonate's known effects on fluid balance and tissue edema, particularly at high doses [23,24]. Previous studies have linked bicarbonate administration to increased fluid retention, which could explain the elevated risk of pulmonary edema and respiratory failure [25]. Additionally, rapid IV bicarbonate infusion in pediatric patients has been associated with intraventricular hemorrhage, which may contribute to coma development [26]. Although the increased risk of hypokalemia in the bicarbonate group did not reach statistical significance (RD = 0.059; p = 0.059), this finding may still be clinically relevant. Bicarbonate therapy can drive potassium into cells, potentially worsening hypokalemia and increasing the risk of cardiac arrhythmias [18,27]. This is particularly concerning for pediatric DKA patients, who are already susceptible to electrolyte disturbances—where even borderline potassium shifts may have significant clinical implications.

Given the increased incidence of severe neurological and respiratory complications, our findings, alongside prior research, suggest that the routine use of bicarbonate therapy in pediatric DKA should be re-evaluated. These findings have direct implications for clinical practice. Sodium bicarbonate is still used in some settings for treating severe acidosis, despite guideline recommendations to limit its use. Our data suggests that this practice may contribute to avoidable patient complications. Given that bicarbonate administration was associated with increased risk of coma and pulmonary and respiratory complications—even after adjustment for confounding—clinicians should weigh the risks carefully and consider heightened monitoring or alternative management strategies when bicarbonate is administered. Although bicarbonate therapy is generally limited to critically ill DKA patients, providers should carefully consider the potential neurological and respiratory complications when deciding to administer treatment.

While our study provides valuable insights, several limitations must be acknowledged. First, TriNetX does not provide information on medication dosage due to HIPAA constraints, which limits our ability to assess dose-response relationships and introduces uncertainty regarding the clinical applicability of our findings. Second, the platform lacks built-in functionality for conducting statistical power analyses in post–propensity score–matched cohorts. As a result, our study may be underpowered to detect significant differences in outcomes with low event rates, increasing the risk of type II error. Additionally, TriNetX's federated network may not capture follow-up data for patients who receive care outside of participating healthcare organizations. This potential loss to follow-up may lead to underreporting of outcomes. Finally, due to TriNetX platform limitations, we are unable to report detailed distributions of age and sex within the matched cohort's analysis. These demographic characteristics are important for evaluating residual confounding and assessing the balance between groups following matching.

Future research should focus on prospective studies to validate our findings in pediatric populations and further reduce potential confounding. Future studies can consider incorporating platforms or datasets that allow for greater transparency in subgroup distributions and the ability to conduct power analyses to further validate this study's findings. Additionally, given the limited adult literature regarding this interaction, future studies should investigate the outcomes associated with bicarbonate administration in adult DKA populations to determine whether similar risks apply across age groups. Further investigation into the mechanisms underlying bicarbonate's association with severe neurological and respiratory outcomes is also needed to guide clinical decision-making in DKA management.

CRediT authorship contribution statement

Milan Patel: Writing – original draft, Visualization, Methodology, Investigation. **Ahmed M. Afifi:** Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Rhonda L. Hercher:** Writing – review & editing, Supervision. **Mohamad Moussa:** Writing – review & editing, Project administration.

Ethical approval

Not required given the data are unidentified.

Declaration of competing interest

The authors declare no conflicts of interest related to this work. No financial, personal, or professional relationships influenced the design, execution, or reporting of this study.

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