Management of diabetic ketoacidosis following implementation of the JBDS guidelines: Where are we and where should we go?

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Abstract
Background: The Joint British Diabetes Society (JBDS) consensus guideline published in 2010 has provided the framework for the effective management of diabetic ketoacidosis (DKA) in adults in the UK.
Methodology: A retrospective study of 50 patient episodes admitted to our teaching hospital between February and December 2012, with a discharge diagnosis of DKA.
Results: Twenty-seven (54%) patients were male, mean (SD) age was 43 (21) years and duration of diabetes was 11 (9) years. In the first 60 minutes from diagnosis, median (interquartile range [IQR]) time to fixed rate intravenous insulin infusion (FRIII) was 49 (29–110) minutes and to intravenous fluids was 19 (0–42) minutes. During ongoing management, 46% of patients developed hypokalaemia and, of those, in 70% potassium supplementation was not prescribed as per protocol. Forty percent of patients experienced hypoglycaemia in the first 24 hours, of whom 80% had 10% dextrose prescribed appropriately according to protocol. Median time to hypoglycaemia from diagnosis was 12 hours 54 minutes. Median (SD) time to resolution of DKA was 12 hours 6 minutes. Eighty six percent of patients were reviewed by the diabetes specialist team during admission. No deaths due to DKA or complications of its management were reported. Median length of hospital stay was two days.
Conclusions: Adherence to the JBDS DKA guideline was good in the immediate stage of treatment. Inadequate metabolic monitoring, fluid management and iatrogenic hypoglycaemia remain areas of concern. A high proportion of patients received diabetes specialist nurse input with reduced length of stay and no recorded mortality. Our recommendations as a result of this audit include a strengthened programme of teaching and education for nursing and medical staff, focus on metabolic monitoring and improved patient contact after hospital discharge.

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Key words: diabetic ketoacidosis, Joint British Diabetes Society, diabetes mellitus, in-patient care

Introduction
DKA is an acute metabolic emergency occurring in individuals with absolute or relative insulin deficiency and is typically characterised by hyperglycaemia, ketonaemia and acidosis. Untreated or mismanaged, DKA can potentially lead to fatal complications and emerging data indicate that this is inextricably linked to the quality of hospital care.1

DKA is commonly associated with type 1 diabetes and poses a significant threat at the time of diagnosis.2,3 Amidst growing concerns about the rising burden of type 1 diabetes, incidence trends predict a doubling of newly diagnosed cases in Europe by 2020.4 However, the incidence of DKA at diagnosis of type 1 diabetes in the UK has remained unchanged at around 25% over the past 20 years.5 Data from the Diabetes Paediatric Audit in 2010 showed that 15.5% of children and young people had experienced one episode of DKA in the last five years and 10.4% had two or more events in the last five years.6 Furthermore, nearly 31% of individuals with type 1 diabetes in the UK were

Abbreviations and acronyms
ABCD Association of British Clinical Diabetologists
CBG capillary blood glucose
DKA diabetic ketoacidosis
FRIII fixed rate intravenous insulin infusion
ICU intensive care unit
JBDS Joint British Diabetes Society
NaDiA National Diabetes Inpatient Audit
NICE National Institute for Health and Care Excellence
UHL University Hospital of Leicester

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readmitted with DKA within a year from their initial hospital admission. A recent US study showed that period prevalence estimates of DKA in individuals with type 1 diabetes over the last decade were high at around 30% but remained stable over time. In March 2010, the JBDS published guidelines (subsequently revised in September 2013) on the management of DKA in adults. These guidelines were rapidly introduced by diabetes hospital teams across the UK and accepted as the national guideline for managing DKA. It was anticipated that such a move should significantly improve the management of people admitted with DKA which, prior to 2010, was deemed to be inconsistent with wide variations of care between hospitals in the UK. Key features included use of a FRIII, continuation of background (long acting/intermediate acting) insulin, preference for venous blood sampling, bedside blood ketone monitoring and commencement of 10% dextrose solution when blood glucose levels fall to less than 14 mmol/L alongside crystalloid fluid replacement on FRIII treatment. Subsequent to these developments, the NaDia 2012 suggested that nearly 78% of participating hospitals had either implemented or modified the JBDS DKA guidelines.

In February 2012, led by the Adult Inpatient Diabetes Steering Group, the UHL NHS Trust implemented a revised DKA guideline based on the JBDS DKA guidelines. Implementation of the guideline was supported by a dedicated DKA prescription and monitoring chart. It was agreed locally to retain the priming bolus dose of insulin since there was uncertainty about the timing of intravenous insulin administered to patients with DKA in the initial hours after admission to the UHL Emergency Department. A retrospective audit of the management of adult patients with DKA admitted to UHL using our own revised DKA protocol as the gold standard comparator of care, was conducted to review adherence and assess improvements in quality of care.

The aims of this audit were:
1. To assess adherence to DKA guidelines in patients managed according to a dedicated DKA prescription and monitoring chart available within a hospital setting.
2. To analyse outcome measures including immediate management up to 60 minutes after hospital admission, on-going management from 60 minutes to 24 hours, and treatment induced hypoglycaemia.
3. To assess the effectiveness of management including time to resolution of DKA, time to conversion to subcutaneous insulin, and length of hospital stay.

Methods
UHL NHS Trust is one of the six biggest hospital Trusts in the UK, treating in excess of 1 million patients per year. The Leicester Royal Infirmary, one of three hospital sites within UHL, provides the main Accident & Emergency service. We retrospectively reviewed case notes of all adult patients (≥17 years of age) admitted at the Leicester Royal Infirmary, who were identified using a coded discharge diagnosis of DKA between February 2012 and December 2012. All data obtained from patient medical records were anonymised and stored in password protected files in keeping with principles of information governance. Data were collected using an audit tool, modelled from the NICE inpatient foot audit tool and with standards derived from the JBDS DKA guidance. The audit tool covered all aspects of management from admission to discharge and adherence to the protocol/usage of dedicated hospital DKA prescription and monitoring chart and clinical outcomes.

Definitions
DKA was defined as a blood glucose ≥11 mmol/L or known diabetes mellitus, ketonuria (≥2+ on standard urine sticks) or ketonaemia >3.0 mmol/L, venous pH <7.3 and/or bicarbonate <15 mmol/L. Hypoglycaemia was defined as a blood glucose <4.0 mmol/L. Resolution of DKA was defined as pH >7.3, bicarbonate >15.0 mmol/L, and blood ketone level <0.3 mmol/L.

Biochemical measures and statistics
All biomedical measures were carried out using standard operating procedures in the biochemical laboratory, UHL. Data were recorded on a Microsoft Excel spreadsheet. Data analysis was carried out using SPSS version 20.0. We report continuous variables as mean, median, interquartile range and standard deviation (SD). Categorical variables are reported as counts and percentages. Univariate analysis was performed using t-test for continuous and chi-square test for categorical variables. Spearman’s correlation test was used to measure the strength of association between variables; p<0.05 was considered.

Results
Characteristics of patients
One hundred and seventy-two episodes were identified with a coded discharge diagnosis of DKA. Of these, we accessed 100 patient case records. Fifty episodes were excluded from the audit (n=17, not using the hospital prescription and monitoring chart [proforma]; n=5, confirmed diagnosis but protocol not used; n=28, incorrect coded diagnosis). Among the 17 patients in whom the proforma was not used, 11 were admitted directly to the ICU where the proforma was not in use, four received a variable insulin infusion and, in the remaining two, recording on the proforma was stopped after ICU admission. Incorrect diagnoses included patients admitted with lactic acidosis (n=2), impeding DKA (n=11), hyperglycaemia (n=5) and other diagnoses (n=10). Therefore, 50 correctly coded DKA patient episodes (44 single patient episodes, three episodes relating to two patients each) in which the hospital proforma was followed were used in the audit. Each episode was audited as a discrete event. Baseline characteristics of patients are shown in Table 1. Twenty-seven (54%) patients were male and 23 (46%) were female. Mean (SD) age and duration of diabetes of patients was 43 (21) years and 11 (9) years, respectively.

Diagnosis and immediate management (0–60 minutes)
Median time (interquartile range, IQR) to diagnosis from the
Table 1 Baseline characteristics of patients included in the DKA audit

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<tr>
<td>Mean age, years (SD)</td>
<td>43 (21)</td>
<td></td>
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<tr>
<td>Males, n (%)</td>
<td>27 (54%)</td>
<td></td>
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<tr>
<td>females, n (%)</td>
<td>23 (46%)</td>
<td></td>
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<tr>
<td>Mean duration of diabetes, years (SD)</td>
<td>11 (9)</td>
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<td>Number of hospital admissions in last 12 months, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>25 (50%)</td>
<td></td>
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<tr>
<td>1</td>
<td>13 (26%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4 (8%)</td>
<td></td>
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<tr>
<td>≥4</td>
<td>6 (12%)</td>
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<tr>
<td>Mean length of hospital stay, days (SD)</td>
<td>3.2 (3)</td>
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point of entry to the emergency department was 25 (13–55) minutes. After the diagnosis of DKA was confirmed, a stat dose of subcutaneous or intramuscular insulin was administered at a median (IQR) time of 29 (14–64) minutes, FR III commenced at 49 (29–110) minutes and intravenous fluids were commenced at 19 (0–42) minutes. Within 0–60 minutes, 74% and 78% of patients received intravenous fluids and FR III, respectively. Beyond the 0–60 minute period, median time for administration of both intravenous fluids and FR III was 75 (67–125) minutes. Seventy-six percent of patients were managed in an appropriate clinical area (Level 1+ as a minimum) (Figure 1).

Ongoing management (1–24 hours)

Potassium replacement

In the first 24 hours, serum potassium levels were within the normal range in 27/50 (54%) patients (mean baseline potassium at admission 5.13 mmol/L). Potassium replacement was undertaken according to protocol in 42% of patients with no evidence of hyperkalaemia in any patient. Forty-six percent of patients developed hypokalaemia and in nearly 70% of patients of this group, potassium supplementation was not prescribed as per protocol. The average lowest potassium level was 3.1 mmol/L and lowest documented serum potassium was 2.5 mmol/L. Hypokalaemia was managed according to hospital guidelines and no evidence of harm (clinically untoward incident) was documented as a result. Thirty-four patients (68%) had ≤3 interval serum potassium checks and 16 patients (32%) had >3 interval serum potassium checks in the period 1–24 hours after admission. Of the latter, only two patients had all of the seven interval checks (by venous blood gas) as recommended in the protocol.

Hypoglycaemia

Forty percent of patients experienced hypoglycaemia during the 1–24 hour management stage. The median time to hypoglycaemia from diagnosis was 12 hours 54 minutes. The lowest mean CBG reading was 3.0 mmol/L and the lowest documented CBG was 2.0 mmol/L. Eighty percent of patients had appropriate 10% dextrose prescribed when CBG dropped to <14 mmol/L and this was consistent in the patients who experienced hypoglycaemia. Continuation of long-acting insulin analogues occurred in 30% of patients managed according to DKA protocol and was not correlated to the development of hypoglycaemia (r=0.20, p=0.16).

Other aspects of management

Intravenous bicarbonate was not prescribed during any DKA episode. Intravenous phosphate (not advocated in the protocol) was administered to three patients to treat biochemical hypophosphataemia. Appropriate review of metabolic progress which included tracking of key metabolic parameters such as fluid resuscitation, intravenous insulin therapy, regular electrolyte and glucose monitoring, as per proforma occurred in 34 (68%) patients. Median time to resolution of DKA was 12 hours 6 minutes. The introduction of blood ketone meters occurred in a phased manner during the audit period. When available, 26 (52%) patients had blood ketones measured on admission. Median time to FR III in these patients was 40 minutes compared with 52 minutes for patients in whom blood ketone levels were not checked. Fourteen patients had blood ketone levels monitored beyond the 24 hour period and, compared with patients who did not receive blood ketone monitoring, there were no differences in time to resolution of DKA or length of stay (refer to UHL guidelines for blood ketone measurement in the management.
of DKA, Figure 2). Median time to subcutaneous insulin from resolution was 11 hours and, in 66% of patients, changing from FRIII to a subcutaneous insulin regime was inappropriately managed with the most common reason being an inordinate delay in switching to a subcutaneous regime despite resolution of DKA. Forty three (86%) patients were reviewed by the diabetes specialist team during admission and, of the seven patients who did not receive a review, two patients self-discharged contrary to medical advice and, in the remaining five patients, no clear reasons were identified. Psychological support was not offered to any patient during hospital admission.

Complications and mortality
Forty-four percent of patients experienced either hypoglycaemia or hypokalaemia and 12% experienced both. There were no deaths directly related to DKA or due to management of complications. Three elderly patients (aged 75, 76 and 90 years) died during the index admission due to intercurrent illness diagnosed as aspiration pneumonia, pneumonia and myocardial infarction, respectively.

Length of stay and follow-up
Median length of stay was 2 days and 40% of patients had documented follow-up within 30 days from discharge. Length of stay was significantly correlated with increasing age ($r=0.28, p=0.04$) and negatively correlated with frequency of metabolic review ($r=-0.29, p=0.03$).

Discussion
This retrospective audit of management of DKA in adults since the introduction of the JBDS guidance in 2010 has demonstrated three key findings. First, good adherence to the immediate phase of treatment (0–60 minutes) with prompt diagnosis and initiation of intravenous fluids and FRIII. Secondly, a high percentage of patients received appropriate and timely senior review. Finally, among individuals in whom blood ketone levels were checked in the emergency department on admission, the median time to initiation of treatment was shorter compared with those diagnosed with urinary ketone measurements.

Of concern is the finding that 44% of patients experienced either hypoglycaemia or hypokalaemia and 12% experienced both during on-going management. Occurrence of hypokalaemia was related to poor adherence to protocol guidance on potassium supplementation and frequency of venous blood gas (and hence potassium) checks. Hypoglycaemia occurred despite 10% dextrose being initiated appropriately in 80% of patients. It is interesting to note that the median time to hypoglycaemia occurring from diagnosis was longer than the median time to resolution of DKA, suggesting that FRIII was continued inappropriately in some patients. It is likely that this would contribute to the occurrence of hypoglycaemia, particularly in the latter stages of the management. This hypothesis is supported by the finding that the switch from FRIII to subcutaneous insulin regime was managed appropriately in only 34% of patients and median time to initiation of subcutaneous regime from resolution was 11 hours. Encouragingly, our audit demonstrated that DKA can be treated effectively with a median length of stay of 2 days (mean 3.3 days) and with no mortality associated with DKA or as a consequence of management. Length of stay was affected by increasing age and frequency of metabolic review during management.

Eighty-six percent of patients in this audit were reviewed by the diabetes specialist team prior to discharge and 40% were offered follow-up appointments within 30 days of discharge. Involvement of the diabetes specialist nurse team as standard in-patient care for adults with diabetes is vital and evidence suggests that it reduces length of stay and improves safety.$^{12,13}$ Furthermore, JBDS guidance suggests that patients admitted with DKA should receive psychological support prior to discharge. However the advisory group set up to formulate the Best Practice Tariff (BPT) for DKA advised that inclusion of psychological support within the BPT was “a step too far” and that the challenges seemed insurmountable.$^{14,15}$

The results of our audit are consistent with similar reports from other hospitals in the UK. Audit results from hospitals across the UK have shown that, in the first 60 minute period, initiation of intravenous fluids occurred in 39–73%, FRIII initiation in 25–78%, hypokalaemia occurred in 30–46%, hypoglycaemia in 10–40%, continuation of basal insulin in 30–58% and diabetes nurse specialist review in 57–86% of patients.$^{16-21}$ A survey of the
management of DKA in 13 intensive care units across the east of England in 2011, showed that a majority were using local guidelines and had not yet adopted the JBDS guidelines. Only four units used FRII, a minority advocated continuation of long-acting insulin analogues and both 0.9% sodium chloride solution and Hartmann’s solution were equally preferred as resuscitation fluids. Furthermore, a study from a university hospital in south west England showed that there was a need for more understanding of DKA protocols by nursing staff, regular reassessments of patients by doctors after initial admission and management, improvements in continuity of care and accessibility of junior doctor staff in busy hospitals. Since the initial stages of DKA are mostly managed in acute medical and emergency units and rapid change over of staff is a recognised problem, it is imperative that ongoing training and awareness of the revised DKA guidelines is a continual process. Education for both health care providers and patients at risk for DKA may help to increase awareness and decrease the overall prevalence of this condition.

In summary, this audit reinforces a growing evidence base that guideline adherence in the management of DKA is good in the immediate stage of treatment; however inadequate metabolic monitoring, iatrogenic hypoglycaemia and poor fluid/electrolyte management remain areas of concern. Our audit also shows that a high proportion of patients received input from the diabetes specialist nurse team with reduced length of stay and no recorded mortality due to DKA or related complications. Subsequent to our audit report, we have published a Trust wide Education Newsletter for Inpatient Diabetes (ENID, Issue 1) which focused on the management of DKA supplemented by key recommendations including the tag line “Don’t forget the K+ in DKA” and “DKA is DK+A – Diabetic Keto Acidosis Insulin Saline / Senior review Dextrose K+ (potassium) Assessment for metabolic progress and complications”. Our own recommendations as a result of this audit include a strengthened programme of teaching and education for nursing and medical staff (including ThinkGlucose), focus on timely and appropriate potassium supplementation, telephone contact by the specialist team with the patient within 48 hours of discharge, audit of DKA management on the labour ward and plans for re-audit in two years after implementation of these recommendations.

Finally, in recognition of the need to understand the national picture with regard to management of diabetic ketoacidosis and as part of a “service improvement exercise”, ABCD with the backing of JBDS and Diabetes UK are currently undertaking a nationwide audit which should help to inform and aid any necessary revisions to the current national DKA guidelines.

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