Original Article

Diagnosis (by p-RIFLE and KDIGO) and Risk Factors of Acute Kidney Injury in Pediatric Diabetic Ketoacidosis: A Retrospective Study

Abstract

Background: There are two criteria to diagnose and stage acute kidney injury (AKI) in children: pediatric-Risk, Injury, Failure, Loss (p-RIFLE) and Kidney Disease Improving Global Outcomes (KDIGO). This study aims to find out the extent of agreement in diagnosis (by p-RIFLE and KDIGO) and risk factors of AKI in pediatric diabetic ketoacidosis (DKA). **Materials and Methods**: A retrospective cohort study involving children aged ≤15 years with DKA was conducted between January 2014 and December 2022. Those with inborn errors of metabolism, septic shock, and urinary tract disease were excluded. The primary outcome was the extent of agreement in diagnosis of AKI by p-RIFLE and KDIGO. The secondary outcomes were staging agreement, risk factors, complications (hypoglycemia, hypokalemia, and cerebral edema), time to resolution of DKA, and hospital and pediatric intensive care units (PICU) stay. **Results**: Data from 161 patients were collected. Mean (SD) age was 8.6 (3.7) years. Good agreement between p-RIFLE and KDIGO criteria for diagnosis of AKI was noted at admission (Kappa = 0.71, p ≤ 0.001), at 24 hours (Kappa = 0.73, p ≤ 0.001) and discharge (Kappa = 0.60, p ≤ 0.001), and for the staging of AKI at admission (Kappa = 0.81, p ≤ 0.001) at 24 hours (Kappa = 0.75, p ≤ 0.001) and discharge (Kappa = 0.48, p ≤ 0.001). On multivariate analysis, age (≤5 years: aOR = 3.03, 95% CI 1.04–8.79) is an independent risk factor for AKI at discharge by KDIGO. Cerebral edema (n = 6, 3.7%), hypoglycemia (n = 66, 41%), and hypokalemia (n = 59, 36.6%) were noted. Resolution and stay in PICU and hospitals were longer for patients with AKI. **Conclusion**: p-RIFLE and KDIGO criteria showed good agreement in diagnosis and staging of AKI in pediatric DKA.

Keywords: *Acute kidney injury, Children, Complications, Diabetic ketoacidosis, Insulin*

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DOI: 10.25259/IJN_79_2024

Received: 14-02-2024
Accepted: 31-05-2024
Online First: 01-08-2024
Published: 10-04-2025

Introduction

In children, diabetic ketoacidosis (DKA) is a life- and organ-threatening complication of Type-I diabetes mellitus (T1DM) caused by insulin deficiency, and incidence ranges from 15% to 70%.[1] DKA is associated with life-threatening complications and comorbidities: electrolyte disturbance, cerebral edema, hypovolemic shock, acute kidney injury (AKI), and mortality.[2] The importance of AKI in DKA has gained clinical significance as studies have started reporting the impact on clinical outcomes. The incidence of AKI in DKA varies from 35% to 80%.[2,3] Though a higher frequency of AKI was reported, the exact pathophysiology remains not well-studied other than kidney hypoperfusion due to intravascular depletion and hyperglycemia-induced tubular injury and inflammation.[3] AKI is usually masked by ketonemia-associated spurious creatinine elevation and osmotic diuresis.[1] An episode of AKI during DKA is associated with a high risk for diabetic kidney disease (DKD).[4] The pediatric-Risk, Injury, Failure, Loss (p-RIFLE) is commonly used to diagnose AKI in critically ill children. The Kidney Disease Improving Global Outcomes (KDIGO) was adopted to diagnose AKI for uniform reporting. Studies in pediatric DKA used both p-RIFLE and KDIGO for AKI diagnosis and staging. The studies have found that p-RIFLE is more sensitive to diagnosing and staging AKI. These definitions have demonstrated excellent interstage discrimination in pediatric intensive care units (PICU) and non-PICU settings.[5] We still need evidence to substantiate acceptance of KDIGO as compared to p-RIFLE criteria in terms of agreement and ability to discriminate/

How to cite this article: Likhitha S, Rameshkumar R, Delhikumar CG, Selvan T. Diagnosis (by p-RIFLE and KDIGO) and Risk Factors of Acute Kidney Injury in Pediatric Diabetic Ketoacidosis: A Retrospective Study. Indian J Nephrol. 2025;35:373-9. doi: 10.25259/IJN_79_2024

differentiate the various stages of AKI in pediatric DKA. Hence, we planned to study the extent of agreement to diagnosis, staging (by p-RIFLE and KDIGO serum creatinine criteria), and risk factors of AKI in pediatric DKA.

Materials and Methods

The study was a retrospective cohort study conducted in the PICU of a tertiary care academic institute - Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) from January 2014 to December 2022. The institutional ethics committee approved the study with a waiver of written informed consent (IEC approval no. JIP/IEC-OS/2023/186 dated 05-07-2023). This study was conducted in accordance with Helsinki guidelines as revised in 2013. Medical records of children aged ≤15 years with DKA admitted to PICU were screened. Data on 150 patients were collected from three prospective studies.[6,7] Children with any of the following conditions were excluded: (i) inborn error of metabolism (IEM), (ii) septic shock, and (iii) disease of the urinary tract. DKA and severity were defined by the International Society for Pediatric and Adolescent Diabetes (ISPAD) guideline [hyperglycemia (blood glucose >200 mg/dL), acidosis (venous pH <7.30 or bicarbonate <15 mEq/L), and ketonemia (beta-hydroxybutyrate-BOHB ≥3 mmol/L) or moderate or large ketonuria by urine dipstick test]. The severity of DKA was classified into mild (pH 7.20–7.29 or bicarbonate <15 mEq/L), moderate (pH 7.10–7.19 or bicarbonate <10 mEq/L), and severe (pH <7.10 or bicarbonate <5 mEq/L).[8] The patients were managed with an initial normal saline bolus, then maintenance fluid of 85% over 48 h, and insulin (intravenous at a dose of 0.05 to 0.1 unit/kg/hour) or subcutaneous insulin (Lispro at a dose of 0.15 unit/kg every 2 hours). The details of the treatment were described in the previous study.[7]

The pediatric version of p-RIFLE criteria for AKI was defined as a fall of estimated creatinine clearance (eCCl) by 25% (Risk), by 50% (Injury), and by 75% or <35 mL/min/1.73 m^2 (Failure).[9] KDIGO criteria were defined as an increase in serum creatinine by >1.5 to 1.9 times baseline (Stage I), by 2.0 to 2.9 times baseline (Stage II), and by ≥3 times baseline (Stage III) or urine output criteria.[10] Serum creatinine was estimated using the modified Jaffe method by auto analyzer (Olympus® AU 680, Beckman Coulter, California, USA). Creatinine clearance was calculated using the modified Schwartz formula (= Length in cm × 0.413 ÷ Serum creatinine in mg/dL). If the lowest creatinine value in the past 3 months was available, the lowest value was taken as the baseline; otherwise, baseline creatinine was estimated by 120 mL/min/1.73 m^2 with reverse calculation by using a modified Schwartz formula as described in the previous studies.[2,4,11]

Baseline characteristics, details about fluid resuscitation, electrolytes, albumin, blood gas, lactate, blood glucose (BG), glycated hemoglobin (HbA1c), capillary BOHB, complications, blood urea nitrogen (BUN), creatinine, fluid overload balance (FO%), hospital including PICU length of stay (LOS), outcome and risk factors were collected from three prospective studies and medical records including electronic hospital information system in standard case report form. The details of blood investigations and frequency were described in previous studies.[6,7] The resolution of ketoacidosis was defined as (pH ≥ 7.30, bicarbonate ≥ 15 mEq/L, and BOHB < 1 mmol/L).[7] Hypokalemia was defined as serum potassium <3.5 mEq/L and/or suggestive electrocardiographic (ECG) changes. Hypoglycemia was defined as BG ≤60 mg/dL.[7] Cerebral edema was diagnosed as per the criteria given by Muir *et al*.[12] Blood ketone and BG were measured using a bedside meter (Abbott Optium-H) after calibration and blood gas analysis by Cobas b 221 system (Roche Diagnostics). Fluid overload percentage (FO%) was calculated using the formula = [(Total fluid input in liter – Total fluid output in liter ÷ Weight at admission in kilogram) × 100].[13] Hyperchloremia was defined as a serum chloride >75% of the serum sodium concentration.[14] Anion gap (AG) was calculated using [=Na–(Cl+HCO_3), corrected sodium using [= measured sodium + 2 × (blood glucose – 100/100 mg per dL)], and effective osmolarity (mOsm/kg) using [= 2 × (sodium) + (blood glucose/18 in mg per dL) formulas.[8] Malnutrition was defined as per Indian standards (weight for age-matched).[15,16] Patients were advised to follow up in pediatric endocrine and nephrology clinics after discharge.

Statistical analysis

The reported incidence of AKI in pediatric DKA was 35% and 64.2% using p-RIFLE and KDIGO criteria, respectively.[1,11] With a two-sided 95% confidence interval (95% CI), the expected true proportion of success is 70%, and the extent of agreement (Kappa) is 85% with a precision of 10% (distance from Kappa to limit, ω), the sample size of 160 required including 20% attrition rate. The normality of data was checked with Kolmogorov–Smirnov z-test. Between groups (AKI-Yes vs. AKI-No), continuous variables were compared using the Student's t-test if normally distributed or the Mann–Whitney U-test if data were skewed. The proportion was compared by Chi-square test (Fisher exact test when cell frequencies were <5). The agreement between p-RIFLE and KDIGO in the diagnosis of AKI was compared using Cohen's Kappa statistics. Multivariate (Binary) logistic regression analysis with clinically relevant factors was done to predict the risk of developing AKI (by KDIGO criteria). The model fit was assessed with Hosmer and Lemeshow's goodness-of-fit model. The adjusted odds ratio (a-OR) with 95% CI was calculated wherever appropriate. All tests were two-tailed, and a p-value of <0.05 was considered statistically significant. Data were analyzed using IBM SPSS Statistics (Version 26.0. Armonk, NY).

Table 1: Baseline characteristics at admission

Parameter	All patients (n = 161)	AKI by p-RIFLE		p-value	AKI by KDIGO		p-value
		Yes (n = 135)	No (n = 26)		Yes (n = 119)	No (n = 42)	
Age (years)	8.6 (3.7)	8.5 (3.8)	9.2 (3.5)	0.359†	8 (3.8)	10 (3.2)	0.002†
Age, n (%)				0.346‡			0.002‡
≤5 years	39 (24.2)	35 (26)	4 (15.4)		35 (29.4)	4 (9.5)	
>5 to ≤10 years	60 (37.3)	51 (37.8)	9 (34.6)		47 (39.5)	13 (31)	
>10 to ≤15 years	62 (38.5)	49 (36.2)	13 (50)	0.346‡	37 (31.1)	25 (59.5)	
Male:Female, n	44:117	39:96	5:21	0.312‡	35:84	9:33	0.318‡
Body mass index	13.9 (2.7)	14.1 (2.9)	13 (1.7)	0.067†	13.8 (2.6)	14.2 (2.9)	0.493†
Malnutrition, n (%)	84 (52.2)	72 (53.3)	12 (46.2)	0.502‡	67 (56.3)	17 (40.5)	0.078‡
New onset DKA, n (%)	81 (50.3)	67 (49.6)	14 (53.8)	0.694‡	61 (51.3)	20 (47.6)	0.685‡
Established DM, n (%)	80 (49.7)	68 (50.4)	12 (46.2)	0.694‡	58 (48.7)	22 (52.4)	0.685‡
*Duration of DM, month	35.5 (12–48)	35 (12–48)	42 (24–60)	0.310§	27 (12–48)	42 (24–60)	0.155§
With previous DKA, n (%)	63 (39.1)	54/68 (79.4)	9/12 (75)	0.711¶	46/58 (79.3)	17/22 (77.3)	0.842‡
*Duration of symptom, day	1.5 (1–2)	2 (1–5)	4 (2–7)	0.029§	2 (1.5–5)	2.5 (2–7)	0.193§
*Onset of symptom to first medical care contact, day	1 (0.5–1.2)	1 (0.6–3)	3.4 (1–6)	0.010§	1 (0.4–1)	1 (1–1.7)	0.230§
Severity of DKA, n (%)				0.348‡			0.752‡
Mild	18 (11.2)	13 (9.6)	5 (19.2)		12 (10)	6 (14.3)	
Moderate	86 (53.4)	74 (54.8)	12 (46.2)		64 (54)	22 (52.4)	
Severe	57 (35.4)	48 (35.6)	9 (34.6)		43 (36)	14 (33.3)	
Hemoglobin A1c, %	13.5 (2.4)	13.5 (2.5)	13.4 (2.4)	0.745†	13.6 (2.3)	13.3 (2.8)	0.580†
Blood glucose, mg/dL	466 (109)	473 (107)	430 (110)	0.065†	473 (111)	448 (99)	0.201†
pH	7.10 (0.15)	7.10 (0.14)	7.14 (0.15)	0.176†	7.10 (0.15)	7.13 (0.15)	0.260†
Bicarbonate, mEq/L	7.8 (4.6)	7.7 (4.5)	8.7 (5.4)	0.312†	7.7 (4.5)	8.2 (5)	0.550†
PCO2, mmHg	21.2 (8.8)	21.2 (9.2)	21.1 (7.3)	0.953†	21.3 (10)	21 (7)	0.786†
Capillary BOHB, mmol/L	5.2 (1.4)	5.1 (1.4)	5.3 (1.5)	0.670†	5.2 (1.4)	5.1 (1.5)	0.786†
Blood urea nitrogen, mg/dL	15 (8.5)	15.5 (9)	11.7 (5.4)	0.036†	16 (9)	13 (7)	0.106†
Creatinine, mg/dL	0.92 (0.48)	1.00 (0.48)	0.49 (0.09)	<0.001†	1.04 (0.50)	0.57 (0.12)	<0.001†
e-GFR, mL/min/1.73 m^2	65.4 (27.4)	56.4 (18.8)	112 (16)	<0.001†	53 (17)	101 (18.3)	<0.001†
Sodium, mEq/L	133 (7)	133 (8)	131 (6)	0.383†	133 (8)	132 (6)	0.517†
Corrected sodium, mEq/L	138 (8)	139 (8)	137 (6)	0.198†	139 (8)	138 (7)	0.349†
Hyperchloremia, n (%)	77 (47.8)	60 (44)	17 (65)	0.050‡	52 (44)	25 (60)	0.078‡
Effective osmolality, mOsm/kg	291 (16)	292 (16)	287 (14)	0.109†	292 (16)	289 (15)	0.233†
Potassium, mEq/L	4.4 (0.8)	4.4 (0.8)	4.2 (0.8)	0.082†	4.4 (0.8)	4.3 (0.8)	0.233†
Anion gap	23.2 (9.8)	24 (10)	20 (7)	0.050†	24 (11)	21 (7)	0.055†
Lactate, mmol/L	2.3 (0.8)	2.3 (0.8)	2.0 (0.6)	0.065†	2.3 (0.7)	2.3 (0.8)	0.747†
*Fluid received before starting insulin, mL/kg	10 (10–20)	10 (10–20)	10 (10–20)	0.531§	10 (10–20)	10 (10–10)	0.024§

All data are presented in mean (SD) or as stated numbers with percentages except * median (IQR), AKI: Acute kidney injury, p-RIFLE: pediatric version of risk, injury, failure, loss of function criteria, KDIGO: Kidney disease improving global outcomes criteria, DKA: Diabetic ketoacidosis, DM: Diabetes mellitus, PCO2: Partial pressure of carbon dioxide, e-GFR: estimated glomerular filtration rate, SD: Standard deviation, IQR: Inter quartile range. The percentage of patients and blood test parameters were rounded to the nearest number wherever appropriate. †Student t-test, ‡Chi-square test, §Mann–Whitney U–test, ¶Fischer's exact test.

Results

A total of 174 patients with a diagnosis of DKA in medical records were screened; 13 patients were excluded (inborn error of metabolism = 6, associated septic shock = 4, and chronic kidney disease = 3), leaving 161 for analysis. Baseline characteristics for all patients and AKI by p-RIFLE and KIDGO are given in Table 1. Mean (SD) age was 8.6 (3.7) years, and 117 (72.7%) were female. Half of the patients had malnutrition (n = 84, 52.2%). The duration of symptoms, the onset of symptoms to first medical care contact time, and kidney function parameters (creatinine, estimated Glomerular Filtration Rate – eGFR) showed significant differences among AKI versus No-AKI patients [Table 1]. Insulin infusion was received in 150 patients (0.1 unit/kg/hour = 40, 24.8%;

0.05 unit/kg/hour = 110, 68.3%) and subcutaneous insulin in 11 patients (6.8%).

At admission, AKI was diagnosed in 135 patients (83.8%) by p-RIFLE (Risk = 60, 44.4%; Injury = 54, 40%, Failure = 21, 15.6%) and 119 patients (74%) by KDIGO (Stage-I = 45, 37.8%, Stage-II = 49, 41.2%, Stage-III = 25, 21%). The extent of agreement between p-RIFLE and KDIGO was good (Kappa = 0.71, p < 0.001). For staging by two criteria showed significant agreement for Stage-0 (No-AKI) at 61.9%, Stage-I (= Risk) at 95.6%, Stage-II (= Injury) at 98%, and Stage-III (= Failure) at 84% [Table 2]. At 24 hours, AKI was diagnosed in 104 patients (64.6%) by p-RILFE (Risk = 64, Injury = 28, Failure = 12) and 82 patients (51%) by KDIGO (Stage-I = 43, Stage-II = 24, Stage-III = 15). The extent of agreement between p-RIFLE and KDIGO was good (Kappa = 0.73, p = <0.001). Staging by two criteria showed significant agreement for Stage-0 (No-AKI) at 72.2%, Stage-I (= Risk) at 95.3%, Stage-II (= Injury) at 95.8%, and Stage-III (= Failure) at 80%. At discharge, AKI was diagnosed in 69 patients (42.9%) by p-RIFLE (Risk = 49, Injury = 15, Failure = 5) and 39 patients (24.2%) by KDIGO (Stage-I = 32, Stage-II = 5, Stage-III = 2). The extent of agreement between p-RIFLE and KDIGO was good (Kappa = 0.60, p = <0.001). Staging

Table 2: Outcomes of the study

Outcome		AKI by KDIGO criteria (At admission)				p-value*
		AKI – Yes		AKI – No		
AKI by p-RIFLE criteria (At admission)	AKI – Yes	119 (100%)		16 (38.1%)		<0.001
	AKI – No	0		26 (61.9%)		Cohen's Kappa = 0.71
	Total	(n = 119)		(n = 42)		
		AKI stage by KDIGO criteria (At admission)				
		0	I	II	III	
AKI stage by p-RIFLE criteria (At admission)	No-AKI (0)	26 (61.9%)	0	0	0	<0.001
	Risk (I)	16 (38.1%)	43 (95.6%)	1 (2%)	0	Cohen's Kappa = 0.81
	Injury (II)	0	2 (4.4%)	48 (98%)	4 (16%)	
	Failure (III)	0	0	0	21 (84%)	
	Total	(n = 42)	(n = 45)	(n = 49)	(n = 25)	
		AKI by KDIGO criteria (At 24 hours)				
		AKI – Yes		AKI – No		
AKI by p-RIFLE criteria (At 24 hours)	AKI – Yes	82 (100%)		22 (27.8%)		<0.001
	AKI – No	0		57 (72.2%)		Cohen's Kappa = 0.73
	Total	(n = 82)		(n = 79)		
		AKI stage by KDIGO criteria (At 24 hours)				
		0	I	II	III	
AKI stage by p-RIFLE criteria (At 24 hours)	No-AKI (0)	57 (72.2%)	0	0	0	<0.001
	Risk (I)	22 (27.8%)	41 (95.3%)	1 (4.2%)	0	Cohen's Kappa = 0.75
	Injury (II)	0	2 (4.7%)	23 (95.8%)	3 (20%)	
	Failure (III)	0	0	0	12 (80%)	
	Total	(n = 79)	(n = 43)	(n = 24)	(n = 15)	
		AKI by KDIGO criteria (At discharge)				
		AKI – Yes		AKI – No		
AKI stage by p-RIFLE criteria (At discharge)	AKI – Yes	39 (100%)		30 (24.6)		<0.001
	AKI – No	0		92 (75.4%)		Cohen's Kappa = 0.60
	Total	(n = 39)		(n = 122)		
		AKI stage by KDIGO criteria (At discharge)				
		0	I	II	III	
AKI stage by p-RIFLE criteria (At discharge)	No-AKI (0)	92 (75.4%)	0	0	0	<0.001
	Risk (I)	28 (23%)	21 (65.6%)	0	0	Cohen's Kappa = 0.48
	Injury (II)	2 (1.6%)	9 (28.1%)	4 (80%)	0	
	Failure (III)	0	2 (6.3%)	1 (20%)	2 (100%)	
	Total	(n = 122)	(n = 32)	(n = 5)	(n = 2)	

All data are presented in mean (SD) or as stated numbers with percentages, AKI: Acute kidney injury, p-RIFLE: pediatric version of risk, Injury, failure, loss of function criteria, KDIGO: Kidney disease improving global outcomes, * Kappa statistics.

Table 3: Multivariate logistic regression analysis for predictors of AKI by KDIGO criteria at discharge (AKI – yes = 39 and AKI – no = 122)

Variables	Unadjusted odds ratio, 95% CI	p-value	Adjusted odds ratio, 95% CI	p-value
Age				
(≤5 years)	2.32 (0.91–5.89)	0.077	3.03 (1.04–8.79)	0.042
(>5 to ≤10 years)	1.55 (0.64–3.71)	0.330	1.68 (0.66–4.28)	0.274
Gender (female)	1.12 (0.49–2.55)	0.786	1.29 (0.54–3.10)	0.571
Malnutrition (yes)	1.44 (0.69–2.98)	0.330	1.65 (0.73 3.71)	0.228
DKA severity				
Moderate	2.27 (0.48–10.75)	0.302	2.13 (0.43–10.53)	0.354
Severe	3.69 (0.77–17.79)	0.103	3.64 (0.72–18.50)	0.120
Duration of symptoms (>2 days)	0.63 (0.30–1.31)	0.211	0.48 (0.22–1.09)	0.078
Hemoglobin A1c (%)				
>12 to ≤15	1.12 (0.45–2.77)	0.808	1.27 (0.48–3.35)	0.636
>15	1.47 (0.54–3.97)	0.451	1.46 (0.46–4.68)	0.525
BOHB (>5 mmol/L)	1.31 (0.63–2.75)	0.468	1.55 (0.69–3.47)	0.287
Lactate (>2 mmol/L)	1.10 (0.50–2.39)	0.815	1.01 (0.43–2.36)	0.978
Hyperchloremia (yes)	0.70 (0.34–1.44)	0.330	0.66 (0.30–1.43)	0.290

Variables entered in the model: age (≤5/>5 to ≤10/>10 to 15-ref), gender (male-ref/female); malnutrition (Yes/No-ref); DKA severity (mild-ref/moderate/severe); Duration of symptom (≤2-ref/>2); Hemoglobin A1c (up to 12-ref/>12-≤15/>15); BOHB (≤5-ref/>5); lactate (≤2-ref/>2); hyperchloremia (Yes/No-ref). Hosmer and Lemeshow's goodness-of-fit model p = 0.611. The overall percentage of the model is 79.5%, and r^2 = 0.13. AKI: Acute kidney injury, KDIGO: Kidney disease improving global outcomes, DKA: Diabetic ketoacidosis, BOHB: Beta-hydroxybutyrate, CI: Confidence interval.

by two criteria showed significant agreement for Stage-0 (No-AKI) at 75.4%, Stage-I (= Risk) at 65.6%, Stage-II (= Injury) at 80%, and Stage-III (= Failure) at 100%. [Table 2]. Overall, p-RIFLE had identified extra 16 (10%) cases of AKI at admission, 22 (13.7%) cases at 24 hours, and 30 (18.6%) cases at discharge as compared to KDIGO.

On multivariate regression analysis, age (≤5 years) predicted the AKI at discharge based on KDIGO criteria [Table 3]. The mean (SD) time to resolve DKA was 23 (14.6) hours. A total of 119 (69.6%) patients achieved resolution of DKA within 24 hours [Mean (SD) was 15.8 (6.6) hours] and 49 (30.4%) patients achieved resolution after 24 hours [Mean (SD) 39.1 (15.1) hours]. There was a significant difference in the mean (SD) resolution of DKA among the AKI versus No-AKI group by both p-RIFLE [25.6 (18) vs. 21 (11.1) hours; p = 0.047)] and KDIGO [27.8 (19.3) vs. 20.3 (10.5); p = 0.002)] criteria at discharge, respectively. Hypoglycemia was noted in 66 (41%), hypokalemia in 59 (36.6%), and cerebral edema in 6 (3.7%). Two patients (1.2%) required mechanical ventilation, and one patient (0.6%) required continuous kidney replacement therapy (CKRT). The median (IQR) LOS in the PICU was 1.3 (1–2) days, and in hospital was 8 (6–11) days, respectively. There was a significant difference in the median (IQR) of LOS in PICU among the AKI versus No-AKI group by both p-RIFLE [2 (1–3) days vs. 1 (1–2) days; p = 0.025] and KDIGO [2 (1–3) days vs. 1.1 (1–2) days; p = 0.010] criteria at discharge, respectively. There was a significant difference in the median (IQR) of LOS in hospital among the AKI versus No-AKI group by both p-RIFLE [9 (6–12) days vs. 8 (6–10) days; p = 0.056] and KDIGO [11 (6.5–13.5) days vs. 8 (6–11) days; p = 0.009] criteria at discharge, respectively. There was no mortality. At discharge, patients had stable vitals, normal urine output, and not on any dialysis.

Discussion

The current study reported the agreement of two commonly used AKI criteria and risk factors of AKI in 161 children with DKA. Age (≤5 years) was a predictor of AKI at discharge. Resolution of DKA and LOS in PICU and hospital was longer in AKI patients (by both p-RIFLE and KDIGO). The highest prevalence of AKI reported was 80.57% using KDIGO criteria by Al Khalifah *et al.*, involving 213 children with DKA.[2] The author mentioned young age (<5 years), more severe DKA, recurrent DKA, and recurrent AKI for the high prevalence of AKI in their study.[2] Similar to our study finding, a high prevalence of AKI at admission is due to young age (≤5 years), severe DKA, and previous DKA episodes. Different ethnic groups have different risks of AKI in adult and pediatric patients with or without DKA.[2] The possible ethnic difference needs to be studied in the future.

In our study, most of the patients had Stage I (= Risk) of AKI, followed by Stage II (= Injury) and Stage III (= Failure). This is similar to previous studies where most of the patients were presented with Stage I (39% to 75%) or II (21% to 44.3%) and a lower proportion of Stage III (1.4% to 4%).[2,17] The previous studies reported that none of the patients required kidney replacement therapy (KRT),[2,17] contrasting our study's finding that one patient required

CKRT. However, the KRT is rarely required in pediatric DKA-associated/complicated AKI.[11,17] The common reason for AKI in DKA is reduced intravascular volume. After fluid resuscitation and subsequent fluid and insulin therapy, there is a significant AKI response noted (called volume-responsive AKI). The concept of volume-responsive AKI, improvement of higher stage namely Stage-III (= Failure) to lower stage, and resolution of ketoacidosis could be the possible reason for no AKI in the different time points of analysis in our study.[2,8,18] Recent pediatric studies reported an increased risk of AKI with increasing age, male gender, dehydration (severity), acidosis, and higher heart rate with higher BG, sodium, chloride, and BUN.[1,2,11,17] All these factors are directly related to the severity of DKA. The interaction of these factors during regression model construction cannot be ignored, and in recent studies, the regression model explains only 16% of the variability.[2] In our study, age (≤5 years) predicts AKI. Future studies are required to validate our risk factors model for developing clinical risk scores for AKI in pediatric DKA.

Similar to our setting, a study by Baalaaji *et al*.[1] involving 74 pediatric DKA patients showed that AKI was seen in 28 (37.8%) patients using p-RIFLE criteria. Most studies, including a systematic review involving 4087 pediatric T1DM with 4500 DKA episodes and a recent study involving 213 pediatric DKA patients, found that any stage of AKI was 47% (95% CI 40%–55%) and 80.75% by using KDIGO criteria, respectively.[2,3] In our study, AKI by p-RIFLE was 83.8%, and KDIGO was 74% at admission. There was significantly good agreement between the two criteria for diagnosing and staging AKI. The studies in PICU and non-PICU settings demonstrated that p-RIFLE and KDIGO criteria can discriminate interstage AKI excellently.[9,10] In adult settings, KDIGO criteria have shown a higher incidence of AKI; in pediatric settings, p-RIFLE criteria have shown more sensitivity to diagnose AKI because it identified more Risk (Stage-I).[19–21] This is similar to our study results as p-RIFLE had gathered an extra 10%, 13.7%, and 18.6% of AKI cases at admission, 24 hours, and discharge, respectively.

The most proposed hypothesis in AKI in pediatric DKA is hypoperfusion due to intravascular volume depletion. The exact pathophysiology has not been studied well.[2] A recent study reported AKI in new-onset T1DM without DKA.[2] In our study, all patients received an initial normal saline bolus even with normal blood pressure and perfusion. A study by Al Khalifah *et al*.[2] found that those who received normal saline bolus had similar AKI prevalence despite having normal blood pressure. In addition to the concept of volume depletion, other factors, namely age (younger) prone to AKI, higher BG-induced tubular injury, hyperchloremia-associated kidney inflammation/injury/hypoperfusion of cortex, the severity of ketoacidosis and conservative fluid approach's contribution cannot be ignored. We found that age is a predictor of AKI. We found differences in the resolution of DKA and LOS in PICU and hospital among AKI patients. This is similar to previous studies that found that those with AKI were associated with a longer time to resolve DKA and stay in the PICU and hospital.[1,2] The possible reasons for no AKI patient outcome are optimal fluid resuscitation, including uniform fluid bolus to all patients, which leads to lower fluid overload balance, predominantly receiving 0.05 unit/kg/hour insulin infusion, which leads to smooth fall in BG and resolution in the particularly high prevalence of malnutrition.

There are limitations in our study. This a retrospective study. We calculated baseline creatinine using eGFR of 120 mL/min/1.73 m^2 because most patients' baseline creatinine was unavailable. This remains the case for the current study and all studies that have used this conservative method to calculate baseline creatinine. Future studies are needed to evaluate the accuracy and validation of this eGFR. We have also not studied the kidney biomarkers and the follow-up of those with AKI for chronic DKD. The long-term follow-up study on AKI in pediatric DKA (CTRI/2018/01/011242) results are awaited. Both p-RIFLE and KDIGO showed good agreement and can be used for diagnosing and staging AKI in pediatric DKA. As suggested, KDIGO criteria can be considered for diagnosing and staging AKI in pediatric DKA for uniform reporting. Future studies on kidney biomarkers and long-term follow-up are required.

p-RIFLE and KDIGO criteria have shown good agreement in diagnosing and staging AKI in pediatric DKA. A younger age of 5 years is a predictor of AKI at discharge using KDIGO criteria. Future studies are needed to validate results to create a clinical risk score for AKI in pediatric DKA.

Acknowledgments: We acknowledge the contribution of Mrs. S. Raja Deepa B. Com, MCA (Puducherry, India) for reviewing and editing the manuscript, and Dr. Thenmozhi M (M.Sc, Ph.D. Post Doctoral Fellow, McMaster University, Canada) for helping with the statistical analysis.

Conflicts of interest: There are no conflicts of interest.

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