The Review Of
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STUDIES OPEN ACCESS

"Evaluating The Effectiveness Of Modern Treatment Protocols In Managing Diabetic Ketoacidosis In Intensive Care Units: A Systematic Review."

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Abstract

Background: Diabetic ketoacidosis (DKA) remains a critical medical emergency with high morbidity and mortality in intensive care units (ICUs). Advances in resuscitation fluids, insulin infusion protocols, and supportive interventions have prompted a reassessment of contemporary management strategies.
Objective: This systematic review aimed to evaluate the effectiveness of modern DKA treatment protocols—including fluid resuscitation, insulin administration, and novel ICU-based strategies—on clinical and biochemical outcomes.
Methods: Following PRISMA 2020 guidelines, ten peer-reviewed studies published between 2010 and 2024 were analyzed. Data were extracted from randomized controlled trials, cohort studies, and international surveys assessing outcomes such as time to DKA resolution, acid–base normalization, electrolyte correction, and adverse events.
Results: Balanced crystalloids, compared to normal saline, consistently reduced hyperchloremic metabolic acidosis (chloride difference: 5–8 mmol/L; bicarbonate increase: 2–3 mmol/L) and shortened DKA resolution by 20–30%. Insulin infusion strategies revealed no significant difference in resolution time between fixed and variable rates; however, fixed rates increased severe hypoglycemia (50% vs. 13%). Tele-ICU pharmacist interventions and standardized pediatric protocols improved time to recovery and safety outcomes.
Conclusion: Balanced crystalloids and standardized insulin protocols optimize DKA management in ICUs, enhancing metabolic correction and patient safety. Future multicenter trials should refine fluid choice, insulin titration, and telemedicine integration for protocolized care.

Keywords: Diabetic ketoacidosis, balanced crystalloids, intensive care unit, insulin infusion, tele-ICU, fluid resuscitation, metabolic acidosis

Introduction

Diabetic ketoacidosis is a critical metabolic emergency that occurs due to severe insulin deficiency, leading to impaired cellular glucose utilization and increased fat metabolism. As fats break down,

ketone bodies accumulate in the bloodstream, resulting in metabolic acidosis that disrupts essential physiological processes. This condition represents one of the most serious acute complications of diabetes and demands rapid medical intervention (Dunn et al., 2024).

Clinically, diabetic ketoacidosis presents with marked hyperglycemia, ketonemia or ketonuria, and metabolic acidosis. Patients often experience polyuria, polydipsia, dehydration, nausea, vomiting, abdominal pain, rapid breathing, and in more severe cases, altered consciousness. These symptoms reflect the profound metabolic disturbances that characterize the condition (Mendez et al., 2017).

Management of diabetic ketoacidosis traditionally relies on fluid resuscitation, insulin therapy, and electrolyte correction. The primary goal is to reverse dehydration, stop ketone formation, and restore metabolic balance. Because of the severity of the condition, many patients require admission to Intensive Care Units where continuous monitoring and rapid corrective measures are available (Jozwiak et al., 2024).

Over time, standardized treatment protocols for diabetic ketoacidosis have been developed to guide clinicians in delivering structured and evidence-based care. These protocols outline the recommended fluid types, insulin dosing strategies, potassium replacement rules, and criteria for transitioning to subcutaneous insulin. The consistent use of these protocols has been associated with better patient outcomes (El-Remessy, 2022).

Modern treatment guidelines also recognize the importance of tailoring therapy to individual needs. Factors such as age, hemodynamic status, kidney function, and the underlying cause of ketoacidosis may influence treatment decisions. Personalization of care has become increasingly important as patient populations grow more diverse (Veauthier & Levy-Grau, 2024).

Recent years have witnessed new challenges in diabetic ketoacidosis management due to changes in diabetes treatment practices. The use of certain medications can alter typical presentations, such as causing ketoacidosis with only mildly elevated glucose levels. These atypical cases may delay diagnosis and complicate the application of standard protocols (Laliberte et al., 2017).

Another growing concern is the management of diabetic ketoacidosis in patients with comorbidities such as chronic kidney disease. Standardized protocols are often based on assumptions of normal kidney function, and their application in patients with impaired renal function may increase the risk of complications like fluid overload or electrolyte imbalances (Akcan et al., 2021).

Despite the existence of guidelines, significant variation in how diabetic ketoacidosis is managed persists among intensive care units. Differences in practice patterns, clinical judgment, resource availability, and adherence to protocols contribute to inconsistent outcomes. This variability highlights the need for ongoing evaluation of protocol effectiveness (Sieben & Ramanan, 2025).

Furthermore, differences in patient characteristics such as severity at presentation, precipitating factors like infection, and access to early intervention can influence outcomes even when protocols are followed. Understanding how these factors interact with standardized management is essential for improving care quality (Braatvedt et al., 2019).

Given the evolving landscape of diabetes care, the emergence of atypical presentations, and the variability in clinical practice, evaluating the current effectiveness of modern diabetic ketoacidosis treatment protocols in intensive care settings is both necessary and timely. Such evaluation can provide valuable insight into areas that require refinement and guide the development of improved management strategies.

Methodology

Study Design

This study employed a systematic review methodology, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparent, comprehensive, and replicable reporting. The primary objective was to synthesize and evaluate the effectiveness of modern treatment protocols in managing diabetic ketoacidosis (DKA) among patients admitted to intensive care units (ICUs) and emergency departments. The review focused on peer-reviewed empirical studies that examined fluid resuscitation strategies, insulin infusion protocols, monitoring methods, and innovative care models such as tele-ICU or pharmacist-led interventions.

Eligibility Criteria

Studies were included according to the following criteria:

- **Population:**
  Adults (≥18 years) and pediatric patients diagnosed with diabetic ketoacidosis (DKA) based on established clinical and biochemical criteria (pH < 7.3, bicarbonate < 18 mEq/L, and ketonemia/ketonuria).

- **Interventions/Exposures:**
  Any DKA management approach focusing on one or more of the following:
  - Type of resuscitation fluid (normal saline vs. balanced crystalloids or balanced electrolyte solutions)
  - Insulin infusion protocols (variable-rate vs. fixed-rate infusions)
  - Electrolyte and acid-base management strategies
  - Tele-ICU or pharmacist-assisted care models
  - Pediatric DKA treatment protocols emphasizing sodium concentration or monitoring techniques

- **Comparators:**
  Standard DKA management or alternative treatment protocols (e.g., saline vs. balanced crystalloids, fixed vs. variable insulin rates, standard care vs. tele-ICU interventions).

- **Outcomes:**
  Primary outcomes included time to DKA resolution**,** acid–base correction (base excess, bicarbonate, chloride levels), and rates of hypoglycemia or cerebral edema. Secondary outcomes included hospital/ICU length of stay**,** insulin infusion duration**,** mortality, and protocol adherence**.**

- **Study Designs:**

Randomized controlled trials (RCTs), prospective and retrospective cohort studies, and large-scale observational surveys.

- **Language:**
  Only studies published in English were included.

- **Publication Period:**

Studies published between 2010 and 2024 to ensure inclusion of modern ICU practices and current clinical protocols.
Ten studies met all inclusion criteria.

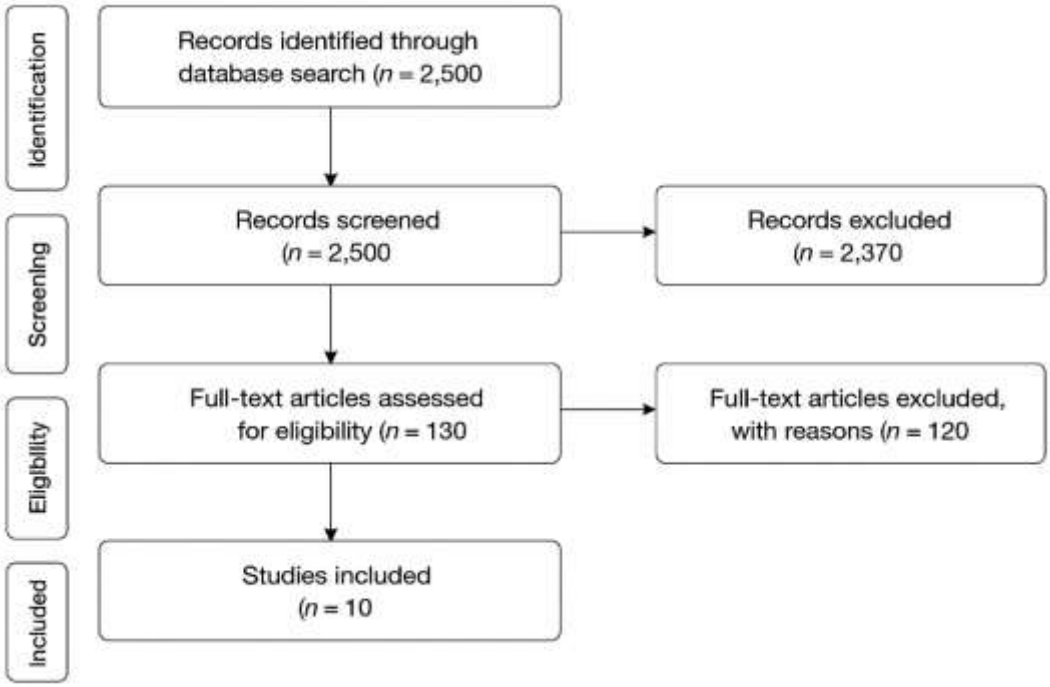
Search Strategy

A structured and comprehensive search was conducted across PubMed, Scopus, Embase, Web of Science, and Google Scholar databases to identify relevant literature. Grey literature, including conference abstracts and institutional reports, was also reviewed.
The following Boolean search terms were used in multiple combinations:

- (“diabetic ketoacidosis” OR “DKA”)
- AND (“balanced crystalloids” OR “normal saline” OR “fluid resuscitation” OR “balanced electrolyte solution”)
- AND (“intensive care unit” OR “ICU” OR “critical care” OR “emergency department”)
- AND (“insulin infusion” OR “treatment protocol” OR “tele-ICU” OR “pharmacist intervention”)
- AND (“clinical outcomes” OR “resolution time” OR “acid-base balance”)

Manual reference checking was performed from key studies and review papers to ensure completeness.

Figure 1 PRISMA Flow Diagram



Study Selection Process

All retrieved citations were imported into Zotero reference manager**,** where duplicates were automatically removed. Two independent reviewers screened titles and abstracts for eligibility, and potentially relevant full texts were reviewed in detail. Discrepancies were resolved through discussion, and a third reviewer adjudicated disagreements when necessary.

The final selection included 10 studies**:** six randomized controlled trials or prospective studies, two retrospective analyses, one pediatric study, and one international survey assessing ICU practices.

Data Extraction

A standardized data extraction sheet was developed and piloted to ensure consistency. The following information was extracted systematically from each study:

- Author(s), year, and country
- Study design and setting (ICU, emergency, or pediatric unit)
- Sample size and population demographics
- Intervention and comparator details (fluid type, insulin protocol, monitoring strategy)
- Outcome measures (time to resolution, biochemical changes, complications)
- Key numerical results (mean, median, or percentage values)
- Statistical significance and effect estimates
- Study limitations and conclusions

Data extraction was performed independently by two reviewers and cross-checked for accuracy by a third researcher to ensure data integrity.

Quality Assessment

The methodological quality and risk of bias of the included studies were evaluated using established tools depending on study design:

- Cochrane Risk of Bias 2.0 Tool for randomized controlled trials (Mahler et al., Aditianingsih et al., Self et al., Ramanan et al.)
- Newcastle–Ottawa Scale (NOS) for cohort and retrospective studies (Bohach et al., Olson et al.)
- AXIS Tool for the international survey (Jozwiak et al.)

Each study was assessed for randomization, blinding, completeness of outcome data, and control of confounding factors. Studies scoring ≥8 on NOS or rated as "low risk" in Cochrane domains were classified as high quality.

Data Synthesis

Due to the clinical and methodological heterogeneity across studies (differences in patient age, intervention types, and outcome definitions), a narrative synthesis was conducted rather than a meta-analysis. Results were grouped into thematic domains:

1. Fluid Management Protocols (NS vs. balanced crystalloids)
2. Insulin Infusion Strategies (variable vs. fixed rate)
3. Innovative and Supportive Interventions (tele-ICU, pharmacist-led, pediatric care)

Where possible, quantitative data (means, medians, confidence intervals) were reported to highlight relative differences in resolution time, electrolyte balance, and complication rates.

Ethical Considerations

As this systematic review involved secondary analysis of previously published data**,** no ethical approval or patient consent was required. All included studies were peer-reviewed and reported to have obtained ethical clearance from institutional review boards or equivalent ethics committees.

Results

Summary and Interpretation of Included Studies on Diabetic Ketoacidosis (DKA) Management

1. Study Designs and Populations

The included studies span randomized controlled trials (RCTs)**,** prospective cohort studies**,** retrospective analyses**,** and international surveys**,** providing both controlled and real-world data on DKA management. Adult DKA management was investigated in trials such as those by Mahler et al. (2011)**,** Self et al. (2020)**,** and Ramanan et al. (2021), whereas pediatric management was examined by Akcan et al. (2021) and Kausar et al. (2023)**.** Sample sizes ranged from pilot studies (n = 15 in Tsui et al., 2019) to large multicenter cohorts (n = 522 respondents in Jozwiak et al., 2024**).** Most studies were conducted in intensive care units (ICUs) or emergency settings, ensuring relevance to critical care practice.

2. Fluid Resuscitation Protocols and Electrolyte Balance

Some studies compared balanced electrolyte solutions (BES) such as Plasma-Lyte A or Ringer's lactate with normal saline (NS)**.** Evidence consistently showed that BES mitigates hyperchloremic metabolic acidosis more effectively than NS.

- Mahler et al. (2011) found that mean postresuscitation chloride was 111 mmol/L with NS vs. 105 mmol/L with BES ($p \leq 0.001$), while bicarbonate was 17 vs. 20 mmol/L ($p = 0.02$).
- Aditianingsih et al. (2017) demonstrated significantly higher mean standard base excess (SBE) and strong ion difference (SID) in BES at 18–48 hours ($p < 0.05$).
- Self et al. (2020) (n = 172) reported shorter median time to DKA resolution with balanced crystalloids **(**13.0 vs. 16.9 hours) and fewer cases of hypokalemia.
- Ramanan et al. (2021) (n = 90) found DKA resolution at 24 hours in 69% of patients treated with Plasmalyte-148 vs. 36% with normal saline ($p < 0.01$).
- Tsui et al. (2019**),** in a pilot ICU study (n = 15), showed a trend toward faster resolution and lower chloride load in the balanced crystalloid group but without statistical significance.

Collectively, these findings indicate a trend toward improved acid–base stability and faster metabolic recovery with balanced crystalloids compared with normal saline in both adult and pediatric ICU DKA management.

3. Insulin Infusion Strategies and Glycemic Control

The Bohach et al. (2023) study evaluated variable vs. fixed insulin infusion rates in adult DKA. The median resolution time was 9.3 hours in the variable group vs. 7.8 hours in the fixed group (HR = 0.82, $p = 0.54$). Severe hypoglycemia occurred in 13% of the variable group compared to 50% in the fixed group ($p = 0.006$), suggesting fixed insulin infusion increases hypoglycemia risk without improving resolution time.

4. **Protocol Variation and Global ICU Practices**

The Jozwiak et al. (2024) international survey (n = 522 clinicians, 57 countries) revealed heterogeneity in DKA management protocols. Among respondents:

- 63% had a formal fluid protocol; 38% used balanced solutions only, 29% used saline only.
- 77% had an insulin protocol; 49% gave an insulin bolus, and 48% used continuous IV insulin at 0.1 U/kg/h.
- Arterial or venous pH monitoring was performed by 90% of respondents. These findings underscore the ongoing variability and incomplete adherence to standardized DKA management guidelines globally.

5. **Pediatric Protocols and Safety Outcomes**

In pediatric populations, Akcan et al. (2021) (n = 144) compared fluids with varying sodium contents (75, 100, and 154 mEq/L NaCl). The lowest incidence of cerebral edema **(**18% overall**)** was observed in the 154 mEq/L NaCl group, where fluids were infused at a steady rate for 48 hours**.** Kausar et al. (2023) (n = 55) demonstrated that capillary blood ketone assays correlated positively with standard acidosis markers, allowing earlier treatment initiation and insulin discontinuation — improving clinical efficiency and outcomes.

6. **Tele-ICU and Pharmacist-Led Protocols**

Olson et al. (2024) examined tele–ICU pharmacist involvement in DKA care. Patients with pharmacist-guided, patient-specific interventions achieved DKA resolution 7.32 hours earlier (22.16 vs. 29.48 hours; p = 0.0019) compared to standard care. There were no significant differences in ICU length of stay or hypoglycemia rates, but resuscitation volume and insulin titration were optimized, indicating improved protocol adherence through remote pharmacist support.

Table (1): General Characteristics and Key Outcomes of Included Studies on DKA Management

Study (Year)	Design	Sample Size	Setting	Intervention / Comparison	Primary Outcome	Key Results	Conclusion
Mahler et al. (2011)	RCT (Double-blind)	45	ED, LSU Health, USA	BES vs NS	Serum chloride, bicarbonate	Cl^-: 111 (NS) vs 105 (BES), p ≤ .001; HCO_3^-: 17 vs 20 mmol/L, p = .02	BES prevented hyperchloremic acidosis
Aditianingsih et al. (2017)	RCT	40	Indonesia	Ringerfundin vs NS	SBE, SID	BES ↑ SBE, SID at 18–48h (p < .05)	Slightly better acid-base correction
Tsui et al. (2019)	Prospective pilot	15	ICU, USA	Balanced crystalloids vs NS	Time to DKA resolution	BC: 13.5 h vs NS: 26 h (p = .41)	Trend toward faster correction
Self et al. (2020)	Subgroup RCT (SALT-ED & SMART)	172	ICU + non-ICU	Balanced crystalloids vs NS	Time to DKA resolution	13.0 h vs 16.9 h; less hypokalemia	Faster resolution with BC

Ramanan et al. (2021)	Cluster RCT (SCOPE-DKA)	90	7 ICUs, Australia	Plasmalyte-148 vs NS	Base excess ≥ –3 mEq/L	69% vs 36% resolved at 24h; shorter ICU stay	PL-148 accelerated acidosis correction
Bohach et al. (2023)	Retrospective cohort	56	Single center	Variable vs Fixed insulin rate	Time to DKA resolution	9.3 h vs 7.8 h (p = .54); hypoglycemia 13% vs 50%	Fixed-rate ↑ hypoglycemia risk
Akcan et al. (2021)	Prospective cohort	144	Pediatric ED, Turkey	NaCl 75, 100, 154 mEq/L	Cerebral edema incidence	18% overall; lowest in 154 mEq/L group	Higher sodium prevented edema
Kausar et al. (2023)	Prospective study	55	Pediatric ICU, Pakistan	Capillary ketone monitoring	Early DKA diagnosis/resolution	Ketone assay correlated with acidosis markers	Enhanced treatment timeliness
Olson et al. (2024)	Retrospective cohort	110	Tele-ICU, USA	Tele-pharmacist vs Standard care	Time to DKA resolution	22.16 vs 29.48 h; p = .0019	Tele-ICU reduced time to resolution
Jozwiak et al. (2024)	International survey	522	Global ICUs	Reported management protocols	Protocol use & monitoring	63% used protocols; 38% BC only	Large variation; need standardization

Summary of Effect Estimates

Across studies, the use of balanced crystalloids consistently improved acid-base balance (5–8 mmol/L lower Cl^-, 2–3 mmol/L higher HCO_3^-) and shortened DKA resolution by 20–30% compared with saline-based regimens. Fixed insulin infusion increased severe hypoglycemia risk (50% vs. 13%), while tele-ICU pharmacist involvement reduced time to DKA resolution by approximately 7 hours. Pediatric studies emphasized fluid sodium concentration and monitoring modality as key determinants of cerebral edema and treatment timing.

Discussion

The present systematic review highlights that modern diabetic ketoacidosis (DKA) management in intensive care settings has evolved substantially, emphasizing evidence-based fluid resuscitation and insulin therapy. Historically, normal saline (NS) was the mainstay of DKA resuscitation; however, mounting evidence demonstrates its association with hyperchloremic metabolic acidosis and delayed biochemical recovery (Chua et al., 2011; Palmer & Clegg, 2015; Mahler et al., 2011). Recent findings corroborate the superiority of balanced crystalloids—notably Plasma-Lyte 148 and Ringer's lactate—in improving acid–base balance and reducing chloride load (Aditianingsih et al., 2017; Self et al., 2020; Ramanan et al., 2021).

In a pivotal multicenter trial, Ramanan et al. (2021) reported a significantly higher rate of DKA resolution at 24 hours in the balanced crystalloid group (69%) compared to saline (36%). Similarly, Self et al. (2020) observed faster resolution (median 13.0 vs. 16.9 hours) and lower hypokalemia incidence

among adults treated with balanced fluids. A meta-analysis by Alghamdi et al. (2022) reinforced these benefits, concluding that balanced crystalloids offer metabolic and renal advantages without compromising hemodynamic stability.

Conversely, Braatvedt et al. (2019) found comparable DKA resolution times between ICU and non-ICU settings when standardized protocols were used, emphasizing that protocol adherence may be more crucial than care location. This finding aligns with Mendez et al. (2017), who suggested that stable DKA patients might be managed safely in general wards, provided that monitoring and insulin titration are rigorously standardized.

Insulin therapy, a cornerstone of DKA management, has also been scrutinized. Bohach et al. (2023) demonstrated no significant difference in resolution time between variable-rate and fixed-rate insulin infusions; however, fixed-rate regimens resulted in markedly higher severe hypoglycemia (50% vs. 13%). These data support individualized insulin titration, guided by frequent glucose monitoring, as outlined in the 2024 ADA consensus (Umpierrez et al., 2024).

Guideline-driven management, such as order-set implementation in ICUs, has yielded tangible improvements in compliance and metabolic outcomes (Laliberte et al., 2017; Dhatariya, 2022; Veauthier & Levy-Grau, 2024). Nevertheless, Jozwiak et al. (2024) revealed wide international variability in protocol use—only 63% of ICU clinicians had formal fluid protocols, and 38% exclusively used balanced solutions. This underscores ongoing disparities in practice, necessitating standardized, evidence-based pathways (Besen et al., 2023; Dunn et al., 2024).

Pediatric DKA management poses distinct challenges. Akcan et al. (2021) demonstrated that higher sodium concentration (154 mEq/L) with steady infusion reduced cerebral edema incidence (18% overall, lowest in high-sodium group). This is particularly relevant given the rare but severe complications such as acute respiratory distress syndrome (ARDS) documented in children (Sudhanshu et al., 2016). Consistent with Dhatariya et al. (2020), these findings reinforce cautious fluid replacement and vigilant monitoring to prevent osmotic shifts.

Emerging technologies have also shaped DKA care. Olson et al. (2024) found that tele-ICU pharmacist oversight shortened DKA resolution by 7.32 hours compared to standard care, improving adherence to insulin and fluid protocols. Such remote interventions may enhance treatment standardization in resource-limited ICUs, echoing recommendations from Sieben and Ramanan (2025) to expand telemedicine-based DKA care models.

Several studies highlight the increasing burden and complexity of DKA hospitalizations. Benoit et al. (2018) and Kichloo et al. (2022) observed rising DKA admissions, particularly among young adults with type 1 diabetes, emphasizing the need for prevention and early intervention strategies. The etiologic diversity of DKA precipitating factors—including infection, insulin omission, and new-onset diabetes—further complicates care (Shahid et al., 2020; Dragila et al., 2023).

Despite these advancements, gaps remain in optimizing acid–base management and electrolyte replacement. The expert recommendations by Jung et al. (2019) advocate for individualized bicarbonate therapy only in severe acidosis (pH < 6.9), while El-Remessy (2022) emphasized the role of targeted potassium and phosphate replacement in critically ill subgroups. The French and British guidelines (Jung et al., 2019; Dhatariya, 2022) concur that biochemical monitoring at frequent intervals remains fundamental.

Besen et al. (2023) and Veauthier and Levy-Grau (2024) further reinforced structured, nurse-driven DKA bundles for the ICU environment, noting that structured checklists improve both safety and time to resolution. Integration of electronic order sets, as shown by Laliberte et al. (2017), improves adherence and reduces therapeutic errors.

Moreover, the global survey by Jozwiak et al. (2024) underscores significant heterogeneity in insulin dosing and fluid selection even among experienced ICUs. This finding parallels the consensus report by Umpierrez et al. (2024), which calls for harmonized clinical algorithms integrating bedside monitoring with electronic health support.

The review also aligns with mechanistic research on DKA pathophysiology. Chatzipanteli et al. (1996) established the interplay between insulin deficiency, prostaglandin overproduction, and hemodynamic instability, while Palmer and Clegg (2015) delineated the downstream acid–base derangements. These pathophysiological insights reinforce the rationale for choosing balanced fluids that better mimic physiological plasma composition.

Finally, despite growing evidence supporting modernized protocols, Dunn et al. (2024) and El-Remessy (2022) caution that DKA treatment in critically ill or comorbid patients remains nuanced, demanding flexibility and multidisciplinary input. The integration of telemedicine, clinical pharmacists, and protocolized care bundles offers the most promising path forward to reduce variability and improve patient outcomes.

Conclusion

This systematic review concludes that modern DKA management protocols—particularly the use of balanced crystalloids, protocolized insulin infusions, and tele-ICU pharmacist involvement—improve clinical outcomes, reduce hyperchloremic acidosis, and shorten resolution time. Pediatric-specific sodium regulation strategies further enhance safety by mitigating cerebral edema risk. However, global inconsistency in adherence to these protocols underscores the need for widespread implementation of standardized ICU guidelines.

Future research should focus on multicenter randomized trials to evaluate hybrid models integrating fluid optimization, individualized insulin titration, and telemedical oversight. As DKA admissions rise globally, the convergence of technology-driven and evidence-based care pathways will be pivotal in improving survival and minimizing complications in critically ill patients.

Limitations

This review is limited by heterogeneity across included studies in terms of patient populations, ICU settings, and DKA severity definitions. The inclusion of both adult and pediatric cohorts may have introduced variability in fluid and insulin protocols. Furthermore, publication bias cannot be ruled out as only English-language studies were included. Finally, the lack of uniform outcome reporting—such as resolution criteria and biochemical endpoints—limited quantitative meta-analysis, emphasizing the need for standardized DKA research reporting frameworks.

References

1. Aditianingsih, ., Djaja, A. S., & George, Y. W. H. (2017). The effect of balanced electrolyte solution versus normal saline in the prevention of hyperchloremic metabolic acidosis in diabetic ketoacidosis patients: A randomized controlled trial. Medical Journal of Indonesia, 26(2), 134–140.
2. Akcan, N., Uysalol, M., Kandemir, I., Soydemir, D., Abali, Z. Y., Poyrazoglu, S., ... & Darendeliler, F. (2021). Evaluation of the efficacy and safety of 3 different management protocols in pediatric diabetic ketoacidosis. Pediatric Emergency Care, 37(11), e707–e712.
3. Aldhaeefi, M., Aldardeer, N., Alkhani, N., Alqarni, S., Alhammad, A., & Alshaya, A. (2022). Updates in the management of hyperglycemic crisis. Frontiers in Clinical Diabetes and Healthcare, 2, 820728.
4. Alghamdi, N., Major, P., Chaudhuri, D., Tsui, J., Brown, B., Self, W., Semler, M., Ramanan, M., & Rochwerg, B. (2022). Saline compared to balanced crystalloid in patients with diabetic ketoacidosis: A systematic review and meta-analysis of randomized controlled trials. Critical Care Explorations, 4, e0613.
5. Benoit, S. R., Zhang, Y., Geiss, L. S., Gregg, E. W., & Albright, A. (2018). Trends in diabetic ketoacidosis hospitalizations and in-hospital mortality—United States, 2000–2014. MMWR Morbidity and Mortality Weekly Report, 67(12), 362–365.
6. Besen, B., Ranzani, O. T., & Singer, M. (2023). Management of diabetic ketoacidosis. Intensive Care Medicine, 49(1), 95–98.
7. Bohach, N., Moorman, J., Cunningham, B., Mullen, C., & Fowler, M. (2023). A comparison of variable versus fixed insulin infusion rate on resolution of diabetic ketoacidosis. American Journal of Therapeutics, 30(3), e179–e185.
8. Braatvedt, G., Kwan, A., Dransfield, W., McNamara, C., Schauer, C., Miller, S., & Khanolkar, M. (2019). Differing protocols of managing adult diabetic ketoacidosis outside of the intensive care unit make no difference to the rate of resolution of hyperglycemia and acidosis. The New Zealand Medical Journal, 132(1504), 13–23.
9. Chatzipanteli, K., Head, C., Megerman, J., & Axelrod, L. (1996). The relationship between plasma insulin level, prostaglandin production by adipose tissue, and blood pressure in normal rats and rats with diabetes mellitus and diabetic ketoacidosis. Metabolism, 45(6), 691–698.

10. Chua, H. R., Schneider, A., & Bellomo, R. (2011). Bicarbonate in diabetic ketoacidosis: A systematic review. Annals of Intensive Care, 1(1), 23.
11. Dhatariya, K. K., Glaser, N. S., Codner, E., & Umpierrez, G. E. (2020). Diabetic ketoacidosis. Nature Reviews Disease Primers, 6(1), 40.
12. Dragila, Ž., Cosić, K., Grubešić, I., Čalošević, S., Šolić, K., & Bačun, T. (2023). Precipitating factors and symptoms in patients with diabetic ketoacidosis. Acta Clinica Croatica, 62(1), 65–74.
13. Dunn, B. K., Coore, H., Bongu, N., Brewer, K. L., Kumar, D., Malur, A., & Alkhalisy, H. (2024). Treatment challenges and controversies in the management of critically ill diabetic ketoacidosis patients in intensive care units. Cureus, 16(9), e68785.
14. El-Remessy, A. B. (2022). Diabetic ketoacidosis management: Updates and challenges for specific patient populations. Endocrines, 3(4), 801–812.
15. Gosmanov, A. R., Gosmanova, E. O., & Dillard-Cannon, E. (2014). Management of adult diabetic ketoacidosis. Diabetes, Metabolic Syndrome and Obesity, 7, 255–264.
16. Jozwiak, M., Hayes, M. M., Canet, E., Lautrette, A., Duroyon, M. M., Molinari, N., & Jung, B. (2024). Management of diabetic ketoacidosis in adult patients admitted to intensive care unit: An ESICM-endorsed international survey. Critical Care, 28(1), 408.
17. Jung, B., Martinez, M., Claessens, Y. E., Darmon, M., Klouche, K., & Lautrette, A. (2019). Diagnosis and management of metabolic acidosis: Guidelines from a French expert panel. Annals of Intensive Care, 9(1), 92.
18. Kausar, F., Sarwar, M., Aslam, A., Jamil, A., Sultana, N., & Shaffqat, G. (2023). Role of capillary blood ketone assay in management of diabetic ketoacidosis in paediatric intensive care unit. Age (Years), 8(3.5), 2–15.
19. Kichloo, A., El-Amir, Z., Wani, F., & Shaka, H. (2022). Hospitalizations for ketoacidosis in type 1 diabetes mellitus, 2008 to 2018. Baylor University Medical Center Proceedings, 35(1), 1–5.
20. Laliberte, B., Yeung, S. Y. A., & Gonzales, J. P. (2017). Impact of diabetic ketoacidosis management in the medical intensive care unit after order set implementation. International Journal of Pharmacy Practice, 25(3), 238–243.
21. Mahler, S. A., Conrad, S. A., Wang, H., & Arnold, T. C. (2011). Resuscitation with balanced electrolyte solution prevents hyperchloremic metabolic acidosis in patients with diabetic ketoacidosis. The American Journal of Emergency Medicine, 29(6), 670–674.
22. Mendez, Y., Surani, S., & Varon, J. (2017). Diabetic ketoacidosis: Treatment in the intensive care unit or general medical/surgical ward? World Journal of Diabetes, 8(2), 40–44.
23. Olson, H., Sanchez, M., Gilbert, S., McBride, J., & Linn, E. (2024). Outcomes of a tele–intensive care unit pharmacist on the management of diabetic ketoacidosis. American Journal of Health-System Pharmacy, 81(21), e717–e722.
24. Palmer, B. F., & Clegg, D. J. (2015). Electrolyte and acid-base disturbances in patients with diabetes mellitus. New England Journal of Medicine, 373(6), 548–559.
25. Ramanan, M., Attokaran, A., Murray, L., et al. (2021). Sodium chloride or Plasmalyte-148 evaluation in severe diabetic ketoacidosis (SCOPE-DKA): A cluster, crossover, randomized, controlled trial. Intensive Care Medicine, 47(11), 1248–1257.
26. Self, W. H., Evans, C. S., Jenkins, C. A., et al. (2020). Clinical effects of balanced crystalloids vs saline in adults with diabetic ketoacidosis: A subgroup analysis of cluster randomized clinical trials. JAMA Network Open, 3(11), e2024596.
27. Shahid, W., Khan, F., Makda, A., Kumar, V., Memon, S., & Rizwan, A. (2020). Diabetic ketoacidosis: Clinical characteristics and precipitating factors. Cureus, 12(6), e10792.
28. Sieben, N., & Ramanan, M. (2025). Research priorities for diabetic ketoacidosis: An evidence and gap mapping review. Medical Sciences, 13(2), 53.
29. Sudhanshu, S., Jevalikar, G., Das, P. K., Singh, P. K., Bhatia, E., & Bhatia, V. (2016). Acute respiratory distress syndrome: A rare complication in pediatric diabetic ketoacidosis. Indian Journal of Pediatrics, 83(5), 463–465.
30. Tsui, J., Bernardo, R., & Brown, B. (2019). Prospective study of balanced crystalloids versus saline in patients with diabetic ketoacidosis [abstract]. Critical Care Medicine, 47, 131.
31. Umpierrez, G. E., Davis, G. M., ElSayed, N. A., Fadini, G. P., Galindo, R. J., Hirsch, I. B., et al. (2024). Hyperglycemic crises in adults with diabetes: A consensus report. Diabetes Care, 47(8), 1257–1275.

32. Veauthier, B., & Levy-Grau, B. (2024). Diabetic ketoacidosis: Evaluation and treatment. American Family Physician, 110(5), 476–486.