Rate of Admission to the Intensive Care Unit in Patients with Diabetic Ketoacidosis and Its Associated Risk Factors: A Single-Center Experience

ABSTRACT

Objective: Diabetic ketoacidosis is one of the most common causes of admission to the intensive care unit in Saudi Arabia. This study aimed to investigate the rate of diabetic ketoacidosis-related intensive care unit admission and related risk factors and to determine the rate of intensive care unit readmission and mortality in a single tertiary health care center.

Methods: This retrospective record review study was based on diabetic ketoacidosis patients aged ≥15 years admitted to the intensive care unit of King Abdulaziz University Hospital from 2018 to 2020. Associations between variables such as patient demographics, precipitating factors, biochemical data, intensive care unit stay details, complications within the study period, and history of readmission to intensive care unit were performed. Statistical analysis was done using RStudio program. Factors associated with the primary outcome variables were further entered in a multivariate binary logistic regression analysis to assess the independent relationships.

Results: Of all diabetic ketoacidosis-related admissions, 28.4% of the admissions matched the study criteria. In 50% of cases, the precipitating cause for diabetic ketoacidosis which leads to intensive care unit admission was medication nonadherence, followed by infectious disease and severe diabetic ketoacidosis. Based on the multivariate regression analysis using patients’ age and medication incompliance as independent variables, being an older adult (>60 years) was the sole risk factor for death among patients under study (odds ratio = 23.3, 95% confidence interval, 3.0-65.3, P = .005).

Conclusion: Our findings highlight that the intensive care unit admission rate of diabetic ketoacidosis remains a significant health problem. Significant independent associated factors for intensive care unit admission were old age and medication nonadherence.

Keywords: Diabetes, diabetic ketoacidosis, ICU admission, medication nonadherence

Introduction

Diabetes mellitus (DM) is an epidemic of the modern era. A notable portion of the Saudi population is diagnosed with DM. Throughout the years, the number of DM cases in Saudi Arabia has been increasing. It is reported that the prevalence of DM in Saudi Arabia is among the highest in the Middle East and worldwide. Diabetic ketoacidosis (DKA) is a common and potentially fatal yet preventable acute complication of DM. A systematic review conducted in Qatar found that Saudi Arabia had the highest incidence of type 1 DM (T1DM)-related DKA at 35 per 100 000, across multiple Arabian nations, characterized by the triad of hyperglycemia, ketosis, and acidosis (Table 1).

In recent years, it has been observed that the admission rate of DKA patients to the ICU due to DKA or DKA-precipitated critical illness has escalated by nearly 5-fold. There are many proposed scoring systems modules to assess ICU admissions of severe DKA. The indications of DKA severity requiring ICU or high dependency unit admission suggested by the Saudi Ministry of Health are:

- Glasgow Coma Scale (GCS) <12
- pH <7.1
- Serum ketones >6.0 mmol/L
- HCO₃⁻ <5.0 mmol/L
- K⁺ <3.3 or >6.0 mmol/L
- Systolic blood pressure <90 mmHg
- SpO₂ <92% at room temperature and pulse rate >100 or <60 bpm
- Urine output <0.5 mL/kg/h or evidence of an acute kidney injury.


DOI: 10.5152/erp.2023.23265
province of Saudi Arabia. Thus, we performed this study to identify the rate of DKA-related ICU admission and its outcomes in the western region of Saudi Arabia.12

In an earlier study by our group, we identified 176 adult DKA patients treated at our hospital, most of whom were aged between 21 and 40 years, and ICU admission was documented in 10.1% of patients.9 Another study from Saudi Arabia found that the most prevalent causes of admission to the ICU were DKA and neurological emergencies, each comprising 21.6% of all ICU admissions.10 Additionally, it also showed that patients with 2 or more DKA-related admissions per year tended to be readmitted to ICU more repeatedly than those with 1 episode (P = .001).1 Researchers in Canada reported that their readmission and mortality rates were 36% and 9% over 1 year, respectively.11 However, little is known about the actual situation of DKA-related ICU admission and its outcomes in the western province of Saudi Arabia.12 Thus, we performed this study to identify the rates of ICU admission and its associated risk factors among adult patients admitted with DKA, as well as their rates of readmission and mortality.

Materials and Methods

Aim and Objectives

This study aimed to investigate the rate of (ICU) admissions of (DKA) patients and to determine risk factors associated with the admissions, rate of readmission and mortality.

Study Design, Setting, and Population

This retrospective observational study was conducted at King Abdulaziz University Hospital, a tertiary care center in Jeddah, Saudi Arabia. The investigators reviewed the electronic files of all patients who presented to the emergency department of King Abdulaziz University Hospital with DKA between January 2018 and December 2020. The study was approved by the Institutional Review Board of King Abdulaziz University Hospital (ref: 388-21).

Table 1. Criteria for Diagnosing DKA

<table>
<thead>
<tr>
<th>Marker</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose level</td>
<td>250 mg/dL</td>
</tr>
<tr>
<td>Serum bicarbonate (HCO₃⁻) level</td>
<td>≤18 mEq/L</td>
</tr>
<tr>
<td>pH</td>
<td>&lt;7.30</td>
</tr>
<tr>
<td>Ketonemia</td>
<td>Positive</td>
</tr>
</tbody>
</table>

DKA, diabetic ketoacidosis.

Table 2. Demographic Characteristics, Precipitating Factor, Hospital Stay, and Patients-Related Data During the First Admission (n = 50)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Missing</th>
<th>Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0 (0%)</td>
<td>Female</td>
<td>26 (52.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Male</td>
<td>24 (48.0%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0 (0%)</td>
<td>15-40</td>
<td>34 (68.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>41-60</td>
<td>8 (16.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>&gt;60</td>
<td>8 (16.0%)</td>
</tr>
<tr>
<td>Nationality</td>
<td>0 (0%)</td>
<td>Saudis</td>
<td>24 (48.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Non-Saudis</td>
<td>26 (52.0%)</td>
</tr>
<tr>
<td>Precipitating factors</td>
<td>0 (0%)</td>
<td>Infections or wounds</td>
<td>16 (32.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Incompliance to medications</td>
<td>25 (50.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Incompliance to diet</td>
<td>15 (30.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Start hyperglycemic medicationsa</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Insulin-related issues</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Pregnancy</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>First presented as DM</td>
<td>9 (18.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>More than 1 precipitating factor</td>
<td>20 (40.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Miscellaneous</td>
<td>6 (12.0%)</td>
</tr>
<tr>
<td>Type of miscellaneous conditionsb</td>
<td>0 (0%)</td>
<td>ACS</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>AKI on top of CKD</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Pancreatitis</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Stroke</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Type of diabetes</td>
<td>0 (0%)</td>
<td>T1DM</td>
<td>44 (88.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>T2DM</td>
<td>6 (12.0%)</td>
</tr>
<tr>
<td>Length of hospital stay, median (IQR)</td>
<td>0 (0%)</td>
<td>Days (overall)</td>
<td>3.0 (2.0, 4.8)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Days (T1DM)</td>
<td>3.0 (2.0, 4.3)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Days (T2DM)</td>
<td>3.0 (2.3, 4.5)</td>
</tr>
<tr>
<td>Duration of DM, median (IQR)</td>
<td>7 (14%)</td>
<td>Years</td>
<td>5.0 (1.0, 10.5)</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>0 (0%)</td>
<td>Yes</td>
<td>7 (14.0%)</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>39 (78%)</td>
<td>Yes</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Blood lactic acid</td>
<td>20 (40%)</td>
<td>Negative</td>
<td>16 (33.3%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>Positive</td>
<td>14 (46.7%)</td>
</tr>
<tr>
<td>Blood pH on admission, median (IQR)</td>
<td>0 (0%)</td>
<td>pH</td>
<td>7.0 (6.9, 7.0)</td>
</tr>
<tr>
<td>pH categories</td>
<td>0 (0%)</td>
<td>≥7.0</td>
<td>26 (52.0%)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>&lt;7.0</td>
<td>24 (48.0%)</td>
</tr>
<tr>
<td>Serum bicarbonate, median (IQR)</td>
<td>4 (8.0%)</td>
<td>Unit</td>
<td>6.0 (5.0, 8.0)</td>
</tr>
<tr>
<td>Serum potassium, median (IQR)</td>
<td>0 (0%)</td>
<td>Unit</td>
<td>3.5 (3.2, 4.5)</td>
</tr>
</tbody>
</table>

DM, diabetes mellitus; T1DM, type 1 diabetes; T2DM, type 2 diabetes. ACS, acute coronary syndrome; AKI, acute kidney injury; CKD, chronic kidney disease; IQR, interquartile range.
aKnown to increase blood glucose as steroids.
bDescriptive data are based on 6 patients with miscellaneous conditions.

King Abdulaziz University Hospital (ref: 388-21). The study protocol followed the ethical standards of the responsible committee based on the Good Clinical Practice Guidelines. All eligible participants or their relatives were provided with comprehensive information about the study, including its purpose, benefits, and data protection measures, and informed consent was obtained.
Data Collection and Definitions

Diabetic ketoacidosis was defined in this study based on a blood glucose level >250 mg/dL, serum bicarbonate level ≤18 mEq/L, serum pH <7.30, and the presence of ketosis. Severe DKA was considered for patients with a pH <7.0.13 The DKA International Classification of Diseases (ICD) 10 code was used to retrieve admission data from the Health Information System database. Patients who fulfilled the criteria of DKA and were ≥15 years of age, the legal age based on our institutional policy, were included in this study. Patients with missing data and a hyperosmolar hyperglycemic state were excluded. The retrieved data were categorized into demographic data, clinical and biochemical data, precipitating factors, and admission outcomes. Patients’ demographic data included age at presentation with DKA, age at which the first diabetes manifestation was diagnosed, gender, and nationality. The clinical laboratory tests included glycated hemoglobin (HbA1c; HbA1c above 10% indicated poorly controlled diabetes), lactic acid, and blood pH. The presence of complications such as renal impairment and cerebral edema was also recorded. Precipitating factors were grouped as follows: infections, missing insulin doses, nonadherence to diet, receiving medications known to increase blood glucose levels (e.g., steroids), injection technique-related issues, pregnancy, and miscellaneous. Outcomes such as length of ICU stay, history of readmission to the ICU within the study period, duration between the first and second ICU admission, and, if applicable, the cause of death were recorded.

Statistical Analysis

Statistical analysis was carried out using RStudio (R version 4.1.1). The rate of readmission was assessed using a 1-sample proportions test with continuity correction. Due to the small proportions of patients in distinct study groups, factors associated with readmission and mortality were assessed using a Fisher’s exact test for categorical data with simulated P-values based on 2000 replicates. For continuous data, a Wilcoxon rank-sum test was applied. Factors associated with the primary outcome variables were further entered in a multivariate binary logistic regression analysis to assess the independent relationships. Results were expressed as odds ratio (OR) and 95% confidence intervals (95% CIs). Statistical significance was considered at P < .05.

Results

Demographic Characteristics and Precipitating Factors

The data of a total of 176 adult DKA admissions were retrieved during the study period, of whom only 50 were admitted to the ICU and met the study inclusion criteria, corresponding to (28.4%) of all DKA-related admissions. More than half of the patients were females (52.0%), Saudis (52.0%) and aged 15-40 years (68.0%). Incompliance to medications and diet was prevalent among 50.0% and 30.0% of patients, respectively. Less than a half of them had more than 1 precipitating factor. The remaining characteristics are demonstrated in Table 2.

Characteristics of the First Hospital Admission

All the included patients were admitted to the ICU during hospitalization. The majority of patients had T1DM (88.0%), and the median (interquartile range [IQR]) duration of the disease was 5.0 years (1.0-10.5). The median (IQR) length of ICU stay was 3.0 days (2.0-4.8). In regard to DKA-related complications, renal impairment was documented in 7 (14%) patients out of the whole cohort. None of the patients developed cerebral edema, whereas 46.7% of patients had lactic acidosis. Blood pH was <7.0 among 48.0% of patients. More details about other laboratory characteristics are provided in Table 2.

Characteristics of Readmission

Generally, 17 patients were readmitted to the hospital during the study period, representing 34.0% of patients (95% CI, 21.6-48.9). Notably, 6 patients were readmitted to the ICU in the current study. This accounted for 12.0% of the whole sample (95% CI, 5.0-25.0) and 35.3% of those who were readmitted (95% CI, 15.3-61.4). All the patients who were readmitted had T1DM. The median (IQR) period between the first and second readmissions was 5.0 weeks (2.5-24.0) and the majority of them (71.4%) had a HbA1c level of ≥10%. Renal impairment occurred in 23.5% of readmitted patients (Table 3). The characteristics of the second readmission were not significantly different between those who were admitted to ICU and those who did not (Table 3).

Factors Associated with Intensive Care Unit Readmission and Death

Focusing on the overall cohort (n = 50), readmission to ICU was not associated with any of the demographic and health-related characteristics, as well as the characteristics of the first admission (Table 4 and Figures 1-5). Regarding group-based differences in mortality, results showed no significant difference between dead and alive patients in terms of ICU readmission during the second hospitalization and other demographic, health-related, and first-admission-related characteristics (Table 4 and Figures 6-10). However, the proportion of dead patients was significantly higher among older adults (aged >60 years, 55.6%) compared to other age categories (22.2% among the 41-to-60-year age category and 22.2% among the 15-to-40-year age category, P = .001).
Additionally, incompliance to medications was significantly lower among dead patients compared to their counterparts (11.1% vs. 58.5%, respectively, \(P = .023\), Table 5). However, based on the multivariate regression analysis using patients’ age and medication incompliance as independent variables, being an older adult (>60 years) was the sole risk factor for death among patients under study (OR = 23.3, 95% CI, 3.0-65.3, \(P = .005\), Table 6).

**Discussion**

**Admission and Readmission Rates**

This study explored the ICU admission rates and associated risk factors among adult patients with DKA. The results showed that the rate of ICU admission in this current study was 28.4%, slightly higher than the study of Chang and Shapiro, which reported an admission rate between 12.2% and 26.5%. Diabetic ketoacidosis patients usually require ICU care due to disease severity, comorbidities, or complications.

![Figure 1. The differences between DKA patients based on ICU readmission during the study period. The result was nonsignificant for length of stay (\(P = .149\)). DKA, diabetic ketoacidosis; ICU, intensive care unit.](image1)

![Figure 2. The differences between DKA patients based on ICU readmission during the study period. The result was nonsignificant for duration of diabetes (\(P = .697\)). DKA, diabetic ketoacidosis; ICU, intensive care unit.](image2)

The present study results also revealed that one-third of the patients had a recurrent admission to the ICU within the subsequent 5 weeks. Similar to our study, a study conducted in Australia and New Zealand reported a readmission rate of 21% out of 115 admissions to the ICU over a period of 13 years. Al Dawish et al. concluded that DKA patients with at least 2 DKA crises per year were more likely to be readmitted to ICU.

**Age**

In our study, most of the cases were aged 15-40 years, and we found that patients from the geriatric group had the highest odds of ICU admission compared to ICU admission per age for each DKA crisis.
admission. Similarly, Ramaesh\textsuperscript{15} and Blanchard et al\textsuperscript{16} reported a median age of 44 (IQR 29-56) and 46 (IQR 29-58) years in their studies, respectively, but did not assess the effects of age on ICU admission.

**Precipitating Factors for Intensive Care Unit Admission**

This study concludes that treatment nonadherence was the prime precipitant for DKA, followed by infectious diseases. Our results are similar to those of Venkatesh et al\textsuperscript{7} and Mendez et al,\textsuperscript{17} who reported that insulin nonadherence was the most important precipitating factor for ICU admission. Comparatively, George et al\textsuperscript{18} found that infectious disease was the leading precipitant for DKA in their study cohort. We believe that treatment nonadherence might be multifactorial, including social and insurance-related factors.\textsuperscript{19}

By broadening the scope beyond our major precipitant, it could be observed that the rate of medication nonadherence in patients with chronic diseases in Saudi Arabia is considerably high.\textsuperscript{20} In a study conducted in 2021 by Altamimi et al,\textsuperscript{21} who investigated the reasons for patients’ nonadherence to chronic disease medications, they observed that forgetfulness was the main reason behind the nonadherence, followed by worries about the side effects of the medications. Furthermore, a review study has shown that structured self-management education of diabetes and regular blood glucose monitoring, especially during times of illness, stress, or when experiencing symptoms of hyperglycemia, results in the reduction of DKA rates. Acknowledging these risk factors and strategies for risk
mitigation is crucial to identify patients with elevated DKA risk such as (T1DM).\textsuperscript{22}

**Severe Diabetic Ketoacidosis**

One of the most highlighted findings from the analysis was that severe DKA (pH <7.0) was significantly associated with increased rates of admission to the ICU, which is one of the DKA markers warranting ICU admission that was mentioned previously. These results were concordant with those of a previous similar cohort study, which revealed that most DKA patients admitted to the ICU were classified as severe DKA.\textsuperscript{15} This finding was also supported by Lee et al,\textsuperscript{23} performed in Australia, which concluded that lower pH levels were related to delayed DKA resolution and possible ICU admission. Similar results were also reported by Al Dawish et al,\textsuperscript{1} who found that low pH, in addition to comorbidities and complications, was related to ICU admission, and a study from India, which found that ICU care was required in 6.7\% and 47.4\% of those with moderate and severe DKA, respectively.\textsuperscript{18} Multiple risk factors were associated with ICU admission in a retrospective study done in Qatar, it included 229 patients with DKA who were admitted to the ICU compared to patient who did not, they have concluded that ICU group had older age, higher body mass index and were predominantly males. In addition, they had higher levels of urea, creatinine, C-reactive protein, anion gap, and lower venous pH and bicarbonate level at admission than those not requiring ICU management of DKA ($P < .001$).\textsuperscript{24}

![Figure 7](image7.png)
**Figure 7.** The differences between DKA patients based on the status of death during the study period. The result was nonsignificant for duration of diabetes ($P = .132$). DKA, diabetic ketoacidosis.

![Figure 8](image8.png)
**Figure 8.** The differences between DKA patients based on the status of death during the study period. The result was nonsignificant for blood pH on admission ($P = .116$). DKA, diabetic ketoacidosis.

![Figure 9](image9.png)
**Figure 9.** The differences between DKA patients based on the status of death during the study period. The result was nonsignificant for serum bicarbonate ($P = .100$). DKA, diabetic ketoacidosis.

![Figure 10](image10.png)
**Figure 10.** The differences between DKA patients based on the status of death during the study period. The result was nonsignificant for serum potassium ($P = .234$). DKA, diabetic ketoacidosis.
concluded that lactic acidosis was observed in 55% of DKA patients, or mortality.25 On the other hand, a cohort study published in 2021 with DKA found no correlation between lactic acidosis and morbidity associated with ICU admissions. Likewise, a study involving 68 patients of DKA patients had lactic acidosis but was not significantly associated with AKI on top of metabolic acidosis. Furthermore, we found that a high percentage (46.7%) of the patients presented as T2DM, type 2 diabetes. It is worth mentioning that 14% of the patients in our study had renal impairment, which has also contributed to the worsening of metabolic acidosis. Furthermore, we found that a high percentage (46.7%) of DKA patients had lactic acidosis but was not significantly associated with ICU admissions. Likewise, a study involving 68 patients with DKA found no correlation between lactic acidosis and morbidity or mortality.25 On the other hand, a cohort study published in 2021 concluded that lactic acidosis was observed in 55% of DKA patients, while significantly high levels of lactic acid were detected in only 16% of the patients.26 Altogether, these findings showed that lactic acidosis in DKA was more common than previously reported. However, it should also be noted that lactic acidosis may result from other causes such as secondary to an infection, dehydration or ischemia.

### Glycated Hemoglobin

Glycated hemoglobin is an essential indicator of hyperglycemia, and most patients in our study with ICU admission had poorly controlled DM (HbA1c is more than 10%). Likewise, in a study by George et al,18 the mean reported HbA1c was 12.1 ± 2.7 for DKA patients admitted to ICU. Moreover, it is crucial to maintain blood glucose levels at their lowest to normal levels as this slows the progression of possible complications; this can be achieved by regular blood glucose monitoring.27 It is supported by a prospective study published in the USA, which found that better glycemic control is attained by regular blood glucose monitoring.28

### Length of Intensive Care Unit Stay

The median length of ICU stay in this present study was 3.0 (IQR 2.0, 4.8) days. Freire et al29 found similar outcomes with a mean of 4 ± 2.5 days. On the contrary, Ramaesh15 observed that the hospital stay related to the original precipitating factor even after the resolution of DKA.

### Mortality Rate

In this study, 9 patients died during the study period, and we found that DKA was not the prime cause in any of them after carefully examining the patients’ data. Comparatively, an earlier Saudi publication in 2020 reported a mortality rate of 1.83%.1 However, many studies that investigated DKA-related mortality did not differentiate between death directly related to DKA or its precipitating factors. Although our study reached its aim of determining the rates of ICU admission, there were some limitations that should be highlighted. Since this was a single-center retrospective study, it contained some of the limitations inherent in retrospective studies, including incomplete data or limited documentation in some patients that reduced the number of our sample as patients with missing information were excluded. Additionally, no information about the direct cause of ICU admission was collected.

### CONCLUSION

Our findings highlight that the ICU admission rate of DKA still remains a significant health problem. The leading factors for ICU admission were old age and medication nonadherence. Although the mortality...
observed in the patients of this study was not related to DKA, it was associated with the underlying admitting condition.

**Ethics Committee Approval:** This study was approved by Ethics Committee of King Abdulaziz University Hospital (Approval No: 388-21, Date: August 9, 2021).

**Informed Consent:** All eligible participants or their relatives were provided with comprehensive information about the study, including its purpose, benefits, and data protection measures, and informed consent was obtained.

**Peer-review:** Externally peer-reviewed.


**Declaration of Interests:** The authors have no conflict of interest to declare.

**Funding:** This study received no funding.

**References**