The Journal of Health Design

AUDIT

Determinants of diabetic ketoacidosis (DKA) severity and clinical characteristics of DKA: A retrospective audit in a metropolitan ICU in Australia

Areeb Athar[1], Fraser Magee[2], Mainak Majumdar[2]

1. The Alfred Hospital, Melbourne, VIC, Australia
2. Intensive Care Unit, Werribee Mercy Hospital, Werribee, VIC, Australia

SUMMARY

The incidence and prevalence of diabetes mellitus is of growing clinical concern in Australia. Diabetic ketoacidosis (DKA) is a serious metabolic complication. We audited baseline characteristics of patients admitted to a metropolitan intensive care unit (ICU) in Australia with a discharge diagnosis of DKA. In our cohort, 97.8 per cent of patients had elevated HbA1c suggesting poor long-term diabetes control; 28 per cent of ICU admissions represented repeat presentations; and treatment non-compliance was identified as a significant contributor.

Key Words: Diabetic ketoacidosis; DKA; ICU; diabetes; hyperglycaemia; non-compliance

To Cite: Athar A, Magee F, Majumdar M. Determinants of diabetic ketoacidosis (DKA) severity and clinical characteristics of DKA: A retrospective audit in a metropolitan ICU in Australia. JHD. 2025;10(1):699–706. https://doi.org/10.21853/JHD.2025.239

Corresponding Author: Areeb Athar (areebathar99@gmail.com): The Alfred Hospital, Melbourne, VIC, Australia

ABSTRACT

We undertook a retrospective review of patients admitted to a metropolitan intensive care unit (ICU) in Victoria, Australia with diagnosis of diabetic ketoacidosis (DKA) between January 1, 2020 and March 31, 2023 to identify baseline characteristics and markers of severity. The average age of patients in our cohort was 42 years, with a female preponderance. Eighty per cent of presentations admitted to ICU had mild to moderate DKA at presentation to the Emergency Department. We found a significant incidence of recurrent presentations and non-compliance. Antecedent glycaemic control was uniformly poor and absence of previous diagnosis of diabetes was associated with severe DKA on presentation to hospital.

BACKGROUND

Diabetes represents a significant epidemiological concern in Australia, with prevalence rising from 3.3 per cent in 2001 to 5.3 per cent in 2022.[1] It was the seventh most common cause of mortality in Australia, accounting for more than 3 per cent of all deaths in 2021 and 2022 alone.[2]

Diabetic ketoacidosis (DKA) is a severe metabolic complication of diabetes, involving a state of relative or absolute insulin deficiency, characterised by a triad of hyperglycaemia (blood glucose >13.9mmol/L), acidaemia (pH <7.30), and ketosis (serum ketones >3 mmol/L).[3] DKA is a largely preventable and treatable condition, but it can result in significant morbidity, prolonged hospital stays, and at times can be fatal.[4] Although predominantly seen in individuals with Type 1 diabetes mellitus (T1DM)[5], DKA is increasingly also recognised as a complication in patients with Type 2 diabetes mellitus (T2DM).[6]

Although risk-adjusted mortality rates from DKA in Australasia have remained stable over recent decades, there has been a five-fold increase in the incidence of intensive care unit (ICU) admissions due to DKA—from 0.97/100,000 ICU admissions in 2000 to 5.3/100,000 ICU admissions in 2013, representing a substantial burden on the individual and on the healthcare system.[7] Previously published data from Victoria show a rise in DKA presentations for patients with T1DM between 2002 to 2016.[8]

Increasingly, patients also present with euglycemic ketoacidosis with increasing use of sodium glucose-linked transport protein-2 (SGLT-2) inhibitors.[9]

The aims of this study were two-fold:

1. To investigate the baseline characteristics of patients with DKA admitted to a metropolitan ICU in Melbourne, Australia, where DKA has been a top-five diagnosis since the ICU opened in August 2018, at variance from trends observed in the Adult Patient Database (APD) maintained by the Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcomes and Research (CORE).

2. To determine the relationship between DKA severity and demographics-specific precipitants (sex, diabetes status, age), antecedent glycaemic control (HbA1c), and resource use (ICU length of stay, hospital length of stay).

METHOD

Following approval from the Human Research Ethics Committee (HREC), we queried the ANZICS APD to identify patients admitted to the ICU at a metropolitan teaching hospital in the western suburbs of Melbourne, Australia between January 1, 2020 and March 31, 2022 with the primary diagnosis of DKA, using the APACHE IIIJ diagnosis code 702.01.

We reviewed clinical records of eligible patients to confirm they met diagnostic criteria for DKA:[4]

- Hyperglycaemia (blood glucose >11mmol/L)
- Ketonemia (capillary serum ketones >3mmol/L)
- Acidaemia: pH <7.3 and/or serum bicarbonate <15 mmol/L

We also included patients with euglycemic ketoacidosis states (blood glucose <14mmol/L) in the audit to capture SLGT-2 associated presentations but excluded presentations with hyperglycaemic hyperosmolar states (HHS) (i.e., serum osmolality >320 mOsm/L) and mixed hyperglycaemic states. We also excluded patients with insufficient or incomplete data.

We collected patient data, including demographic data, ICU and hospital data (ICU length of stay, hospital length of stay, mortality), and data specific to diabetes (pH, HbA1c, documented precipitant) using both patient records and ANZICS APD data. We categorised patients as having severe (pH<7.0), moderate (pH ≥7.0–7.24), and mild (pH 7.25–7.3) DKA.[4]

We categorised underlying reasons for presentation of DKA from clinical notes and discharge summaries as follows:

- Missed/recently changed medication dose(s)
- Non-compliance/poor control (as per collateral history/clinician assessment)
- Sepsis/infection
- Recently diagnosed Type 1 diabetes mellitus (diagnosed during admission)
- Recently diagnosed Type 2 diabetes mellitus (diagnosed during admission)
- SGLT2-related
- First presentation of DKA
- Not other specified (NOS), where the cause could not be classified as above.

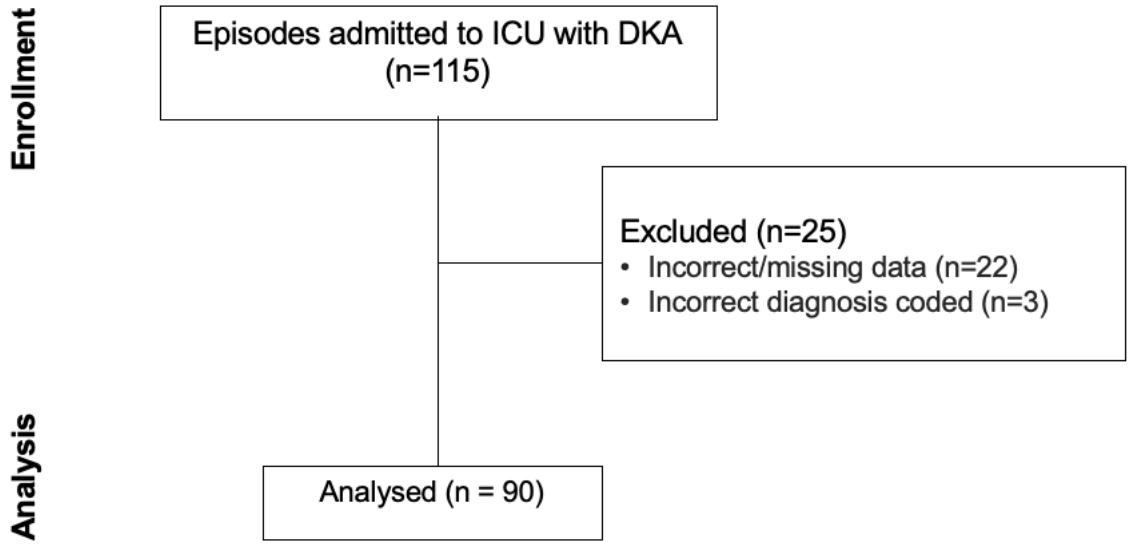
We entered data into an Excel spreadsheet (Microsoft Excel, Redmond, WA). We report results as numbers and proportions, means with standard deviations (SDs), or medians with interquartile range (IQRs). We assessed for normality, and groups compared using chi-squared, Student's t, or Wilcoxon

rank-sum tests as appropriate. Patients with missing data were excluded from the final analysis. We performed data analysis using STATA version 15.1 (StataCorp, College Station, TX).

RESULTS

Between January 1, 2020 and March 31, 2022, we identified 115 episodes of admission to ICU with a discharge diagnosis of DKA, representing 55 per cent of all admissions to our hospital via the Emergency Department with DKA over the same time period. On chart review, 22 DKA episodes had missing data on the clinical patient record. Three episodes of HHS were misclassified as DKA. We included 90 episodes meeting the biochemical criteria for DKA in the final analysis (Figure 1). Of these, 28 per cent (n=25) were repeat presentations.

Figure 1: Consort diagram for DKA episodes analysed



The mean age was 42.16 (SD 17.04) years and the sex distribution was 47.8 per cent male (n=43) versus 52.2 per cent female (n=47). We determined that 59.8 per cent (n=52) were diagnosed with Type I diabetes (T1DM), and 27.6 per cent (n=24) were diagnosed with Type 2 diabetes (T2DM), while 12.6 per cent (n=11) were either previously undiagnosed or awaiting completion of diabetes workup as per clinical documentation. We have provided demographic characteristics (Table 1).

Table 1: Baseline characteristics of DKA admissions

Variable	Values
Age (SD)	42.16 (17.04)
Male (%)	43 (47.8)
Diabetes status Type 1: Type 2 (n)	52:24
Repeat presentations of DKA (%)	28
ICU length of stay (days: IQR)	1.65 (1.09–2.86)
Hospital length of stay (days, IQR)	4.74 (2.78–7.10)
Severe DKA (pH<7.0) (%)	20.0 (18)
HbA1c >7%	97.8

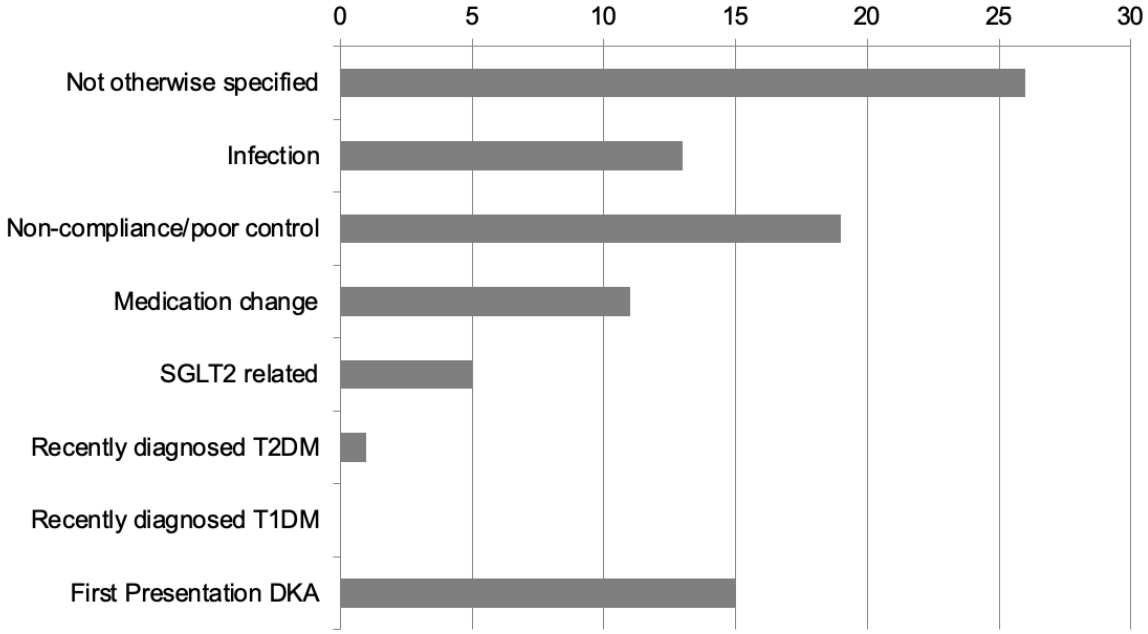
For patients admitted to the ICU, the median length of hospital stay (LOHS) was 4.74 days (IQR 2.78–7.10), and the median LOS in ICU (ICU-LOS) was 1.65 days (IQR 1.09–2.86). For comparison, the median LOHS for DKA admissions not admitted to the ICU and managed in the ward during this period

in the study hospital was 3.86 days (IQR 1.78–5.48). The median time from presentation to Emergency Department to ICU admission was 4.57 hours (IQR 3.12–6.97).

The median HbA1c was 11.75 percent (IQR 10.3–13.4), with 97.8 per cent of values ranging >7.0 per cent, indicating poor glycaemic control.

According to the data, 20 per cent (n=18) of presentations to the Emergency Department had severe DKA (pH<7.0), while 80 per cent (n=72) presented with mild to moderate DKA (pH 7 to 7.3). Non-compliance/poor control (21.1 per cent; n=19) was the most common precipitating factor identified for DKA episodes admitted to the ICU, followed by the first presentation of DKA for that patient (16.7 per cent; n=15). Other precipitants included infection (14.4 per cent; n=13), medication change (12.2 per cent; n=11), SGLT2-related (5.6 per cent; n=5), and recently diagnosed T2DM (1.1 per cent; n=1). No specified causes were identified in 28.9 per cent (n=26) of presentations (Figure 2).

Figure 2: Distribution of DKA precipitants



The data show that both Type 1 diabetes (p=0.01) and Type 2 diabetes (p=0.01) were associated with presentation of severe DKA, as was absence of previous diabetes status (p=0.01). Age and sex were not associated with presentation with severe DKA (Table 2).

Table 2: Association of baseline variables with DKA severity

Variable	pH <7.0	pH ≥7.0	*p* value
Age	42.5	41.1	0.83
Male Sex (%)	9 (50)	34 (47.2)	0.83
Type 1 diabetes	8 (44.4)	44 (63.8)	0.01*
Type 2 diabetes	4 (22.2)	20 (29)	0.01*
No previous diabetes/not overwise specified	6 (33.3)	5 (7.25)	0.01*
ICU length of stay (days, IQR)	1.65 (1.3–3.6)	1.67 (1.1–2.7)	0.83
Hospital length of stay (days, IQR)	5.18 (2.3–7.8)	4.61 (2.8–6.9)	0.6
HbA1c (%, IQR)	12.95 (11.5–14.5)	11.4 (10.0–13.05)	0.11

Resource use (ICU and hospital length of stay) was not different between severe and non-severe DKA presentations and LOHS for patients admitted to ICU was longer than those managed in a ward setting. HbA1c levels were not significantly different between presentations with severe and non-severe DKA (12.95 per cent vs 11.4 per cent; p=0.11). We present age- and sex-based distribution of DKA severity on presentation (Tables 3 and 4).

Table 3: Sex-based distribution of DKA severity

Sex	pH 7.25–7.3	pH ≥7.0–7.24	pH <7.0
Male	10	24	9
Female	6	32	9

Table 4: Age-based distributions of DKA severity

Sex	pH 7.25–7.3	pH ≥7.0–7.24	pH <7.0
17–30	2	24	3
31–40	2	10	7
41–50	4	7	3
51–60	2	8	3
61–70	2	6	1
71–80	2	1	1
> 80	2	0	0

DISCUSSION

Our data reflect practice at a metropolitan hospital in Victoria, Australia. More than half of patients (55 per cent) presenting to the Emergency Department with DKA were admitted to the ICU.

In our cohort of 90 presentations admitted to the ICU with DKA, more episodes involved female patients (n=47, 52.2 per cent) than males (n=43, 47.8 per cent). This finding is consistent with international data.[10,11] Of note, the gender distribution in our cohort differs from previously published Australian data from Queensland (119 presentations in 2013 across three major Emergency Departments servicing a population catchment of more than 1 million where the male-to-female ratio of presentations with DKA was 1.4:1)[12] and Victoria (23,628 presentations with DKA to Emergency Departments between 2002–2016, 50.5 per cent males).[8] The difference may reflect that our cohort was restricted to adult patients only, with most patients younger than 40, an age group shown to have a female predominance for DKA.[13]

Our study population comprised more Type 1 than Type 2 diabetics. This finding matches a previous study where 75.8 per cent of patients had Type 1 diabetes and 24.1 per cent had Type 2 diabetes.[6]

Twenty per cent of our cohort presented with severe DKA, whereas previously published data suggest an incidence of 11.8–16.1 per cent for presentation with severe DKA.[3] While most episodes had no clear underlying cause, the type of diabetes had a significant association with presentation to hospital with severe DKA. Other parameters such as age, sex, length of ICU and hospital stay, and different precipitants assessed in the present study of DKA were not associated with severity of DKA presentation.

The most common specific precipitant was non-compliance/poor control followed by first presentations of DKA. Our findings are similar to previously published data, where the most common specific precipitant reported was non-compliance/poor control (as noted in the patient history).[12,14] This is concerning as medication non-compliance has been shown to be a major contributor of economic

burden.[15] Systemic factors such as limited access to endocrine specialists and limited engagement with primary care may also contribute to non-compliance/poor control, exacerbating both incidence and severity of DKA presentations. Infection[16] and medication changes[5] have also been reported as common precipitants of DKA and our sample also included these precipitants. We also identified a small number of patients with SLGT-2 medication–related DKA, contributing to the growing evidence for this drug class as a precipitant.[17]

Elevated HbA1c (>7.0 per cent) is a significant risk factor for cardiovascular disease and stroke in patients with diabetes[18] and a prognostic marker for morbidity and mortality in critically ill patients.[19] Median HbA1c in our study was 11.75 per cent, with most of the HbA1c values above >13.01 per cent. HbA1c levels were comparable between episodes of severe and non-severe DKA admitted to the ICU. Median HbA1c in our cohort is comparable to previously reported median HbA1c of 11.4 per cent[5] and suggests poor long-term control in this group of patients. This is also evidenced by the high rate (28 per cent) of repeat presentations. Protocolised inpatient diabetes education and referrals to structured outpatient diabetes education, with particular focus on first and repeat DKA presenters, which have been shown to reduce HbA1c levels, may have been of potential benefit to patients in our cohort.[20] Recurrent presentation with DKA is associated with increased mortality and healthcare fragmentation.[21]

Most DKA episodes admitted to ICU were of moderate severity on presentation to the hospital. Median time to ICU admission (4.57 hours; IQR 3.12–6.97) is similar to previously published Australian data (4 hours; IQR 1.8–6.5).[7] Median ICU LOS (1.65 days; IQR 1.09–2.86) is comparable to previously published Australian data (1.74 days; IQR 1.03–2.80).[5,7] Median LOHS (4.74 days; IQR 2.78–7.10) for patients admitted to the ICU was longer at our centre than previously published Australian data (3.75 days; IQR 2.39–6.74)[7] and also longer than for DKA admissions not admitted to the ICU and managed in the ward at the study hospital (3.86 days; IQR 1.78–5.48). It is unclear whether the disparity in LOHS between patients admitted to ICU versus managed in the ward reflects differences in patient complexity or patient flow issues in the hospital.

The sample size and retrospective nature of the data from this single-centre audit limit generalisability, but provide important insights into the design of future prospective multi-centre studies. Further, as we accessed the paper-based medical records accessed by the investigators retrospectively, we cannot exclude the possibility of missing documentation. The HbA1c level was not available for all patients, nor were there specific records on the ethnicity of patients, outcome comparison between Type 1 and Type 2 diabetes, and consideration of the impact of COVID-19. These could be areas for future studies. Nevertheless, this audit may provide a snapshot of population characteristics, antecedent glycaemic control, and severity of presentation within the hospital's catchment.

CONCLUSION

The present study reinforces findings of previous audits and allows benchmarking of the hospital with previously published Australian DKA data. ICU-LOS was similar to previously published data while LOHS somewhat longer than previously published may reflect an improvement opportunity for inpatient management. High median HbA1c (11.8 per cent) suggests poor long-term diabetes control in our cohort and non-compliance in community and outpatient settings were major precipitants for DKA episodes in our cohort.

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ACKNOWLEDGEMENTS

The coauthors made the following contributions:

- AA planned, collected the data, conducted data analysis, and drafted the manuscript;
- FG conceptualised, planned, conducted the statistical analysis, and reviewed the manuscript;
- MM conceptualised, planned, and drafted the manuscript.

The authors also acknowledge the ANZICS CORE Committee's assistance in extracting hospital-specific and comparator data from contributing Australasian ICUs for this study.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

FUNDING

None

ETHICS COMMITTEE APPROVAL

Human Research Ethics Committee (HREC), Mercy Health.