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ORIGINAL ARTICLE

Hyponatremia and Severe Diabetic Ketoacidosis in Children with Type 1 Diabetes at an Indonesian Referral Hospital: A Cross-Sectional Study

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is the leading acute cause of death in children with type 1 diabetes. Indonesian data on its severity and biochemical profile are scarce.

Objective: To examine whether admission sodium, potassium and urine ketone status are associated with severe DKA.

Methods: This retrospective cross-sectional study included children aged 1–18 years admitted in DKA (International Society for Pediatric and Adolescent Diabetes 2022 criteria) to a tertiary hospital in Bali in 2022–2024. Hyponatremia (<135 mmol/L), hypokalemia (<3.5 mmol/L) and urine ketone 3+ were compared between severe and mild–moderate DKA with exact tests and Firth-penalized logistic regression across all joint tables compatible with the observed pairwise counts.

Results: Of 54 children (mean age 11.22 years; 74.1% girls), 37 (68.5%; 95% confidence interval [CI] 55.3–79.3) had severe DKA. Hyponatremia occurred in 24 of 37 children with severe DKA (64.9%) and 4 of 17 with mild–moderate DKA (23.5%) (odds ratio 6.00, 95% CI 1.62–22.20; Fisher p = 0.008; Holm-adjusted p = 0.023). In Model 1, the adjusted odds ratio for hyponatremia ranged from 4.83 to 4.90 and was significant in every admissible joint table. Hypokalemia (53.7%; odds ratio 1.05, p = 1.000) and urine ketone 3+ (57.4%; odds ratio 1.85, p = 0.379) were not associated with severity.

Conclusion: Two-thirds of children admitted in DKA to this Indonesian referral hospital had severe acidosis. Measured hyponatremia at admission was associated with severe DKA. It should prompt calculation of the glucose-corrected sodium. Potassium and dipstick ketone grade were not associated with severity.

1. Introduction

Diabetic ketoacidosis (DKA) is the most frequent life-threatening acute complication of type 1 diabetes in children and the main cause of diabetes-related death in this age group.[1] It has become more common at diagnosis over two decades. Across 13 national registries, DKA at diagnosis rose by 1.6% per year between 2006 and 2019 and reached 39.4% in 2020.[2] By 2020 the proportion stood at 44.1% to 52.9% in the United States and England,[3] and a 2026 meta-analysis pooled a prevalence of 41.9%, with country estimates running from 15.6% in Sweden to 78.5% in Thailand.[4] Severity is climbing as well. In a complete Polish regional cohort, the severe share of DKA went from 15.5% in 2006–2014 to 27.7% in 2015–2023.[5] Where resources are limited, the consequences are gravest. In-hospital mortality reached 13.3% among Ethiopian children with DKA,[6] and mortality in referral hospitals of the Amhara region was 10.6 per 1,000 person-days,[7] while national Thai data show mortality falling from 2.2% to 0.6% as pediatric care improved.[8] Almost half of pediatric DKA episodes are complicated by acute kidney injury, with a pooled incidence of 47%.[9]

Southeast Asian centers carry some of the highest burdens. At a Malaysian tertiary center, 73.2% of newly diagnosed children presented in DKA and 54.9% of these episodes were severe;[10] 38.7% of Malaysian children had been misdiagnosed before diabetes was recognized,[11] and the share with severe DKA reached 46.8% during the COVID-19 pandemic.[12] In Thailand, national data show DKA admissions rising from 4.8 to 7.3 per 100,000 child-years. Recurrent episodes made up 52% of admissions, and girls were admitted more often than boys (7.6 vs 4.3 per 100,000 child-years).[13] Thai girls also had a higher cumulative incidence of DKA and of referral.[14] In Vietnam, 57.8% of newly diagnosed children presented in DKA,[15] and a nationwide Chinese registry recorded 52.7%.[16] Indonesian evidence is thinner. Recent indexed studies describe what families of children with type 1 diabetes must bear—97.6% paid for travel to care and 31.7% paid out of pocket for insulin[17]—and suboptimal self-monitoring, with fewer than half of children reaching four glucose checks a day.[18] Two older single-center series describe DKA in Surabaya (58 children, 2002–2013; 37.9% severe)[19] and in Jakarta (37 children, 2006–2011; ketone monitoring during treatment).[20] No recent Indonesian cohort has described the severity and biochemical profile of children admitted in DKA.

Serum sodium is measured routinely at admission, but reading it in DKA is not simple. Hyperglycemia pulls water from the intracellular to the extracellular compartment and so lowers the measured sodium concentration. Glycosuria drives osmotic loss of sodium and water, and hypovolemia stimulates antidiuretic hormone, which promotes free-water retention.[1] The measured value thus reflects the depth of hyperglycemia, natriuresis and water handling together. In 1,681 episodes from the Pediatric Emergency Care Applied Research Network (PECARN) FLUID trial, presenting glucose correlated with blood urea nitrogen (r = 0.44), creatinine (r = 0.42) and glucose-corrected sodium (r = 0.32),[21] and falls in corrected sodium during treatment were associated with presenting sodium and chloride concentrations and with

hypotonic fluids.[22,23] Sodium also has prognostic value. A higher initial sodium distinguished children who died or needed a prolonged intensive-care stay,[24] hypernatremia was more frequent in severe pediatric DKA in Saudi Arabia,[25] and children with acute kidney injury had higher corrected sodium.[26] In Ethiopia, both hyponatremia (adjusted odds ratio [aOR] 4) and hypernatremia (aOR 7.4) were associated with death.[6] Few investigators have asked whether a low measured sodium at admission marks more severe acidosis.

Potassium behaves differently. Insulin deficiency and acidosis push potassium out of cells, so serum potassium at presentation is usually normal or high even though total-body stores are depleted; insulin and fluids then drive it back into cells.[1] In a multicenter Chinese cohort of adults, 16.6% were hypokalemic on admission, yet 67.9% became so during treatment, and the figure rose to 73.6% in severe DKA.[27] A Japanese national database linked lower potassium concentrations in initial fluids to higher 28-day mortality (odds ratio [OR] 1.69).[28] Pediatric series report hypokalemia in 24.4% to 50.9% of children, depending on when it was counted.[29–31] A 2026 meta-analysis found that balanced crystalloids reduced hypokalemia compared with 0.9% saline (risk ratio 0.66).[32] The measured value depends so heavily on timing and treatment that potassium may be a poor marker of how severe the underlying episode is.

Ketone testing raises a third problem. Urine dipsticks detect acetoacetate through the nitroprusside reaction but cannot detect beta-hydroxybutyrate (BOHB), the predominant ketone body in acidotic patients.[33] Among Pakistani children, finger-stick BOHB outperformed the urine dipstick in sensitivity (90.4% vs 84.9%) and accuracy (92.7% vs 86.5%).[34] Even blood BOHB tracked pH only moderately ($r = -0.44$),[35] admission BOHB was unrelated to pH in Japanese children,[36] and a plasma BOHB below 1.5 mmol/L suits the definition of resolution better than the grading of severity.[37] In Zambia, ketonuria lost its association with length of stay once DKA severity was taken into account (hazard ratio 0.90).[38] In many Indonesian hospitals, however, the urine dipstick is still the only ketone test routinely available.

Whether these three routine measurements separate severe from milder DKA remains unsettled. One comparative series found no difference in electrolyte profiles between mild-to-moderate and severe DKA,[39] while others tie sodium disturbances to severe disease and adverse outcomes.[6,24,25] To our knowledge, no study has examined these relationships in Indonesian children, whose biochemical picture at a tertiary hospital may be shaped by delayed referral from district facilities, treatment before transfer and undernutrition. The novelty of this study lies in three features. It relates three routine admission measurements, not clinical features alone, to the ISPAD severity grade in a recent consecutive cohort from a provincial referral hospital. It uses exact methods suited to 54 children. It also quantifies how far unrecorded joint distributions, sex and referral status, and the absence of glucose correction could change the sodium finding.

This study therefore had three aims: (1) to describe the demographic, nutritional and biochemical profile of children with type 1 diabetes admitted in DKA to the main tertiary referral hospital of Bali, Indonesia, and to compare it with published cohorts; (2) to estimate, with exact methods suited to a small sample, the association of admission hyponatremia, hypokalemia and urine ketone 3+ with severe DKA; and (3) to determine whether any association persisted after mutual adjustment and under sensitivity analyses for covariates whose joint distribution was not recorded.

2. Methods

2.1. Study Design and Setting

This was a retrospective, single-center, analytical cross-sectional study of routinely collected electronic medical records. It is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies.[40]

The study was conducted at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia, the teaching hospital of the Faculty of Medicine, Universitas Udayana, and the main pediatric referral center for the province. Children with DKA reach the hospital either directly through its emergency department or after transfer from district hospitals and primary-care facilities.

2.2. Participants and Eligibility

The electronic medical records of all children admitted with type 1 diabetes and DKA between 1 January 2022 and 31 December 2024 were reviewed consecutively. Inclusion criteria were age 1–18 years at admission, a diagnosis of type 1 diabetes, DKA fulfilling the International Society for Pediatric and Adolescent Diabetes (ISPAD) 2022 criteria as documented by the attending pediatrician, and complete admission records for serum sodium, serum potassium, urine ketone, venous pH and bicarbonate. Admission glucose was used to confirm the diagnosis of DKA and was not analyzed as an exposure (see Limitations). Whether an admission occurred at diagnosis or in established diabetes was not recorded. Children with incomplete records or with comorbidities that affect electrolyte or acid–base balance, such as chronic kidney disease, were excluded. The unit of analysis was the child, and the selection of participants is shown in Figure 1.

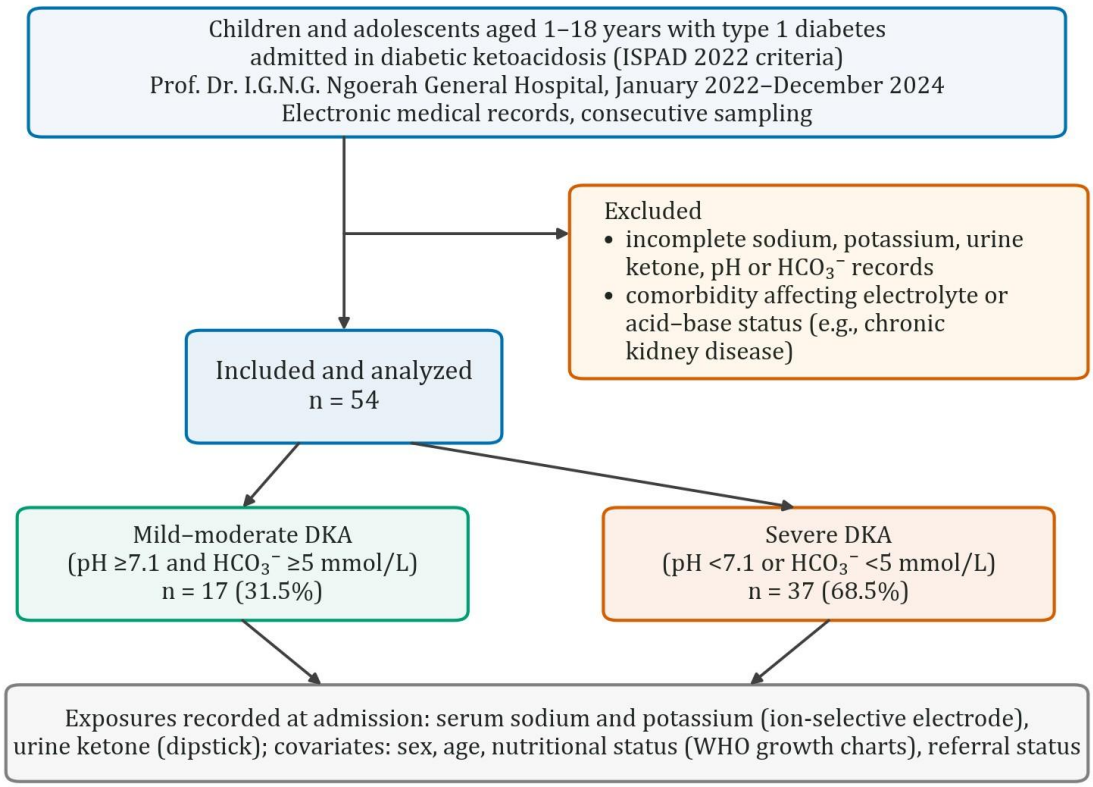


Figure 1. Study flow (STROBE). Children aged 1–18 years with type 1 diabetes admitted in diabetic ketoacidosis to Prof. Dr. I.G.N.G. Ngoerah General Hospital between January 2022 and December 2024 were identified from electronic medical records; 54 met the eligibility criteria and were analyzed, 17 with mild–moderate and 37 with severe DKA (ISPAD 2022). [Author query: numbers of children screened and excluded for each criterion are not reported; please add them to this figure.]

2.3. Variables and Data Collection

The outcome was DKA severity at admission, classified according to ISPAD 2022.[1] DKA was defined by blood glucose >11 mmol/L (>200 mg/dL), venous pH <7.3 or serum bicarbonate <18 mmol/L, and ketonemia (BOHB ≥3 mmol/L) or moderate-to-large ketonuria. Severity was graded as mild (pH <7.3 or bicarbonate <18 mmol/L), moderate (pH <7.2 or bicarbonate <10 mmol/L) or severe (pH <7.1 or bicarbonate <5 mmol/L). A child was classified as severe when either criterion was met (Figure 1). Mild and moderate episodes were combined into one mild–moderate category and compared with severe DKA.

The three pre-specified exposures were measured on the admission blood and urine samples. Hyponatremia was defined as a measured serum sodium concentration <135 mmol/L, without correction for glucose, and hypokalemia as a serum potassium concentration <3.5 mmol/L; both were measured by ion-selective electrode in the hospital's central laboratory. Laboratory values were those of the first sample obtained at this hospital; for referred children, this sample may have been drawn after treatment had begun at the referring facility. Urine ketone was measured by semi-quantitative urine dipstick and dichotomized as 3+ versus <3+. Covariates were sex, age in completed years at admission, nutritional status and referral status. Nutritional status was classified from weight and height on the World Health Organization growth charts (2006 standards for children younger than 5 years;[41] 2007 reference for ages 5–19 years[42]) as undernutrition (mild-to-moderate protein–energy malnutrition), normal, or overweight/obesity. Referral status distinguished children transferred from another health facility from those who presented directly.

Data sources and measurement. Data were abstracted by the first author onto a standard form. DKA severity, sodium, potassium, urine ketone and nutritional status were cross-classified with one another. Sex, age and referral status were recorded as summary descriptors without linkage to severity or laboratory findings, so their potential confounding was examined by sensitivity analysis rather than by direct adjustment.

Bias. Consecutive inclusion of all eligible admissions over three years limited selection bias within the hospital, although excluding children with incomplete records may itself introduce selection bias. Severity and laboratory variables were defined by fixed numeric thresholds from a single central laboratory, which limited measurement bias. Records with missing exposure or outcome data were excluded, so the analysis was complete-case by design.

2.4. Statistical Analysis

Study size. All eligible admissions in the three-year window were included, so the study size was fixed by the number of eligible children. With two-sided α = 0.05, 54 children provided 80% power to detect a correlation of |r| ≥ 0.37, or an odds ratio of 5.51 to 6.25 for an exposure present in 25% to 50% of children with mild–moderate DKA. The minimum sample size estimated before data collection assumed r = 0.40, one-sided α = 0.05 ($z\alpha$ = 1.64) and power 0.90 ($z\beta$ = 1.28), using Fisher's z transformation:

$$n = \left[\frac{z_\alpha + z_\beta}{0.5\ \ln\left(\frac{1+r}{1-r}\right)}\right]^2 + 3$$

$$= \left[\frac{1.64 + 1.28}{0.5 \ln\left(\frac{1.40}{0.60}\right)}\right]^2 + 3 = 50.5 \approx 51$$

With a two-sided α, the same assumptions would require 62 children.

Analyses were performed in Python 3.14 with SciPy 1.18, NumPy 2.4 and statsmodels 0.15, and figures were drawn with matplotlib 3.10. All tests were two-sided with α = 0.05, and p values are reported to three decimal places.

Univariate analysis. Categorical variables were summarized as counts and percentages with Wilson score 95% confidence intervals (CI), which retain nominal coverage at small n:

$$\text{CI} = \frac{x + \frac{z^2}{2} \pm z\sqrt{\frac{x(n - x)}{n} + \frac{z^2}{4}}}{n + z^2}$$

where x is the count, n the sample size and z = 1.96. Age was summarized as mean ± standard deviation with a t-based 95% CI of the mean. Proportions were tested against equal shares with exact binomial tests. To place the cohort in context, each proportion was compared with the corresponding proportion reported in recent cohorts (pediatric, and adult for hypokalemia) identified through PubMed (2021–2026), using exact one-sample binomial tests with Holm adjustment across all comparisons. The magnitude of each difference was expressed as Cohen's h:

$$h = 2 \arcsin\sqrt{p_1} - 2 \arcsin\sqrt{p_2}$$

Bivariate analysis. The association of each exposure with severe DKA was assessed with Fisher's exact test, with the mid-p and Boschloo's unconditional test as sensitivity analyses. Effect sizes were the odds ratio (OR) with Woolf 95% CI, the conditional maximum-likelihood OR with exact 95% CI, the risk difference with Newcombe hybrid-score 95% CI, the risk ratio (RR), and the φ coefficient. The three laboratory exposures formed the primary family, and their p values were Holm-adjusted. Nutritional status was analyzed with the Fisher–Freeman–Halton exact test and Cramér's V, and undernutrition was also compared with all other categories. For each exposure considered as a marker of severe DKA, sensitivity, specificity and predictive values were reported with Wilson CIs, likelihood ratios with log-method CIs, the area under the curve of a binary marker (equal to [sensitivity + specificity]/2) with Hanley–McNeil CI, and Youden's index J = sensitivity + specificity − 1. Robustness to unmeasured confounding was summarized with the E-value on the risk-ratio scale:

$$E = \text{RR} + \sqrt{\text{RR} \times (\text{RR} - 1)}$$

Multivariable analysis. Severe DKA was modelled with Firth-penalized logistic regression, which removes the small-sample bias of maximum likelihood and remains finite under separation, by maximizing the penalized log-likelihood

$$\ell^*(\beta) = \ell(\beta) + \frac{1}{2} \log|I(\beta)|$$

where I(β) is the Fisher information matrix. Coefficients were tested with penalized likelihood-ratio tests, and CIs were obtained by profile penalized likelihood. Model 1 contained hyponatremia, hypokalemia and urine ketone 3+; Model 2 added undernutrition. The two-way cross-classifications of every pair of these variables were available, but their three- and four-way joint cells were not. For a main-effects logistic model, the likelihood depends only on the outcome-by-predictor counts and on the joint distribution of the predictors. Every integer joint table consistent with all observed one- and two-way counts was therefore enumerated exhaustively, and the model was fitted in each. Given these counts, a four-variable binary table has five free cells, one for each three-way combination and one four-way cell, and the enumeration covered every integer value of these cells that kept all 16 cells non-negative. For Model 2, the enumeration covered the joint table of the four predictors, and integer programming confirmed that each candidate admitted an allocation of severe and mild–moderate cases consistent with the observed severity-by-predictor counts; because the fit does not depend on how outcomes are distributed within a predictor table, one feasible allocation per table suffices. Newton–Raphson fitting with a quasi-Newton fallback was used, and no fit was discarded. For each predictor we report the attainable range of the adjusted OR (aOR), the aOR and profile 95% CI in the table yielding the median aOR, and the percentage of admissible tables in which $p < 0.05$; the table yielding the median aOR is shown for illustration and is no more probable than any other admissible table. A range lying entirely on one side of 1 was interpreted as a finding that holds for every dataset consistent with the observations; a range spanning 1 was interpreted as an association that the data cannot identify.

Sensitivity analysis for sex and referral status. Because sex and referral status were not cross-classified with other variables, three complementary analyses were performed. First, an exact tipping-point map was computed. For a model containing hyponatremia and one binary covariate C, the Firth fit depends only on the number of children with C among those with severe DKA and the number with C among those with hyponatremia, so every feasible pair of these counts was fitted (168 for sex and 290 for referral status). To anchor the maps, we report the share of configurations in which hyponatremia remained significant when the covariate's odds ratios with severity and with hyponatremia both lay between 0.5 and 2, and between one-third and 3; published effects of female sex on DKA are close to 1.1.[43,44] Second, sex and referral labels were randomly assigned to the 54 children, preserving their totals, and the full model (Model 2 plus sex and referral) was fitted in 400 datasets for each of three admissible base tables spanning the range of Model 2. This represents the scenario in which neither covariate is associated with severity or sodium and is not a bound. Third, simulated annealing searched for the most extreme aOR values attainable. For pairs with no cross-classification at all (for example, sex by severity), every 2 × 2 table consistent with the two totals was enumerated and the attainable OR range reported.

Robustness to glucose correction and to outcome changes. Glucose was not analyzed, so the glucose-corrected sodium could not be calculated. Correction can only raise the sodium value and can therefore only move children from hyponatremia to normonatremia. We determined the smallest number of hyponatremic children whose reclassification would remove statistical significance, first assuming that reclassification affected only children with severe DKA, who are expected to have higher glucose, then allowing one or two reclassifications among children with mild–moderate DKA, and finally reclassifying the same proportion (10% to 50%) of hyponatremic children in both groups. The fragility index was defined as the number of outcome changes in one exposure group that raised the two-sided Fisher p to 0.05 or above.

Precision and planning. The sample size required to estimate each proportion within ±10 and ±5 percentage points, and the sample size a future study would need to detect the observed difference in each exposure between severity groups (two-sided α = 0.05, power 0.80, allocation 37:17), were calculated with standard normal-approximation formulas.

2.5. Ethical Approval

The study protocol was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana (approval No. 2405/UN14.2.2.VII.14/LT/2025). Because only anonymized, routinely collected medical records were analyzed, the requirement for individual informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki (2013 revision). Records were abstracted after ethical approval was granted in 2025.

3. Results

3.1. Participants and Characteristics

Fifty-four children with type 1 diabetes admitted in DKA between January 2022 and December 2024 met the eligibility criteria and were analyzed; 17 had mild–moderate and 37 severe DKA, as shown in Figure 1. Their characteristics are detailed in Table 1. Girls predominated: 40 children were female (74.1%; 95% CI 61.1–83.9), a proportion that exceeded an equal sex ratio (exact binomial p = 0.001). The mean age was 11.22 ± 5.18 years (95% CI of the mean 9.81–12.63). Twenty-eight children (51.9%) had been referred from another facility and 26 (48.1%) presented directly (p = 0.892). Nutritional status was normal in 35 children (64.8%), while 14 (25.9%; 95% CI 16.1–38.9) had undernutrition and 5 (9.3%) overweight or obesity.

Table 1. Characteristics of 54 Children with Type 1 Diabetes Admitted in Diabetic Ketoacidosis.

Characteristic	n	%	Wilson 95% CI (%)	CI half-width (pp)	n for ±5 pp
Sex					
Female	40	74.1	61.1–83.9	11.4	296
Male	14	25.9	16.1–38.9	11.4	296
Age, years, mean ± SD (95% CI of mean)	54	11.22 ± 5.18	9.81–12.63		
Referral status					
Referred from another facility	28	51.9	38.9–64.6	12.9	384
Self-presented	26	48.1	35.4–61.1	12.9	384
Nutritional status (WHO)					
Undernutrition (mild-to-moderate PEM)	14	25.9	16.1–38.9	11.4	296
Normal	35	64.8	51.5–76.2	12.3	351
Overweight/obesity	5	9.3	4.0–19.9	7.9	130
DKA severity (ISPAD 2022)					
Mild–moderate	17	31.5	20.7–44.7	12.0	332
Severe	37	68.5	55.3–79.3	12.0	332
Serum sodium					
Hyponatremia (<135 mmol/L)	28	51.9	38.9–64.6	12.9	384
Normal (≥135 mmol/L)	26	48.1	35.4–61.1	12.9	384
Serum potassium					
Hypokalemia (<3.5 mmol/L)	29	53.7	40.6–66.3	12.9	383
Normal (≥3.5 mmol/L)	25	46.3	33.7–59.4	12.9	383
Urine ketone (dipstick)					
3+	31	57.4	44.2–69.7	12.8	376
<3+	23	42.6	30.3–55.8	12.8	376

Note: PEM, protein–energy malnutrition; SD, standard deviation; pp, percentage points. Proportions with Wilson score 95% confidence intervals; age with a t-based 95% CI of the mean. The last column gives the sample size needed to estimate the proportion within ±5 pp. Exact binomial tests against equal proportions: female sex p = 0.001; severe DKA p = 0.009; referral p = 0.892.

Severe DKA was the dominant presentation, affecting 37 children (68.5%; 95% CI 55.3–79.3; p = 0.009 against an equal split). On admission, 28 (51.9%; 95% CI 38.9–64.6) children had hyponatremia, 29 (53.7%; 95% CI 40.6–66.3) hypokalemia and 31 (57.4%; 95% CI 44.2–69.7) a urine ketone result of 3+. As shown in Figure 2, every interval was wide: the half-widths of the 95% CIs ranged from 7.9 to 12.9 percentage points, and estimating these proportions within ±5 percentage points would require 130 to 384 children.

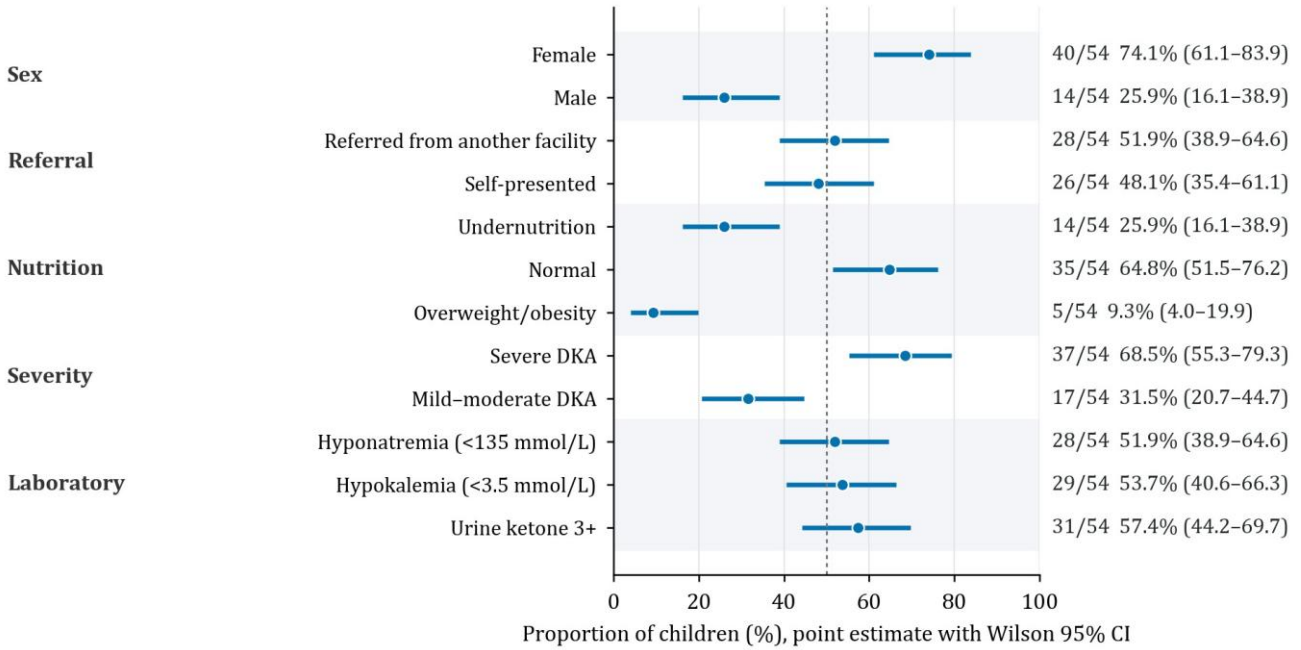


Figure 2. Characteristics of the 54 children. Points show proportions and horizontal bars Wilson 95% confidence intervals; the dashed line marks 50%. Undernutrition denotes mild-to-moderate protein–energy malnutrition on WHO growth charts.

3.2. Comparison with Published Cohorts

The cohort's proportions are compared with 22 published reference proportions in Table 2. The share of severe DKA (68.5%) exceeded that reported in Poland (27.7%; Holm-adjusted p <0.001; h = 0.84), Hangzhou, China (33.9%; p <0.001), Argentina, Chile and Peru (36.4%; p <0.001) and Egypt (43.2%; p = 0.004),[5,45–47] but was compatible with a Malaysian tertiary center (54.9%; p = 0.492) and a Saudi pediatric intensive-care cohort (61.6%; p = 1.000).[10,48] The female share also exceeded those of new-onset cohorts in China (52.4%; p = 0.021) and Malaysia (53.8%; p = 0.033),[11,16] did not differ significantly from Uganda (56.0%; p = 0.104)[49] and was similar to a Pakistani series of children with established diabetes (77.1%; p = 1.000).[50]

Table 2. Comparison of the Cohort's Proportions with Published Pediatric and Adult Cohorts.

Variable (this cohort)	Comparator	Reference proportion (%)	Exact binomial p	Holm-adjusted p	Cohen's h
Severe DKA: 37/54 (68.5%)	Poland, regional DKA cohort (Niechciał 2025)[5]	27.7	<0.001	<0.001	0.84
	Hangzhou, China, new-onset (Peng 2021)[45]	33.9	<0.001	<0.001	0.71
	Argentina/Chile/Peru, new-onset (Hirschler 2024)[46]	36.4	<0.001	<0.001	0.65
	Egypt, emergency department (Abdou 2022)[47]	43.2	<0.001	0.004	0.52
	Malaysia, new-onset, tertiary (Mavinkurve 2024)[10]	54.9	0.055	0.492	0.28
	Saudi Arabia, PICU, new-onset (Albuali 2023)[48]	61.6	0.330	1.000	0.15
Female sex: 40/54 (74.1%)	Equal sex ratio	50.0	0.001	0.008	0.50
	China, new-onset registry (Li 2022)[16]	52.4	0.002	0.021	0.45
	Malaysia, new-onset (Mavinkurve 2021)[11]	53.8	0.003	0.033	0.43
	Uganda, new-onset (Ahabwenki 2026)[49]	56.0	0.009	0.104	0.38
	Pakistan, DKA in established T1D (Rahak 2023)[50]	77.1	0.627	1.000	−0.07
Hyponatremia: 28/54 (51.9%)	Iran, PICU, any time during admission (Sharifzadeh 2026)[31]	46.6	0.496	1.000	0.11
Hypokalemia: 29/54 (53.7%)	China, adults, on admission (Zhang 2025)[27]	16.6	<0.001	<0.001	0.81
	Saudi Arabia, new-onset (Batwa 2022)[29]	24.4	<0.001	<0.001	0.61
	India, during treatment (Likhitha 2024)[30]	36.6	0.011	0.119	0.35
	Iran, PICU, any time during admission (Sharifzadeh 2026)[31]	50.9	0.686	1.000	0.06
	China, adults, during treatment (Zhang 2025)[27]	67.9	0.029	0.289	−0.29
Urine ketone ≥3+: 31/54 (57.4%)	Pakistan, children with DKA (Lohano 2022)[34]	46.9	0.134	0.806	0.21

Variable (this cohort)	Comparator	Reference proportion (%)	Exact binomial p	Holm-adjusted p	Cohen's h
Undernutrition: 14/54 (25.9%)	India, T1D clinics (Khadilkar 2023)[51]	6.4	<0.001	<0.001	0.56
	Egypt, T1D clinic (Sakhr 2024)[52]	16.0	0.061	0.492	0.25
Overweight/obesity: 5/54 (9.3%)	Hungary, T1D onset (Muzslay 2026)[53]	15.9	0.261	1.000	−0.20
	India, T1D clinics (Khadilkar 2023)[51]	17.7	0.111	0.777	−0.25

Note: Exact two-sided binomial test of the observed proportion against each reference proportion; Holm adjustment across all 22 comparisons is descriptive. Comparators are grouped by characteristic and ordered by reference proportion; each label states the population type (new-onset, established diabetes, intensive care, adults, clinic cohorts) and the time of measurement where relevant. PICU, pediatric intensive-care unit; T1D, type 1 diabetes. Cohen's h: 0.2 small, 0.5 medium, 0.8 large; positive values indicate a higher proportion in this cohort. Comparators for severe DKA report the severe share among DKA episodes; hypokalemia comparators differ in measurement time (on admission vs at any time during treatment); nutritional comparators are clinic cohorts with type 1 diabetes rather than DKA cohorts.

Hypokalemia (53.7%) was about three times more frequent than admission hypokalemia in adults (16.6%; p <0.001)[27] and twice as frequent as in a Saudi series of children with new-onset DKA (24.4%; p <0.001),[29] but it was closer to pediatric series that counted hypokalemia at any time during admission or treatment, in an Iranian intensive-care unit (50.9%; p = 1.000) and India (36.6%; p = 0.119),[30,31] and lower than the treatment-phase frequency in adults (67.9%; p = 0.289). Hyponatremia (51.9% vs 46.6% in Iran; p = 1.000) and urine ketone ≥3+ (57.4% vs 46.9% in Pakistan; p = 0.806)[34] were within the published range. Undernutrition was more frequent than in an Indian multicenter clinic cohort (6.4%; p <0.001) but compatible with an Egyptian cohort (16.0%; p = 0.492).[51,52] These comparisons are summarized in Figure 3.

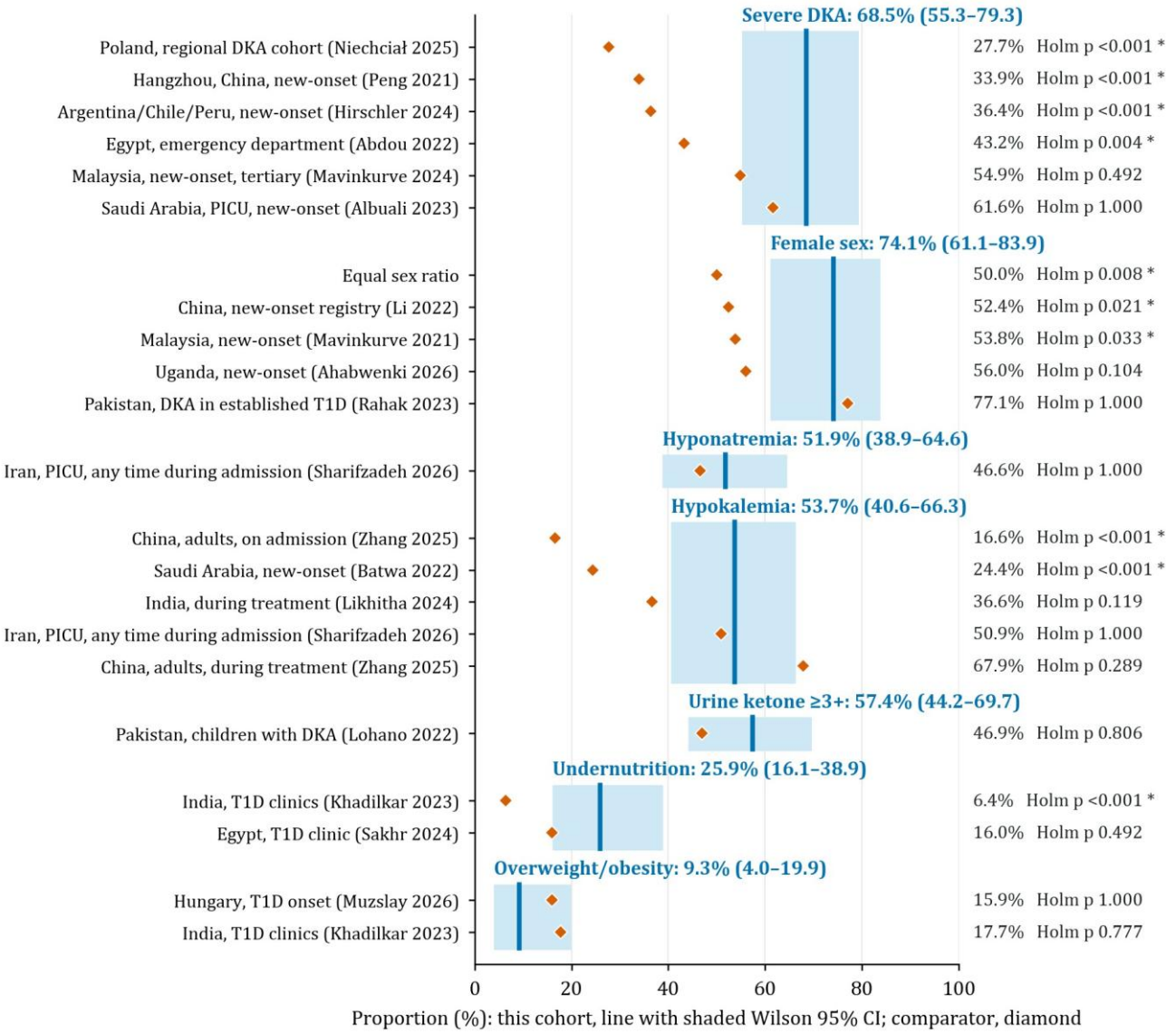


Figure 3. Proportions in this cohort compared with published cohorts. For each characteristic, the vertical line and shaded band give this cohort's proportion and Wilson 95% CI; diamonds give the comparator proportions, ordered within each block by reference proportion and labelled with the comparator population. Holm-adjusted exact binomial p values across all 22 comparisons are shown on the right (p<0.05).*

3.3. Admission Findings by DKA Severity

Hyponatremia was present in 24 of 37 children with severe DKA (64.9%) and in 4 of 17 with mild–moderate DKA (23.5%), as detailed in Table 3. The OR for severe DKA was 6.00 (95% CI 1.62–22.20), and the conditional exact OR was 5.79 (95% CI 1.42–29.54) (Fisher p = 0.008; mid-p = 0.006; Boschloo p = 0.005). The association remained significant after Holm adjustment for the three laboratory exposures (p = 0.023). Severe DKA affected 85.7% of children with hyponatremia and 50.0% of those with normal sodium, a risk difference of 35.7 percentage points (95% CI 10.9 to 55.6; φ = 0.384).

Table 3. Sodium, Potassium, Urine Ketone and Nutritional Status by DKA Severity.

Exposure	Severe DKA, n = 37, n (%)	Mild–moderate DKA, n = 17, n (%)	OR (95% CI)	Conditional exact OR (95% CI)	Fisher exact p	Holm p	Risk difference, pp (95% CI)	φ
Hyponatremia	24 (64.9)	4 (23.5)	6.00 (1.62–22.20)	5.79 (1.42–29.54)	0.008	0.023	35.7 (10.9 to 55.6)	0.384
Hypokalemia	20 (54.1)	9 (52.9)	1.05 (0.33–3.31)	1.04 (0.28–3.84)	1.000	1.000	1.0 (−22.5 to 24.9)	0.010
Urine ketone 3+	23 (62.2)	8 (47.1)	1.85 (0.58–5.90)	1.83 (0.49–6.92)	0.379	0.757	13.3 (−11.0 to 36.8)	0.142
Undernutrition	11 (29.7)	3 (17.6)	1.97 (0.47–8.27)	1.95 (0.42–12.69)	0.507	—	13.6 (−15.6 to 34.4)	0.128
Nutritional status, 3 categories	11 / 22 / 4	3 / 13 / 1	—	—	0.533[a]	—	—	0.166[b]

Note: OR, odds ratio of severe DKA for children with versus without the finding (Woolf 95% CI); conditional exact OR, conditional maximum-likelihood estimate with exact 95% CI; risk difference, difference in the proportion with severe DKA between children with and without the finding (Newcombe hybrid-score 95% CI): hyponatremia 24/28 (85.7%) vs 13/26 (50.0%), hypokalemia 20/29 (69.0%) vs 17/25 (68.0%), urine ketone 3+ 23/31 (74.2%) vs 14/23 (60.9%), undernutrition 11/14 (78.6%) vs 26/40 (65.0%). Holm adjustment across the three pre-specified laboratory exposures. Mid-p and Boschloo p values: hyponatremia 0.006 and 0.005; hypokalemia 0.940 and 0.976; urine ketone 3+ 0.318 and 0.326. Nutritional categories are undernutrition / normal / overweight-obesity. Sample size needed to detect the observed difference in each exposure between severity groups (two-sided α = 0.05, power 0.80, allocation 37:17): hyponatremia 50 (34 severe, 16 mild–moderate); urine ketone 3+ 391; hypokalemia 73,071. [a] Fisher–Freeman–Halton exact test. [b] Cramér's V.

Hypokalemia was almost equally frequent in severe (54.1%) and mild–moderate DKA (52.9%; OR 1.05, 95% CI 0.33–3.31; p = 1.000; risk difference 1.0 percentage point, 95% CI −22.5 to 24.9). Urine ketone 3+ was more frequent in severe DKA (62.2% vs 47.1%), but the difference was compatible with chance (OR 1.85, 95% CI 0.58–5.90; p = 0.379; Holm-adjusted p = 0.757). Undernutrition was present in 29.7% of children with severe and 17.6% of those with mild–moderate DKA (OR 1.97, 95% CI 0.47–8.27; p = 0.507), and the three nutritional categories did not differ in severity (Fisher–Freeman–Halton p = 0.533; Cramér's V = 0.166). Figure 4 shows these proportions with their 95% CIs. The exposures were essentially unrelated to one another (φ = −0.003 for sodium and potassium, 0.144 for sodium and ketone, and 0.026 for potassium and ketone).

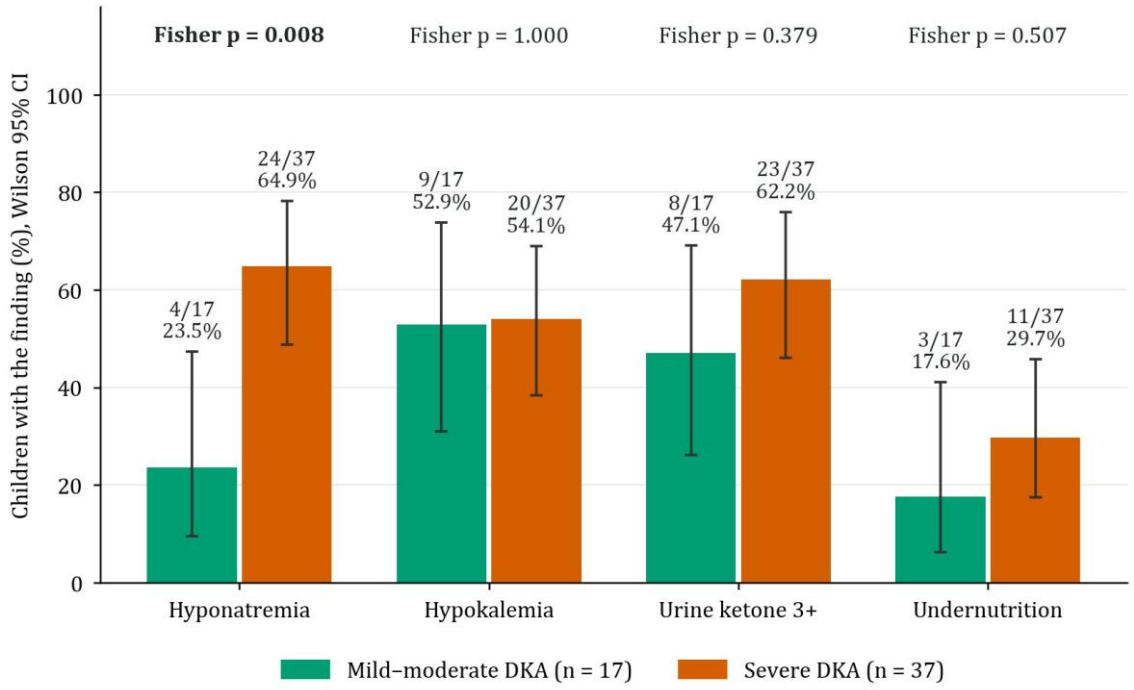


Figure 4. Frequency of hyponatremia, hypokalemia, urine ketone 3+ and undernutrition in children with mild–moderate (n = 17) and severe (n = 37) DKA. Bars show proportions with Wilson 95% CIs; labels give counts and percentages; Fisher exact p values compare the two severity groups.

3.4. Discriminative Performance

As a marker of severe DKA, hyponatremia had a sensitivity of 64.9% (95% CI 48.8–78.2), a specificity of 76.5% (52.7–90.4) and a positive likelihood ratio of 2.76 (1.13–6.71), as detailed in Table 4. Its positive predictive value was 85.7% and its negative predictive value 50.0% at the observed severe-DKA prevalence of 68.5%, and its balanced accuracy—the single point that one cut-off contributes to a receiver-operating characteristic curve—was 0.707 (95% CI 0.565–

0.848). Hypokalemia (balanced accuracy 0.506) and urine ketone 3+ (0.576) did not discriminate better than chance. The risk ratio of severe DKA with hyponatremia was 1.71 (95% CI 1.13–2.59), with an E-value of 2.82 for the point estimate and 1.52 for the lower confidence limit.

Table 4. Discriminative Indices of Each Admission Finding for Severe DKA.

Index (95% CI)	Hyponatremia	Hypokalemia	Urine ketone 3+
Sensitivity for severe DKA, %	64.9 (48.8–78.2)	54.1 (38.4–69.0)	62.2 (46.1–75.9)
Specificity, %	76.5 (52.7–90.4)	47.1 (26.2–69.0)	52.9 (31.0–73.8)
Positive predictive value, %	85.7 (68.5–94.3)	69.0 (50.8–82.7)	74.2 (56.8–86.3)
Negative predictive value, %	50.0 (32.1–67.9)	32.0 (17.2–51.6)	39.1 (22.2–59.2)
Positive likelihood ratio	2.76 (1.13–6.71)	1.02 (0.60–1.75)	1.32 (0.75–2.32)
Negative likelihood ratio	0.46 (0.28–0.77)	0.98 (0.53–1.80)	0.71 (0.39–1.31)
Balanced accuracy (AUC of a binary marker)	0.707 (0.565–0.848)	0.506 (0.338–0.673)	0.576 (0.414–0.737)
Youden index J	0.413	0.011	0.151
Risk ratio for severe DKA	1.71 (1.13–2.59)	1.01 (0.71–1.46)	1.22 (0.83–1.80)
E-value: point estimate / confidence limit	2.82 / 1.52	1.13 / 1.00	1.74 / 1.00

Note: Prevalence of severe DKA 68.5% (37/54); predictive values apply to this prevalence only. Proportions with Wilson score CIs; likelihood ratios with log-method CIs; AUC of a binary marker equals (sensitivity + specificity)/2, Hanley–McNeil CI. The E-value is the minimum strength of association, on the risk-ratio scale, that an unmeasured confounder would need with both the finding and severe DKA to explain away the observed risk ratio (or its confidence limit closest to 1).

3.5. Multivariable Analysis

The Firth-penalized models are summarized in Table 5. In Model 1, 1,096 joint tables were consistent with every observed one- and two-way count. The aOR for hyponatremia ranged only from 4.83 to 4.90 across these tables (in the median table, 4.89; 95% CI 1.50–18.53), and the association was significant in all of them (p = 0.008 in each). The aOR for hypokalemia ranged from 0.95 to 1.17 and that for urine ketone 3+ from 1.51 to 1.56, and neither was significant in any table. Adding undernutrition (Model 2; 1,581 admissible tables) left the hyponatremia estimate essentially unchanged (aOR 4.78–5.23; p = 0.006 to 0.009; significant in 100% of tables), while undernutrition itself (aOR 1.79–2.39) was not significant in any table. The median Model 2 aORs were 4.98 for hyponatremia, 1.02 for hypokalemia, 1.50 for urine ketone 3+ and 2.01 for undernutrition (Figure 5). The unadjusted and adjusted estimates are compared in Figure 5, and the full distribution of adjusted estimates across admissible tables is shown in Figure 6.

Table 5. Firth-Penalized Logistic Regression for Severe DKA Across Every Joint Table Consistent with the Observed Cross-Classifications.

Predictor	Unadjusted Firth OR (95% CI)	Model 1 aOR (95% CI)[a]	Model 1 attainable aOR range	Model 1 datasets with p<0.05 (%)	Model 2 attainable aOR range	Model 2 datasets with p<0.05 (%)
Hyponatremia	5.44 (1.64–21.08)	4.89 (1.50–18.53)	4.83–4.90	100.0	4.78–5.23	100.0
Hypokalemia	1.05 (0.34–3.25)	1.05 (0.31–3.51)	0.95–1.17	0.0	0.85–1.21	0.0
Urine ketone 3+	1.81 (0.58–5.75)	1.51 (0.45–5.07)	1.51–1.56	0.0	1.38–1.70	0.0
Undernutrition	—	—	—	—	1.79–2.39	0.0
Admissible joint tables (n)	—	—	1,096	—	1,581	—

Note: Model 1: hyponatremia, hypokalemia and urine ketone 3+. Model 2: Model 1 plus undernutrition. The observed two-way cross-classifications of every pair of variables fix the outcome-by-predictor counts and the pairwise predictor associations; the higher-order joint cells are unknown, so every integer joint table consistent with all observed one- and two-way counts was enumerated and fitted. [a] Profile penalized-likelihood 95% CI in the table yielding the median aOR. p values from penalized likelihood-ratio tests; for hyponatremia, p = 0.005 unadjusted, 0.008 across all Model 1 tables and 0.006–0.009 across Model 2 tables. The table yielding the median aOR is shown for illustration and is no more probable than any other admissible table. Pairwise associations among the predictors were weak (φ: sodium–potassium −0.003, sodium–ketone 0.144, potassium–ketone 0.026; Cramér's V for nutritional status 0.148–0.184).

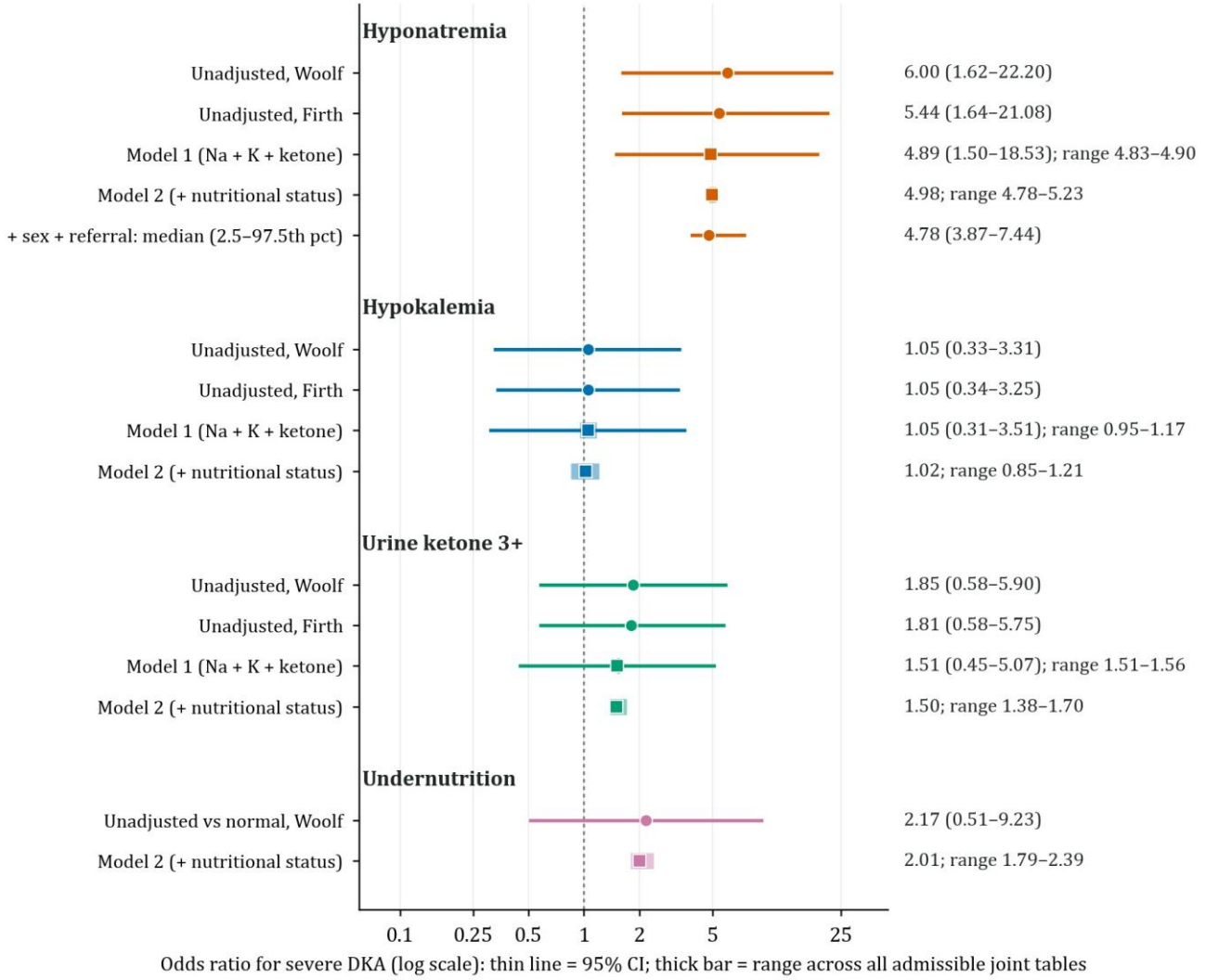


Figure 5. Odds ratios for severe DKA. Thin lines show 95% CIs (Woolf for unadjusted estimates; profile penalized likelihood for Firth models). Thick bars show the range of adjusted odds ratios across every joint table consistent with the observed cross-classifications (1,096 tables in Model 1; 1,581 in Model 2). For hyponatremia, the last row gives the median and 2.5th–97.5th percentiles when sex and referral status were added with randomly assigned labels. Log scale; dashed line, OR = 1. Undernutrition is compared with normal weight only in this figure (OR 2.17, 95% CI 0.51–9.23), whereas Table 3 compares it with all other categories (OR 1.97, 95% CI 0.47–8.27).

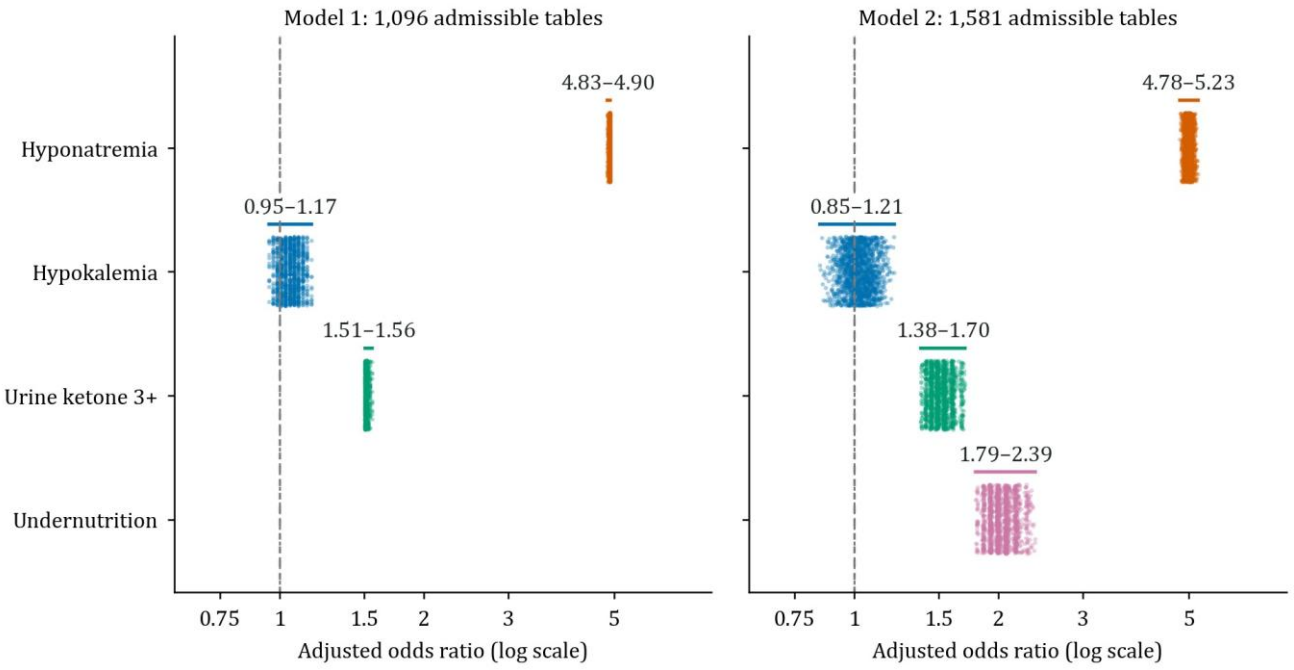


Figure 6. Distribution of adjusted odds ratios across all admissible joint tables. Each point is one table consistent with every observed one- and two-way count (vertical jitter only separates overlapping points and carries no information); the bar and label above each cloud give the attainable minimum and maximum. Model 1 includes hyponatremia, hypokalemia and urine ketone 3+; Model 2 adds undernutrition.

3.6. Sensitivity to Sex and Referral Status

The sensitivity analyses for sex and referral status are presented in Table 6 and Figure 7. If sex were unrelated to both severity and sodium, the aOR for hyponatremia would be 5.33 (p = 0.005). Across all 168 feasible configurations of sex, hyponatremia remained significant in 81.5%. The least extreme configuration that removed significance required 86.5% of children with severe DKA but only 47.1% of those with mild–moderate DKA to be girls (Firth-penalized OR 6.6), together with 92.9% versus 53.8% girls among hyponatremic and normonatremic children (Firth-penalized OR 9.1). For referral status, hyponatremia remained significant in 71.4% of 290 configurations (aOR 5.30 under independence). Significance was lost only if referral were concentrated in severe DKA (64.9% vs 23.5%; Firth-penalized OR 5.4) and in hyponatremia (71.4% vs 30.8%; Firth-penalized OR 5.2). When the covariate's odds ratios with severity and with hyponatremia both lay between 0.5 and 2, hyponatremia remained significant in 100.0% of 16 configurations for sex (aOR 5.06–6.76) and in 100.0% of 16 configurations for referral status (aOR 5.11–6.31); with both odds ratios between one-third and 3, it remained significant in 100.0% of 30 and 100.0% of 56 configurations, respectively.

Table 6. Sensitivity of the Hyponatremia–Severity Association to Sex and Referral Status, Whose Cross-Classification with Other Variables Was Not Recorded.

Analysis	Sex (40 girls)	Referral (28 referred)
A. Exact tipping-point map (severe DKA ~ hyponatremia + covariate)		
Feasible covariate configurations, n	168	290
Configurations with hyponatremia p<0.05, %	81.5	71.4
aOR of hyponatremia if the covariate is unrelated to severity and sodium (p)	5.33 (0.005)	5.30 (0.005)
Configurations with both covariate ORs between 0.5 and 2: n; % with p<0.05 (aOR range)	16; 100.0 (5.06–6.76)	16; 100.0 (5.11–6.31)
Configurations with both covariate ORs between one-third and 3: n; % with p<0.05 (aOR range)	30; 100.0 (4.79–12.98)	56; 100.0 (4.54–13.29)
Weakest configuration with p≥0.05: covariate share in severe vs mild–moderate DKA, %	86.5 vs 47.1	64.9 vs 23.5
… and in hyponatremia vs normonatremia, %	92.9 vs 53.8	71.4 vs 30.8
… implied Firth-penalized OR of the covariate with severe DKA / with hyponatremia	6.6 / 9.1	5.4 / 5.2
… aOR of hyponatremia (p)	3.33 (0.078)	3.55 (0.055)
B. Full model (Model 2 + sex + referral), randomly assigned covariate labels		
Median aOR of hyponatremia (2.5th–97.5th percentile)	4.78 (3.87–7.44)	both covariates in the same model
Datasets with hyponatremia p<0.05, %	99.0–99.8	both covariates in the same model
C. Pairs with no cross-classification: attainable range over all consistent 2 × 2 tables		

Analysis	Sex (40 girls)	Referral (28 referred)
Female sex × severe DKA: OR range; tables with p<0.05, %	0.046–310.7; 60.0	
Referral × severe DKA: OR range; tables with p<0.05, %	0.012–105.0; 61.1	
Referral × hyponatremia: OR range; tables with p<0.05, %	0.002–3021.0; 70.4	
Referral × hypokalemia: OR range; tables with p<0.05, %	0.003–969.0; 69.2	
Female sex × hyponatremia: OR range; tables with p<0.05, %	0.019–66.1; 53.3	

Note: Panel A: for a model with hyponatremia and one binary covariate, the Firth fit depends only on the number of children with the covariate among those with severe DKA and among those with hyponatremia; every feasible pair was fitted. Panel B: covariate labels randomly permuted over the 54 children (400 datasets for each of three admissible base tables spanning the Model 2 range); the most extreme values found by simulated annealing spanned the null and required, for example, all 37 children with severe DKA to be girls. Panel B represents the scenario in which neither covariate is associated with severity or sodium; it is not a bound. Panel C: every 2 × 2 table consistent with the two marginal totals; every range spans 1, so these associations are not identifiable from the recorded data and would require patient-level cross-classification.

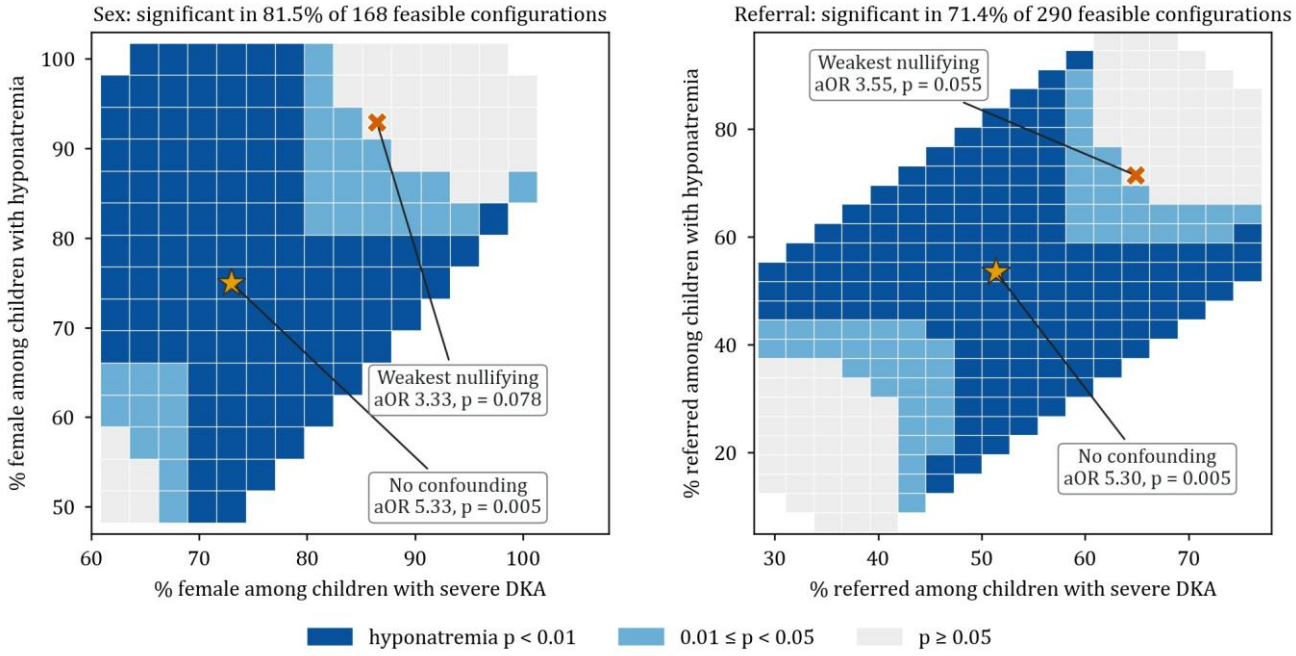


Figure 7. Exact tipping-point maps for confounding by sex (left) and referral status (right). Each cell is one feasible configuration of the covariate among children with severe DKA (x-axis) and among children with hyponatremia (y-axis); color gives the penalized likelihood-ratio p value of hyponatremia after adjustment. The star marks the configuration in which the covariate is unrelated to both; the cross marks the least extreme configuration under which the association loses significance.

When sex and referral labels were assigned at random within the full model—the scenario in which neither is related to severity or sodium—the median aOR for hyponatremia was 4.78 (2.5th–97.5th percentile 3.87–7.44), and the association was significant in 99.0% to 99.8% of datasets. The most extreme values found by simulated annealing spanned the null, but only under alignments such as all 37 children with severe DKA being girls. The associations of sex and referral status with severity, and of referral status with sodium or potassium, could not be identified from the recorded data: every attainable OR range spanned 1, as shown in panel C of Table 6.

3.7. Robustness to Glucose Correction and Outcome Changes

The robustness analyses are detailed in Table 7. If glucose correction reclassified only children with severe DKA, 5 of the 24 hyponatremic children with severe DKA would have to become normonatremic for the association to lose significance (OR 3.43; p = 0.077); with one or two children with mild–moderate DKA also reclassified, 7 or 9 would be required. If the same proportion of hyponatremic children were reclassified in both groups, the association remained significant up to 25% (OR 4.42; p = 0.038) and lost significance at 30% (OR 3.97; p = 0.069), although the OR stayed between 3.43 and 5.11 in every reclassification scenario. The fragility index was 3: changing the outcome of three hyponatremic children from severe to mild–moderate DKA raised the Fisher p = 0.090, and changing three normonatremic children from mild–moderate to severe DKA raised it to 0.063.

Table 7. Robustness of the Hyponatremia–Severity Association to Reclassification of Sodium Status After Glucose Correction and to Changes in Outcome Status.

Scenario	Children changed (severe / mild–moderate)	Hyponatremia in severe vs mild–moderate DKA	OR	Fisher p
Observed	0 / 0	24/37 vs 4/17	6.00	0.008

Scenario	Children changed (severe / mild–moderate)	Hyponatremia in severe vs mild–moderate DKA	OR	Fisher p
A. Differential reclassification (smallest number that removes significance)				
Severe group only	5 / 0	19/37 vs 4/17	3.43	0.077
1 mild–moderate child also reclassified	7 / 1	17/37 vs 3/17	3.97	0.069
2 mild–moderate children also reclassified	9 / 2	15/37 vs 2/17	5.11	0.057
B. Proportional reclassification (same share of hyponatremic children in both groups)				
10% reclassified	2 / 0	22/37 vs 4/17	4.77	0.020
20% reclassified	5 / 1	19/37 vs 3/17	4.93	0.035
25% reclassified	6 / 1	18/37 vs 3/17	4.42	0.038
30% reclassified	7 / 1	17/37 vs 3/17	3.97	0.069
40% reclassified	10 / 2	14/37 vs 2/17	4.57	0.062
50% reclassified	12 / 2	12/37 vs 2/17	3.60	0.181
C. Fragility index (outcome changes until Fisher p ≥ 0.05)				
Hyponatremic children changed from severe to mild–moderate	3	21/34 vs 7/20	3.00	0.090
Normonatremic children changed from mild–moderate to severe	3	24/40 vs 4/14	3.75	0.063

Note: Glucose was not analyzed, so the glucose-corrected sodium could not be computed. Reclassification moves children from hyponatremia to normonatremia, as glucose correction would; differential scenarios assume correction affects mainly children with severe DKA, who are expected to have higher glucose. The fragility index counts the outcome changes in one group that raise the two-sided Fisher p to ≥0.05.

4. Discussion

Over three years at the main pediatric referral hospital of Bali, two-thirds of the children admitted in DKA had severe acidosis, and three of every four were girls. Hyponatremia, as measured at admission, was linked to severe DKA: children with severe episodes were almost three times as likely as those with milder ones to be hyponatremic (64.9% vs 23.5%). The association survived multiplicity correction, mutual adjustment in every joint table compatible with the data, adjustment for undernutrition, and credible confounding by sex or referral status, although its statistical significance would not survive the reclassification of five hyponatremic children with severe DKA. Glucose correction could well produce a shift of that size. More than half of the children had hypokalemia and more than half had a 3+ dipstick ketone result, yet neither was associated with severity. The regional literature has described how often DKA occurs at diagnosis but rarely how routine admission chemistry relates to its severity. These findings help to redress that imbalance.

4.1. The Burden of Severe DKA

A severe-DKA share of 68.5% is among the highest reported. It is more than double the 27.7% of a complete Polish regional cohort and the 33.9% of Hangzhou,[5,45] and it is higher than the 36% from 30 Latin American centers and the 43.2% from an Egyptian pediatric emergency department.[46,47] In Jordan, most DKA at diagnosis was mild or moderate (38% and 33.3%).[54] In an earlier Surabaya series, 37.9% of 58 children had severe DKA.[19] Our estimate lies nearer to a Malaysian tertiary center (54.9%) and a Saudi intensive-care cohort (61.6%),[10,48] both of which, like our hospital, receive the sickest children from a wide catchment. Three mechanisms may contribute; none was measured in this study. The first is referral selection: children with milder DKA are more likely to be managed at district hospitals, whereas those with deeper acidosis are transferred. The second is delayed diagnosis. A meta-analysis found that delay more than doubled the odds of DKA at onset (OR 2.27).[55] Malaysian children were misdiagnosed in 38.7% of cases,[11] and Yemeni children in DKA had longer appraisal and diagnosis intervals.[56] In Sweden, primary-care referral was delayed in 43% of cases, and delay was associated with lower pH.[57] The third is socioeconomic disadvantage, which raises the risk of severe DKA. Relative poverty doubled it in Sweden (RR 2.10).[58] Lack of insurance was associated with DKA in Latin America,[46] and regional deprivation was associated with DKA across six high-income countries.[44] Lower paternal education and poor knowledge of diabetes symptoms predicted DKA in Jordan and Ethiopia.[54,59] Kuwait saw more frequent DKA and intensive-care admission after the COVID-19 pandemic, and Malaysia saw more severe DKA.[12,60] International registry data show that DKA at diagnosis stayed above pre-pandemic trends in 2021.[2] Our study period began in 2022, when these effects may not yet have resolved.

4.2. Hyponatremia as a Correlate of Severity

The prevalence of hyponatremia (51.9%) resembled the 46.6% reported in an Iranian pediatric intensive-care cohort,[31] and sodium disturbances were the commonest electrolyte complication in a Libyan series (36.4%).[61] In the earlier Surabaya series, hyponatremia was recorded in 32.8% of children.[19] Studies of sodium and severity point in different directions. A small comparative series found no electrolyte difference between mild-to-moderate and severe DKA.[39] In Saudi children, hypernatremia rather than hyponatremia was more frequent in severe DKA.[25] In a United States nested case–control study, children with death or prolonged intensive care had higher initial sodium.[24] In Ethiopia, both hyponatremia (aOR 4) and hypernatremia (aOR 7.4) were associated with death.[6] These findings are not contradictory once the measurement is considered. We defined hyponatremia on measured sodium, and the measured value falls by 1.6 to 2.4 mmol/L for every 100 mg/dL rise in glucose as water shifts across cell membranes.[62] In the PECARN FLUID cohort, glucose correlated with urea and creatinine, the markers of dehydration and renal hypoperfusion,[21] and in Korea children with hyperosmolar DKA had more altered consciousness,

intensive-care admission and acute kidney injury than those with isolated DKA.[63] Severe DKA may therefore combine higher glucose, greater osmotic diuresis and stronger antidiuretic stimulation. All three lower measured sodium. Studies that report corrected sodium, or that define hypernatremia on corrected values, capture a different construct, namely the free-water deficit that remains once the glucose effect is removed. Our robustness analysis puts a number on this concern. Suppose glucose correction moved as few as five of the 24 hyponatremic children with severe DKA into the normonatremic range. The association would then lose statistical significance, although the OR would stay above 3. The finding is best read as evidence that measured sodium tracks severity, not as evidence that a sodium deficit independent of glucose does. The setting of the episode may also matter, whether at diagnosis or in established diabetes. In PECARN FLUID, previously diagnosed diabetes was associated with falls in corrected sodium during treatment.[22] The proposed pathways remain a model, not a demonstrated sequence, and are summarized in Figure 8.

Measured hyponatremia should therefore be read as a marker of the depth of the metabolic disturbance. It is not an independent cause of severity, and its discriminative value was modest. A positive likelihood ratio of 2.76 and a positive predictive value of 85.7% mean that a hyponatremic child in this setting probably has severe DKA. A negative predictive value of 50.0% means that normal sodium does not exclude it. Predictive values depend on prevalence, so both would be lower at district hospitals, where severe DKA is less common. Blood gas analysis remains indispensable. The clinical value of the finding lies elsewhere. Hyponatremia at admission should prompt calculation of the glucose-corrected sodium and close monitoring of its trajectory. In PECARN FLUID, falls in corrected sodium were associated with presenting sodium, previously diagnosed diabetes and hypotonic fluids.[22] Corrected sodium stayed stable with 0.9% saline but fell with 0.45% saline.[23] A systematic review of 4,087 children also listed low corrected sodium among the predictors of acute kidney injury.[9] In Polish children, those with acute kidney injury had higher corrected sodium,[26] and in Thai children glucose above 500 mg/dL was associated with acute kidney injury (aOR 13.7).[64] Sodium handling, glucose and kidney injury are thus intertwined, and a hyponatremic child with severe DKA should be regarded as at risk of all three.

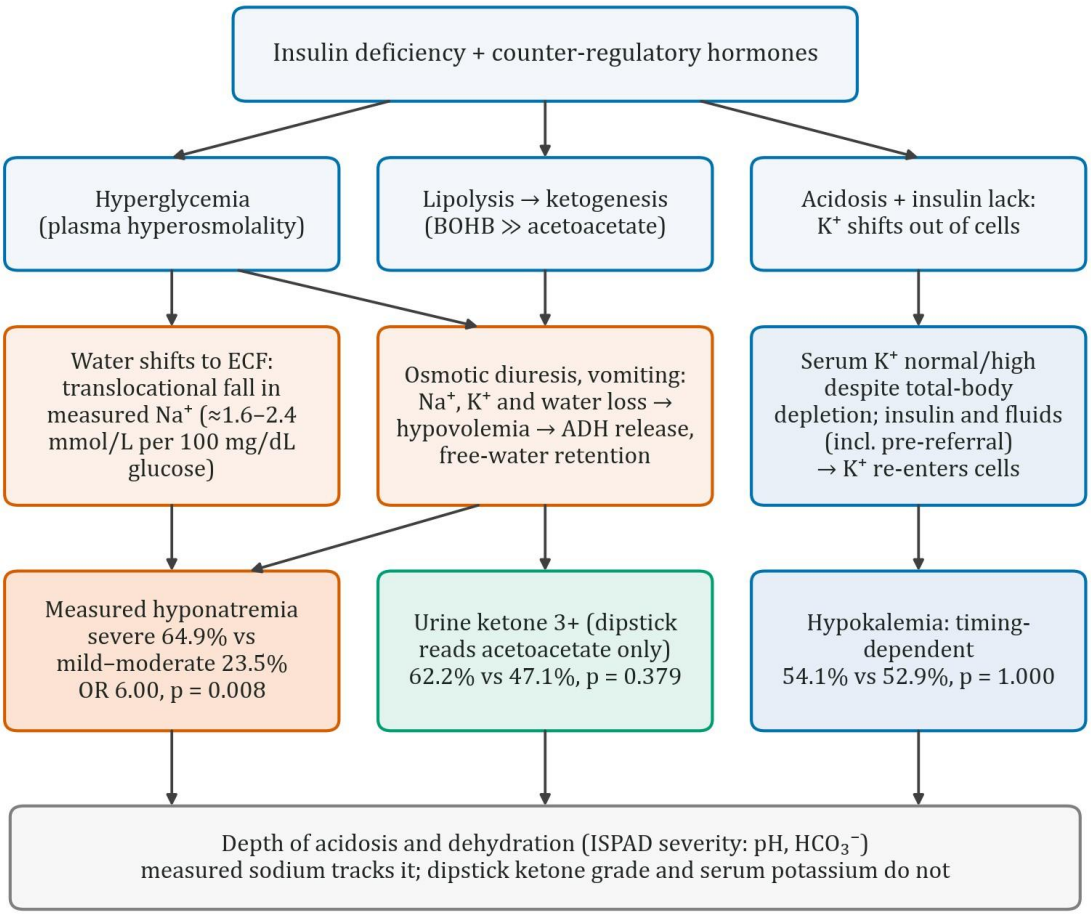


Figure 8. Proposed pathways linking diabetic ketoacidosis to the three admission measurements. Hyperglycemia lowers measured sodium by translocation of water and, with osmotic diuresis and antidiuretic hormone release, tracks the depth of dehydration and acidosis; dipstick urine ketone reads acetoacetate, not beta-hydroxybutyrate (BOHB); serum potassium reflects transcellular shifts and the timing of insulin and fluids rather than total-body stores. Observed proportions and exact p values from this cohort are shown in the bottom row. ECF, extracellular fluid; ADH, antidiuretic hormone.

4.3. Potassium: A Problem of Timing

The frequency of hypokalemia in our cohort (53.7%) was an unexpected finding. Before treatment, insulin deficiency and acidosis shift potassium out of cells. Hypokalemia at admission is therefore uncommon. In a multicenter Chinese cohort of adults, 16.6% were hypokalemic on admission and 21.7% hyperkalemic,[27] and in Saudi children with new-onset DKA hypokalemia was recorded in 24.4%.[29] Our proportion matched instead the series that counted hypokalemia at any time during treatment: 50.9% in Iran, 36.6% in India, and the commonest complication in Brazil.[30,31,65] In the Chinese cohort,

67.9% of patients became hypokalemic during treatment.[27] One explanation, which these data cannot test, is that many values were obtained after treatment had begun. More than half of our children were transferred from other facilities, where insulin and fluids are often started before transfer. If so, pre-referral insulin and fluids would have driven potassium into cells before the first measurement at our hospital, which would decouple the value from the severity of the underlying episode. A Canadian review found that 75% of children received at least one element of management that departed from guidelines, and treatment-related risk factors for cerebral edema were more common in those who first presented to community centers (52% vs 19%).[66] Referral status was not cross-classified with potassium, so this hypothesis could not be examined, as shown in Table 6. Recording the time of the first sample relative to any insulin or fluid, and whether treatment began elsewhere, would test it directly. Recurrent DKA in children with established diabetes, who may have taken insulin before presenting, is a second possible explanation. Either mechanism would also explain the absence of any association with severity (OR 1.05). That agrees with the earlier finding that electrolyte profiles did not differ between severity grades.[39]

Whatever its cause, hypokalemia in half of the children admitted has direct implications for safety. The recommendations that follow rest on the published evidence and were not evaluated in this study. Not receiving potassium replacement was associated with death in Ethiopian children (aOR 7.4),[6] and a Japanese national database linked lower potassium concentrations in initial fluids to higher mortality.[28] In a meta-analysis, balanced crystalloids reduced hypokalemia compared with 0.9% saline (risk ratio 0.66).[32] Ringer's lactate gave better potassium levels at 24 and 48 hours in a Tunisian randomized trial in adults.[67] Potassium acetate in a two-bag system was associated with a shorter hospital stay than potassium chloride in a United States cohort.[68] Hyperchloremia develops in up to 80% of children within 18 hours and prolongs resolution.[69,70] That is one more reason to prefer balanced fluids where they are available. For referring hospitals, a shared provincial protocol would make the admission potassium interpretable and protect children during transfer, specifying potassium measurement before insulin, potassium in the initial fluids once urine output is confirmed, and documentation of all pre-transfer treatment.

4.4. Urine Ketones: Diagnostic Value and Severity

More than half of the children had a 3+ dipstick result, similar to the 46.9% with +++ or ++++ ketonuria among Pakistani children.[34] Yet the dipstick grade did not separate severe from milder DKA. The chemistry predicts this. The nitroprusside reaction detects acetoacetate but not BOHB, and as acidosis deepens the ratio of BOHB to acetoacetate rises, so that the dipstick saturates or understates ketosis just when it is most severe.[33] Even blood BOHB is an imperfect severity marker. It tracked pH only moderately in a mixed adolescent and adult cohort in Qatar ($r = -0.44$),[35] and admission BOHB was unrelated to pH in Japanese children.[36] In a Jakarta series of 37 children, capillary BOHB correlated more strongly than urine ketones with pH ($r = -0.52$ vs -0.49) and with bicarbonate ($r = -0.60$ vs -0.48) during treatment.[20] In Zambia, ketonuria lost its association with length of stay once DKA severity was considered (hazard ratio 0.90).[38] Strongly positive urine ketones nonetheless help early recognition of DKA in a Chinese warning score.[71] They took a median of 24 hours to clear in Ethiopian children, which makes them unsuitable for judging resolution.[72] In a larger Ethiopian cohort, the median time to resolution was 22 hours, and mild DKA resolved faster (adjusted hazard ratio 1.37).[73] Blood BOHB is more useful for monitoring. A plasma value below 1.5 mmol/L identified resolution with 83% sensitivity and 87% specificity.[37] Combined indices may say more than either measure alone. The ketone-to-bicarbonate ratio identified renal tubular damage at diabetes onset in Italian children (area under the receiver-operating characteristic curve 0.94),[74] and initial BOHB correlated with serum creatinine in a United States cohort (Spearman $\rho = 0.42$).[75] Dipstick testing remains useful for diagnosis where blood testing is unavailable, but these data do not support using it to grade severity or to guide the intensity of treatment. Home ketone testing needs attention too. In German families, every adolescent and 98% of caregivers made at least one handling error when demonstrating urine dipstick testing.[76]

4.5. Sex, Age and Nutritional Status

The female share of 74.1% was higher than an equal sex ratio and than the 52.4% to 53.8% reported in Chinese and Malaysian new-onset cohorts,[11,16] but it resembled the 77.1% girls among Pakistani children admitted in DKA with established diabetes.[50] Most comparators for the female share were new-onset cohorts. The significant differences may therefore partly reflect case mix rather than a true excess of girls among children with DKA. The comparison is nonetheless informative. Female sex is a modest risk factor for DKA at diagnosis (OR 1.10 in Germany and 1.06 across six registries).[43,44] It is a stronger and more consistent risk factor for recurrent DKA in established diabetes. The German–Austrian Diabetes-Patienten-Verlaufsdokumentation (DPV) registry,[77] a recent United States cohort[78] and a systematic review[79] have shown this, and the review also identified adolescence, low socioeconomic status and poor mental health. In Thailand, DKA admission rates were higher in girls than in boys and peaked at 13–17 years.[13] Disordered eating affected 43.3% of Ethiopian adolescents with type 1 diabetes,[80] and anxiety disorders were associated with higher DKA rates in the DPV registry.[81] Low parental education and income predicted DKA during established diabetes in Sweden.[82] The mean age of our children was 11.22 years, and many were peri-pubertal, a stage of physiological insulin resistance and growing autonomy in self-management. Female sex was also associated with mortality in Ethiopian children with DKA (adjusted hazard ratio 2.6).[7] The marked female predominance therefore suggests that a substantial proportion of our admissions may have been episodes in children with established diabetes. Whether each episode occurred at diagnosis or in established diabetes was not recorded. The sensitivity analysis showed that confounding by sex would have to be much stronger than published effects of female sex on DKA (OR about 1.1) to remove the sodium association.

Undernutrition affected 25.9% of the children. This is more than the 6.4% in an Indian multicenter clinic cohort[51] and the 5.8% underweight in a second Indian cohort that described a triple burden of undernutrition, anemia and overweight.[83] It agrees with the 16% undernutrition among Egyptian children with type 1 diabetes.[52] Overweight or obesity (9.3%) was less frequent than the 15.9% to 17.7% reported in Hungarian and Indian cohorts.[51,53] In Hungary, overweight was associated with more frequent and more severe DKA at onset.[53] Anthropometry at admission in DKA is hard to interpret because children with DKA at diagnosis have a lower body mass index (BMI) z score,[16] and a lower BMI was associated with DKA in Latin America (OR 0.95),[46] so part of the undernutrition we recorded probably reflects acute catabolic weight loss and dehydration rather than chronic

malnutrition. Undernutrition was not associated with severity in either the bivariate or the multivariable analysis. Its confidence interval (OR 0.47–8.27) is too wide to exclude a meaningful effect. In Malaysian children with DKA, hypophosphatemia affected 70.8% on day 1.[84] The nutritional and electrolyte consequences of DKA reach beyond sodium and potassium.

4.6. Implications for Bali and Indonesia

Read together with the regional literature, the findings suggest three priorities for the province. None was evaluated in this study. The first is earlier diagnosis. Misdiagnosis and delayed referral drive DKA at onset across the region.[11,55] Missed new-onset DKA was associated with cerebral edema (aOR 4.6) and death in a multicenter United States study.[85] Awareness of the classic symptoms among families, schools and primary care, and point-of-care glucose and ketone testing in every primary-care facility, are inexpensive steps. The second priority is a common provincial protocol for the first hours of care and for transfer, so that children reach the referral hospital after appropriate fluids and potassium, with their pre-transfer treatment documented. The fall in Thai DKA mortality from 2.2% to 0.6% over nine years shows what system-level improvement can achieve.[8] The third priority is support for children with established diabetes, particularly adolescent girls. Indonesian families already carry substantial out-of-pocket costs for insulin, syringes and travel,[17] and fewer than half of children in Surabaya reached recommended self-monitoring frequencies.[18] Recurrent DKA is likely to remain common without structured education, mental-health screening and reliable access to supplies. Technology can help where it is affordable. Combined continuous glucose monitoring and insulin-pump use was associated with fewer DKA events in a Californian cohort of young people.[86]

4.7. Methodological Considerations

Small single-center series are often analyzed with correlation coefficients between dichotomized variables. These conceal the size and uncertainty of the association and do not allow adjustment. Exact 2 × 2 analysis with multiplicity control avoids the first problem. A multivariable layer that states what the data can and cannot identify avoids the second. A main-effects logistic model depends only on the outcome-by-predictor counts and the joint distribution of the predictors. The pairwise cross-classifications therefore nearly determined the adjusted estimates, and the aOR for hyponatremia varied only between 4.83 and 4.90 across 1,096 admissible tables. Sex and referral status were not cross-classified. For them, the tipping-point maps turn an unverifiable assumption into an explicit statement of how strong confounding would have to be to change the conclusion. The approach may be applicable to other small cohorts in which only part of the joint distribution is available. The robustness analyses also show the limits of a small sample. A fragility index of 3 means that a handful of misclassified outcomes could change the inference. The estimate therefore needs prospective confirmation.

4.8. Strengths and Limitations

The study has four strengths. It provides a recent description of pediatric DKA severity and admission chemistry from Indonesia, drawn from consecutive admissions over three years at the province's referral hospital. All definitions followed ISPAD 2022 and fixed laboratory thresholds from a single central laboratory. The analysis used exact methods and penalized regression suited to a sample of 54. It reported effect sizes with confidence intervals rather than p values alone and controlled multiplicity across the primary exposures. Finally, the conclusions were tested across every dataset consistent with the observations and against explicit confounding scenarios. This separates the robust finding from those that the data cannot support.

The limitations are equally specific. The study was retrospective, single-center and small, and its confidence intervals are wide. Sodium was analyzed as measured rather than glucose-corrected, and continuous sodium, potassium, glucose, pH and bicarbonate values were not analyzed, so dose–response relationships and corrected-sodium analyses were not possible. The time of the first electrolyte sample relative to insulin and fluid therapy, including treatment before transfer, was not recorded, which limits the interpretation of potassium. Mild and moderate DKA were combined, which ruled out an ordinal analysis of severity. Urine ketone was available only as a dichotomized dipstick grade. Sex, age and referral status were not cross-classified with severity or laboratory findings. Their confounding could be bounded but not adjusted for directly. Whether each episode occurred at diagnosis or in established diabetes was not available, nor were its precipitating cause and clinical outcomes such as cerebral edema, acute kidney injury and length of stay. The number of admissions screened and excluded was not recorded, nor was whether any child contributed more than one admission. Data were abstracted by one investigator, so inter-rater agreement could not be assessed. Finally, the published comparators differ in setting, definitions and the timing of measurement. The benchmark comparisons place the cohort in context. They do not estimate causal differences.

4.9. Future Research

A prospective provincial registry of pediatric DKA in Bali would address these limitations. It should record continuous admission sodium, potassium, glucose, pH and bicarbonate, with the time of sampling relative to any treatment, the three-level ISPAD severity grade, whether the episode occurred at diagnosis or in established diabetes, and outcomes including acute kidney injury, cerebral edema and time to resolution. Glucose-corrected sodium should be analyzed alongside measured sodium. About 50 children (34 severe and 16 mild–moderate) would suffice to confirm the sodium association with 80% power. Detecting the observed difference in urine ketone 3+ would require about 391 children. The potassium difference was too small to be worth pursuing as a severity marker. Two gaps are the most actionable: a pragmatic comparison of capillary BOHB with urine dipstick testing at district hospitals would address one, and an evaluation of a shared pre-transfer protocol would address the other.

5. Conclusion

At the main pediatric referral hospital of Bali, two-thirds of the children with type 1 diabetes admitted in DKA had severe acidosis, and girls predominated. Measured hyponatremia at admission was associated with severe DKA (OR 6.00, 95% CI 1.62–22.20). The association held after mutual adjustment in every dataset compatible with the observations (Model 1 aOR 4.83–4.90; Model 2 aOR 4.78–5.23), but it would lose significance if glucose correction reclassified five of the 24 hyponatremic children with severe DKA. Admission potassium and dipstick ketone grade were not associated with severity. Hyponatremia should prompt calculation of the glucose-corrected sodium and close monitoring. Normal sodium does not exclude severe DKA. Confirmation needs a prospective registry that records continuous, time-stamped

sodium, glucose, potassium, pH, bicarbonate and blood BOHB together with whether each episode occurred at diagnosis, so that the effects of disease severity can be separated from those of treatment before admission.

Declarations

Ethics Approval and Consent to Participate

The study protocol was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana (approval No. 2405/UN14.2.2.VII.14/LT/2025). The study was conducted in accordance with the Declaration of Helsinki. The requirement for individual informed consent was waived because only anonymized, routinely collected medical records were analyzed.

Consent for Publication

Not applicable. No identifying information is reported.

Availability of Data and Materials

Record-level data are available from the corresponding author on reasonable request, subject to approval by Prof. Dr. I.G.N.G. Ngoerah General Hospital.

Competing Interests

The authors declare no competing interests.

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Authors' Contributions

PWW: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Visualization, Writing - original draft. IMA: Conceptualization, Methodology, Supervision, Validation, Writing - review and editing. IMDY: Methodology, Supervision, Validation, Writing - review and editing. All authors approved the final manuscript.

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Use of artificial intelligence

None declared.

Preprint Statement

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