Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes Mellitus

Clinical and Biochemical Differences

Christopher A. Newton, MD; Philip Raskin, MD

Background: Diabetic ketoacidosis (DKA), once thought to typify type 1 diabetes mellitus, has been reported to affect individuals with type 2 diabetes mellitus. An analysis and overview of the different clinical and biochemical characteristics of DKA that might be predicted between patients with type 1 and type 2 diabetes is needed.

Methods: We reviewed 176 admissions of patients with moderate-to-severe DKA. Patients were classified as having type 1 or type 2 diabetes based on treatment history and/or autoantibody status. Groups were compared for differences in symptoms, precipitants, vital statistics, biochemical profiles at presentation, and response to therapy.

Results: Of 138 patients admitted for moderate-to-severe DKA, 30 had type 2 diabetes. A greater proportion of the type 2 diabetes group was Latino American or African American (P < .001). Thirty-five admissions (19.9%) were for newly diagnosed diabetes. A total of 85% of all admissions involved discontinuation of medication use, 69.2% in the type 2 group. Infections were present in 21.6% of the type 1 and 48.4% of the type 2 diabetes admissions. A total of 21% of patients with type 1 diabetes and 70% with type 2 diabetes had a body mass index greater than 27. Although the type 1 diabetes group was more acidic (arterial pH, 7.21 ± 0.12 vs 7.27 ± 0.08; P < .001), type 2 diabetes patients required longer treatment periods (36.0 ± 11.6 vs 28.9 ± 8.9 hours, P = .01) to achieve ketone-free urine. Complications from therapy were uncommon.

Conclusions: A significant proportion of DKA occurs in patients with type 2 diabetes. The time-tested therapy for DKA of intravenous insulin with concomitant glucose as the plasma level decreases, sufficient fluid and electrolyte replacement, and attention to associated problems remains the standard of care, irrespective of the type of diabetes.

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An episode of diabetic ketoacidosis (DKA) was once considered a hallmark feature that would differentiate individuals with type 1 diabetes mellitus from those with type 2 diabetes mellitus. This is a concept that has been perpetuated by such statements as "patients with NIDDM [non–insulin-dependent diabetes mellitus] are [not] ketosis prone" and "many individuals with type 2 DM [diabetes mellitus] (previously NIDDM) do not require insulin therapy to prevent ketoacidosis." The clinical and biochemical characteristics of DKA have been previously well described; however, most patients included in these reports probably had type 1 diabetes mellitus. More recently, there have been multiple reports of DKA occurring in patients with type 2 diabetes mellitus. Additionally, patients with idiopathic type 1 diabetes, also referred to as type 1B, type 1.5, or Flatbush diabetes, will present with DKA but have few other features associated with classic autoimmune type 1 diabetes.

Recent epidemiologic studies estimate that hospitalizations for DKA have increased during the past 2 decades. Part of this increased frequency of admissions may be related to the increased prevalence of type 2 diabetes. With the changes in the frequency of DKA and the increased incidence of DKA in patients with type 2 diabetes mellitus, the question may be posed of whether there has been any change in the clinical or laboratory characteristics of the patients with DKA who present to the emergency department. In this study, we present the clinical and biochemical characteristics of patients with type 2 diabetes compared with type 1 diabetes admitted with DKA to The University Diabetes Treatment Center at Parkland Memorial Hospital, Dallas, Tex, as well as their response to our treatment protocol.
practice guidelines was encouraged. The insulin infusion was continued, duration of insulin infusion, time from presentation to treatment, amount of insulin administered, amount of intravenous fluid administered, amount of insulin administered, duration of insulin infusion, time from presentation to resolution of urine ketones, insulin dose at discharge, and length of hospitalization.

Comparisons between the groups were performed using the t test, Mann-Whitney rank sums tests, and the χ² test as appropriate. Unless otherwise indicated, all data are expressed as mean ± SD. Patients with type 2 diabetes were compared to the subgroup of patients with type 1 diabetes. Patients were assigned to the type 2 diabetes group if they were previously diagnosed as having diabetes and at some time in their disease, other than a time consistent with the "honeymoon period," were managed with diet and exercise alone or with oral hypoglycemic agents or were noncompliant with their insulin regimen for more than 3 weeks preceding admission. Patients with newly diagnosed diabetes were assigned to the type 2 group if they tested negative for autoimmune antibody or if they had phenotypic features of type 2 diabetes (such as obesity, acanthosis nigricans, or a family history of type 2 diabetes) and were noted to have a stressful event (eg, infection) that precipitated the episode of DKA. Based on recent evidence that indicates similar biochemical profiles and physical characteristics, patients with idiopathic type 1 diabetes (type 1B) were included in the type 2 diabetes subgroup for purposes of analysis. Further analyses were performed comparing patients diagnosed as having diabetes on admission for DKA with those with a known history of diabetes. Additionally, patients with multiple admissions were compared with the group of patients with only 1 admission during the year.

RESULTS

A total of 138 patients accounted for the 176 admissions to Parkland Memorial Hospital’s University Diabetes Treatment Center for moderate-to-severe DKA. Eighty (58%) of the patients were male, 24 (17%) of the patients were white, 65 (47%) were African American, 48 (35%) were Latino (mostly Mexican or Mexican American), and 1 patient (1%) was Native American. The patients were between the ages of 15 and 66 years (mean age, 35.0 ± 12.1 years). A total of 18.2% of the patients had a history of polysubstance abuse. A summary of the patient demographics for the subgroups analyzed is presented in Table 1. Differences between groups are noted for age and diabetes duration only.

Symptoms documented to be present at the time of presentation are summarized in Table 2. The duration of the symptoms, when they were reported to be present, is also shown. Although 42% of the patients admitted to weight loss, only 78% of these patients were able to quantify the amount of loss, which was reported to average 13.0 kg over 3 months.

A plausible explanation for the development of DKA was identified in 90.3% of admissions. Thirty-six patients were newly diagnosed as having diabetes. Eighty-five percent of the admissions by patients with a known history of diabetes followed a period of discontinuation of medical therapies during the days preceding presentation. Discontinuation of medication use, mostly insulin, was implicated in 90.2% of the admissions by the 16 patients with more than 1 admission during the year. Five of these patients had a history of polysubstance abuse. Infections were identified in 38% of all the patients and included urinary tract infections, upper respiratory tract infections, pneumonia, cellulitis, and cutaneous abscesses. These infections were present in 22% of the patients with type 1 diabetes and 48% of patients with type 2 diabetes. Pancreatitis was also present in 10% of the admissions. Since patients with an acute myocardial infarction were admitted to the cardiac care service rather than the University Diabetes Treatment Center, none of the patients in this study had a myocardial infarction as described in the original manuscript.
a precipitant for the development of DKA. Similarly, surgical stress was not an observed cause for the development of DKA, since all of the patients in this study presented to the emergency department presumably from home.

On presentation to the emergency department, patients were tachycardic, with an average heart rate of 117±19/min and had a slightly elevated systolic/diastolic blood pressure of 135±23/85±15 mm Hg. By the time of discharge from the hospital, the patients had normalization of the heart rate to 83±9/min and normalization of systolic/diastolic blood pressure to 113±16/73±10 mm Hg. Patients weighed 69.6±18.3 kg (range, 43.1-147.2 kg; median, 65.3 kg) at the time of admission to the hospital, having received an average of 3.7±1.5 L of intravenous fluid in the emergency department. Their weight increased by an additional 2.7±3.2 kg during the hospitalization. Patients newly diagnosed as having diabetes weighed more than those with a known history of diabetes (81.4±22.7 kg vs 67.3±16.5 kg, *P*=.02). Based on weight at the time of discharge from the hospital, 25% of the patients had a body mass index (a measure of weight in kilograms divided by the square of height in meters) greater than 27. Using their admission weights and reported amount of weight lost, 21% of patients with type 1 diabetes and 70% of patients with type 2 diabetes had a body mass index greater than 27 before the onset of symptoms of uncontrolled diabetes.

Table 1. Demographics for Subgroups of Patients Classified by Type and Previous Diagnosis of Diabetes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Previously Diagnosed Type 1 DM</th>
<th>Previously Diagnosed Type 2 DM</th>
<th>Newly Diagnosed Type 1 DM</th>
<th>Newly Diagnosed Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>78</td>
<td>25</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>32.5±11.2</td>
<td>41.0±12.5*</td>
<td>38.2±13.3*</td>
<td>42.5±3.3</td>
</tr>
<tr>
<td>Sex, No. (%) Male</td>
<td>44 (56)</td>
<td>15 (60)</td>
<td>18 (60)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Female</td>
<td>34 (44)</td>
<td>10 (40)</td>
<td>12 (40)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Ethnicity, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>18 (23.1)</td>
<td>3 (12)</td>
<td>3 (10)</td>
<td>0</td>
</tr>
<tr>
<td>African American</td>
<td>36 (46.1)</td>
<td>12 (48)</td>
<td>12 (40)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Latino American</td>
<td>24 (30.8)</td>
<td>9 (36)</td>
<td>15 (50)</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1 (4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Duration of diabetes, mean ± SD, y</td>
<td>12.7±10.0</td>
<td>5.6±4.4†</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: DM, diabetes mellitus; NA, not applicable.
*P<.05 for comparison vs previously diagnosed type 1 DM group.
†P<.001 for comparison vs previously diagnosed type 1 DM group.

Table 2. Frequency and Duration of Symptoms Reported by Patients Admitted With Moderate-to-Severe Diabetic Ketoacidosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency, Percentage of Admissions</th>
<th>Symptom Duration, Mean ± SD, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria</td>
<td>75.2</td>
<td>22.3±33.6</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>74.4</td>
<td>23.1±33.9</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>33.1</td>
<td>26.3±34.2</td>
</tr>
<tr>
<td>Weight loss</td>
<td>42.1</td>
<td>89.9±97.7</td>
</tr>
<tr>
<td>Nausea</td>
<td>83.4</td>
<td>3.2±3.1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>78.5</td>
<td>3.1±3.1</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>51.2</td>
<td>3.4±3.3</td>
</tr>
</tbody>
</table>

Table 3. Frequency of Laboratory Data Findings at the Time of Presentation

<table>
<thead>
<tr>
<th>Component</th>
<th>Reference Range</th>
<th>Low</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>65-110 mg/dL (3.6-6.1 mmol/L)</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.35-7.45</td>
<td>100.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>22-31 mEq/L</td>
<td>100.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sodium</td>
<td>135-145 mEq/L</td>
<td>77.0</td>
<td>21.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.6-5.0 mEq/L</td>
<td>4.6</td>
<td>58.6</td>
<td>36.8</td>
</tr>
<tr>
<td>Chloride</td>
<td>98-109 mEq/L</td>
<td>66.1</td>
<td>31.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Blood urea</td>
<td>7-21 mg/dL (2.5-7.5 mmol/L)</td>
<td>3.5</td>
<td>60.2</td>
<td>36.3</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6-1.2 mg/dL (53.0-106.1 µmol/L)</td>
<td>1.2</td>
<td>57.3</td>
<td>41.5</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.4-10.2 mg/dL (2.1-2.5 mmol/L)</td>
<td>12.4</td>
<td>68.2</td>
<td>19.4</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.4-1.8 mEq/L (0.7-0.9 mmol/L)</td>
<td>10.0</td>
<td>67.5</td>
<td>22.5</td>
</tr>
<tr>
<td>Phosphate</td>
<td>2.4-4.5 mg/dL (0.8-1.5 mmol/L)</td>
<td>8.8</td>
<td>54.1</td>
<td>37.1</td>
</tr>
<tr>
<td>Amylase</td>
<td>29-108 U/L</td>
<td>23.6</td>
<td>59.9</td>
<td>16.5</td>
</tr>
<tr>
<td>Lipase</td>
<td>7-99 U/L</td>
<td>11.6</td>
<td>58.9</td>
<td>29.5</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>4.1-10.9 × 10^3/µL</td>
<td>0</td>
<td>44.3</td>
<td>55.7</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>45±74%</td>
<td>0.6</td>
<td>35.1</td>
<td>64.3</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>16±45%</td>
<td>64.9</td>
<td>34.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Monocytes</td>
<td>4±10%</td>
<td>22.8</td>
<td>69.0</td>
<td>8.2</td>
</tr>
</tbody>
</table>
and creatinine levels were both elevated, but the ratio was similar between the 2 groups.

Patients were classified as having type 2 diabetes, either type 2 diabetes or idiopathic type 1 diabetes, in 17.6% of the admissions. A greater percentage of these patients were of African American or Latino American ethnicity than the group of patients with type 1 diabetes (P < .001 by χ² test). Infections accounted for 15 of the 31 admissions for the 30 patients in this group. Patients previously diagnosed as having type 2 diabetes were found to be noncompliant with their diabetes therapy in 69.2% of the admissions. No significant differences were observed in the frequency of symptom complaints in this group compared with the type 1 diabetes group. This group of patients weighed more than the patients with type 1 diabetes (85.4±25.2 kg vs 66.1±14.4 kg, P = .002).

Other vital signs were not significantly different between the groups.

Laboratory data for the various subgroupsanalyzed are shown in Table 4. The laboratory data from 2 other reviews are also included in Table 4 for comparison. The cholesterol levels were similar in all groups except for the high-density lipoprotein cholesterol levels, which was lower in patients with a history of type 2 diabetes than in those with type 1 diabetes (34.3±13.6 mg/dL [0.9±0.4 mmol/L] vs 46.4±14.2 mg/dL [1.2±0.4 mmol/L], respectively, P < .001) and in those who were newly diagnosed as having classic type 1 diabetes (34.2±10.7 mg/dL [0.9±0.3 mmol/L], P < .001). No differences were observed in liver function test results.

The insulin-glucose infusion algorithm shown in the Figure was used in most admissions. Overall, patients had cleared their urine ketones at an average of 31.7±11.1 hours after presenting to the emergency department and 21.5±10.5 hours after being initiated on an insulin infusion protocol. They received 9.5±3.5 L of intravenous fluid during that time. Patients continued with the intravenous insulin infusions for a total of 36.3±28.4 hours and received a total of 200.3±130.1 U of insulin from this infusion and a total of 13.8±4.9 U of insulin to achieve a negative urine ketone status, patients with newly diagnosed type 1 diabetes and those with type 2 diabetes required both longer periods

### Table 4. Laboratory Findings in Patients Grouped According to Type of Diabetes and Whether Admission Was for Newly Diagnosed Diabetes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Previously Diagnosed Type 1 DM</th>
<th>Previously Diagnosed Type 2 DM</th>
<th>Newly Diagnosed Type 1 DM</th>
<th>Newly Diagnosed Type 2 DM</th>
<th>Foster and McGarry16</th>
<th>Umpierrez et al19</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of admissions</td>
<td>115</td>
<td>26</td>
<td>30</td>
<td>5</td>
<td>88</td>
<td>126</td>
</tr>
<tr>
<td>Glucose, mg/dL (mmol/L)</td>
<td>529±212.4 (29.4±11.8)</td>
<td>480±159.8 (26.7±8.9)</td>
<td>461.4±192.3 (25.6±10.7)</td>
<td>396.6±191.1 (22.0±10.6)</td>
<td>475 (26.4)</td>
<td>628 (34.9)</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.21±0.12</td>
<td>7.27±0.08∗</td>
<td>7.19±0.14</td>
<td>7.28±0.03†</td>
<td>NA</td>
<td>7.16</td>
</tr>
<tr>
<td>Bicarbonate, mEq/L</td>
<td>10.1±5.1</td>
<td>10.2±4.1</td>
<td>9.8±5.0</td>
<td>12.0±4.6</td>
<td>&lt;10</td>
<td>9</td>
</tr>
<tr>
<td>Sodium, mEq/L</td>
<td>131.6±5.0</td>
<td>129.5±5.4</td>
<td>132.5±5.8</td>
<td>130.6±4.6</td>
<td>132 (133)</td>
<td>133</td>
</tr>
<tr>
<td>Potassium, mEq/L</td>
<td>5.1±0.9</td>
<td>4.5±0.9∗</td>
<td>4.4±0.6∗</td>
<td>4.8±0.5</td>
<td>4.8 (5.3)</td>
<td>5.3</td>
</tr>
<tr>
<td>Chloride, mEq/L</td>
<td>94.4±8.1</td>
<td>93.1±8.0</td>
<td>97.9±6.3‡</td>
<td>94.4±6.9</td>
<td>NA</td>
<td>92</td>
</tr>
<tr>
<td>Blood urea nitrogen, mg/dL (mmol/L)</td>
<td>22.8±13.3 (8.1±4.7)</td>
<td>19.7±12.5 (7.0±4.5)</td>
<td>17.6±12.3‡ (6.3±4.4)</td>
<td>13.8±4.8 (4.9±1.7)</td>
<td>25 (8.9)</td>
<td>27 (9.6)</td>
</tr>
<tr>
<td>Creatinine, mg/dL (µmol/L)</td>
<td>1.5±0.9</td>
<td>1.2±0.7 (106.1±61.9)</td>
<td>1.2±0.5‡ (106.1±44.2)</td>
<td>1.2±0.3 (106.1±26.5)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Calcium, mg/dL (mmol/L)</td>
<td>9.5±0.9 (2.4±0.2)</td>
<td>9.4±0.9 (2.3±0.2)</td>
<td>9.2±1.0 (2.3±0.2)</td>
<td>8.9±0.7 (2.2±0.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Magnesium, mEq/L (mmol/L)</td>
<td>1.7±0.3 (0.9±0.1)</td>
<td>1.7±0.3 (0.8±0.2)</td>
<td>1.7±0.3 (0.8±0.2)</td>
<td>1.5±0.4 (0.7±0.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Phosphate, mg/dL (mmol/L)</td>
<td>5.0±2.3 (1.6±0.7)</td>
<td>4.0±2.7 (1.3±0.9)</td>
<td>3.9±2.0‡ (1.3±0.6)</td>
<td>2.9±1.3 (0.9±0.4)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>White blood cells, ×10^9/L</td>
<td>13.0±6.3</td>
<td>13.3±6.8</td>
<td>14.1±7.3</td>
<td>10.0±1.3§</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Neutrophils, %</td>
<td>77.6±10.7</td>
<td>73.2±10.8</td>
<td>74.0±13.5</td>
<td>71.3±12.9</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lymphocytes, %</td>
<td>14.9±9.3</td>
<td>14.0±10.1</td>
<td>14.9±11.4</td>
<td>21.5±10.8</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Monocytes, %</td>
<td>6.0±3.1</td>
<td>6.7±2.9</td>
<td>6.7±2.7</td>
<td>6.0±3.4</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: DM, diabetes mellitus; NA, not applicable.

∗P < .05 vs previously diagnosed type 1 DM.
†P < .01 vs newly diagnosed type 1 DM.
‡P < .05 vs previously diagnosed type 1 DM.
§P < .05 vs previously diagnosed type 2 DM.
charge dose (62±23 U vs 72±28 U, respectively) and more insulin (283±156 U, P=.01; and 175±69 U, P=.23; respectively) to achieve a negative urine ketone status. The patients with a known history of type 1 diabetes and those with type 2 diabetes achieved a negative urine ketone status at similar times following initiation of the intravenous insulin infusion protocol (19.1±8.4 and 23.1±11.6 hours, respectively, P=.22). Patients newly diagnosed as having type 1 diabetes required 31.7±13.3 hours (P=.005) to achieve negative urine ketones after initiating the intravenous insulin protocol.

With regard to complications associated with treatment of DKA, 4 patients had a blood glucose level of less than 70 mg/dL (<3.9 mmol/L) at some point during the insulin infusion. Three of these episodes occurred after the patient received a subcutaneous injection of insulin in anticipation of discontinuing the intravenous insulin infusion but failed to tolerate the associated meal, attesting to the adequacy of the insulin-glucose infusion. None of the episodes of hypoglycemia were reported to be clinically significant. Patients received an average of 235±213mM of potassium during their hospitalizations; however, since a specific protocol for potassium management was not provided to the treating physicians, the frequency of patients developing hypokalemia could not be appropriately assessed. Of note though, 8% of the patients did not receive any potassium supplementation. None of the patients developed cerebral edema, and there were no deaths. One patient developed a deep venous thrombosis during his hospitalization. Another patient was diagnosed as having adult respiratory distress syndrome within a few hours of presentation to the emergency department.

Patients remained hospitalized for an average of 4.5±3.3 days, consistent with the national average length of stay for DKA of 4.5 days.13 Patients with known type 1 diabetes were discharged home on an average daily insulin dose of 1.02±0.25 U/kg per day or 69±22 U/d of insulin. Patients with type 2 diabetes received 1.10±0.38 U/kg daily or 92±39 U/d (P=.03 vs group with type 1 diabetes). Patients with newly diagnosed type 1 diabetes were discharged on a protocol of 89±36 U/d or 69±22 U/d of insulin. Patients with type 2 diabetes received 1.10±0.38 U/kg per day or 69±22 U/d of insulin. Patients with type 2 diabetes also demonstrated a lower percentage of potassium supplementation (39.8±13.3 hours, P=.01; and 36.0±11.6 hours, P=.04; respectively) and more insulin (283±156 U, P=.01; and 175±69 U, P=.23; respectively) to achieve a negative urine ketone status. The patients with a known history of type 1 diabetes and those with type 2 diabetes achieved a negative urine ketone status at similar times following initiation of the intravenous insulin infusion protocol (19.1±8.4 and 23.1±11.6 hours, respectively, P=.22). Patients newly diagnosed as having type 1 diabetes required 31.7±13.3 hours (P=.005) to achieve negative urine ketones after initiating the intravenous insulin protocol.

With regard to complications associated with treatment of DKA, 4 patients had a blood glucose level of less than 70 mg/dL (<3.9 mmol/L) at some point during the insulin infusion. Three of these episodes occurred after the patient received a subcutaneous injection of insulin in anticipation of discontinuing the intravenous insulin infusion but failed to tolerate the associated meal, attesting to the adequacy of the insulin-glucose infusion. None of the episodes of hypoglycemia were reported to be clinically significant. Patients received an average of 235±213mM of potassium during their hospitalizations; however, since a specific protocol for potassium management was not provided to the treating physicians, the frequency of patients developing hypokalemia could not be appropriately assessed. Of note though, 8% of the patients did not receive any potassium supplementation. None of the patients developed cerebral edema, and there were no deaths. One patient developed a deep venous thrombosis during his hospitalization. Another patient was diagnosed as having adult respiratory distress syndrome within a few hours of presentation to the emergency department.

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Our results help illustrate the variability of clinical characteristics of patients who present with DKA and point out the fact that patients with type 2 diabetes also develop ketoacidosis. Even when restricting the population to those patients with moderate or severe DKA, the patients have a variety of clinical and biochemical findings as shown in Table 3. We found that some of the variability relates to the precipitating factors for DKA in that patients with newly diagnosed diabetes have different biochemical findings compared with patients with a known history of diabetes as shown in Table 4. Additionally, we found that patients with type 2 diabetes have a different biochemical presentation of DKA, with less severe aci-
terregulatory hormones contribute to the hyperglycemia through glyco- 
genesis, gluconeogenesis, and decreased peripheral use of glucose. Volume depletion is prob- 
ably the principal factor that results in the marked hyperglycemia seen in DKA. The metabolic acidosis that 
develops in DKA is primarily the result of accumulation of the metabolic acids, acetoacetatic acid and β-hydroxy-
butyric acid, in the plasma. These ketoacids develop as a 
consequence of the lipolysis and proteolysis that occur 
when elevated glucagon-insulin ratios cause in-
ncreased hepatic levels of carnitine and decreased malonyl-
coenzyme A concentrations.

Other electrolyte abnormalities seem to develop as 
a secondary effect of the hyperglycemia and metabolic 
acidosis. The glycosuria that is present leads to at least 
mild dehydration and an associated increase in blood urea 
nitrogen levels, as well as a mild increase in serum creati-
tine levels. Although serum sodium levels might be 
expected to be increased in a dehydrated state, the 
oscmetric effect of glucose draws water into the extracellu-
lar space and tends to reduce the sodium concentration. 
Potassium levels will tend to be high because of the physi-
ologic compensation of the metabolic acidosis and the 
hyperosmolarity and insulin deficiency present, 
although it is known that total body stores of potassium are depleted in DKA.

It is therefore surprising to find 
that nearly 8% of the patients in this review did not re-
quire potassium supplementation during treatment of 
their DKA. Although phosphate is severely depleted be-
cause of glycosuria, the plasma values will vary because of 
transmembrane shifts in the ion distribution caused 
by metabolic acidosis and insulin deficiency. A stress-
induced leukemoid response is responsible for elevated leukocyte counts.

A little more than one fourth of the patients had 
newly diagnosed diabetes, accounting for approxi-
mately 20% of the admissions. Consistent with other re-
ports, newly diagnosed diabetes presenting with DKA was 
diagnosed in a substantial number of overweight pa-
tients, a condition frequently associated with type 2 dia-
betes. Our results suggest that patients with newly di-
agnosed type 1 diabetes have a more normal electrolyte 
profile than patients who have a known history of dia-
betes despite similar degrees of acidosis. This is a bit 
surprising, since they had similar glucose levels, pH levels, 
apparent ketonuria, and duration of symptoms. It is 
known that the severity of ketoacidosis is decreased when 
counterregulatory hormone levels are low.

Furthermore, it would be expected that patients with newly di-
agnosed diabetes would have a more intact counterregu-
atory hormone system than patients with a prolonged 
duration of diabetes. As such, we might predict that 
the newly diagnosed diabetes would be associated with higher glucagon and epinephrine levels, which would 
ultimately induce a greater degree of ketogenesis and a more 
severe picture of DKA. Hyperkalemia would be expected 
in both groups of individuals, since the insulin 
deficiency is present in both, but would be predicted to 
be greater in the more acidic group. Since the groups 
had similar pH levels, the potassium and phosphate lev-
els would be predicted to be similar if this were a major 
contributing factor. Therefore, the normokalemia in the 
newly diagnosed group suggests that another process, 
possibly related to the osmolarity, may be involved.

The newly diagnosed group did not have markedly 
increased blood urea nitrogen levels and only very mildly 
increased creatinine levels, possibly explained by 
the known interference of acetocetate with the assay, which 
might suggest that they are not as dehydrated as the pa-
tients with a known history of diabetes. The new diag-
nosis group required more than 4 L of additional fluid 
and more than 12 additional hours of treatment with the 
insulin-glucose infusion to achieve a ketone-negative sta-
 tus, as well as 10 L of additional fluid during the hospi-
talization compared with the previously diagnosed group.

However, the patients who also had pancreatitis ac-
counted for most of this increased fluid requirement. 
A trend toward increased fluid requirements remained when 
the patients with pancreatitis were excluded from the 
analysis (data not shown). Some of the normalcy of the 
laboratory results in the new diagnosis group could be 
related to fluid intake and maintenance of urine output 
before presentation to the emergency department; how-
ever, this cannot be verified given the retrospective na-
ture of our study. The status of the counterregulatory hor-
mones may or may not be useful in understanding the 
observed differences between these groups; however, since 
these hormones are generally not of practical value in the 
clinical management of DKA, this study cannot address 
this possibility.

Patients with type 2 diabetes can develop more than 
mild ketosis and may experience moderate-to-severe DKA. It has been said that these patients require a precipitat-
ing stressor; however, consistent with other reports, we 
found that 29% of the patients did not have a precipi-
tant other than noncompliance with their medical 
therapy. The tendency for the patients with type 2 dia-
betes who develop DKA being Latino or African Ameri-
can compared with white may only be a reflection of the 
demographics of the overall patient population at Parkland 
Memorial Hospital. However, the possibility of a true eth-
nic variation in patients with type 2 diabetes who are prone 
to develop DKA, possibly from a genetic predisposition, 
cannot be excluded. In contrast to other reports that com-
pared DKA in type 1 and type 2 diabetes, we found a dif-
fERENCE in the serum electrolyte concentrations and other 
biochemical levels of these 2 groups. Some of the dif-
fences we observed may be secondary to differences in 
counterregulation and basal insulin levels in these groups.

Our patients with type 1 diabetes had had their disease 
for a duration of 12.7 years, which is likely long enough 
to place the patients at a time long after the “honey-
moon period” and at a time when they are likely to have 
absolute insulin deficiency. The patients with type 2 dia-
betes had a disease duration of 5.6 years and thus would 
be expected to still have residual β-cell activity. 
Although the type 2 diabetes group had insufficient insu-
lin to prevent DKA, it is theoretically possible that they 
had enough insulin to modulate the disease process. In 
support of this idea is the finding of lower potassium lev-
els in this group, which as noted herein are dependent 
on insulin presence or absence. The less severe acidosis 
suggests a lower level of ketoacids; however, this was not detected in this study. Although we did not observe dif-
ferences in the degree of ketonuria between the subgroups studied, we acknowledge that our method of measuring ketoacids by semiquantitative urine testing fails to identify the ketoacid that is most prevalent in DKA and that a difference in β-hydroxybutyric acid levels could exist, although this has not been studied.

The importance of recognizing DKA in a patient with type 2 diabetes is illustrated by the time it took for these patients to achieve a negative urine ketone status. Once patients with either type 1 or type 2 diabetes were treated by the intravenous insulin infusion protocol, the duration of treatment required to achieve a negative urine ketone status was similar between the 2 groups. Patients with type 2 diabetes, however, required more time from initial presentation to the emergency department to achieve negative urine ketones. Some of this delay may be the result of a failure to suspect DKA in the “atypical patient.”

Our results also show that the insulin-glucose infusion algorithm outlined in the Figure can be used safely in the management of patients who present with DKA irrespective of the type of diabetes. Complications that have been reported with management of DKA were infrequent in our population in part because of the age of our patients but also because of the inclusion of a variable glucose infusion algorithm in the treatment protocol. Resolution of the acidosis caused by the presence of ketoacids is often used as a marker of resolution of DKA. Reports that serum 3-β-hydroxybutyric acid levels are elevated in patients with type 2 diabetes who have normal fasting blood glucose levels raise concerns about their utility in DKA management in patients with type 2 diabetes.25,26 Our use of urine ketone testing does not provide direct evidence of β-hydroxybutyric acid levels, but since acetoacetic acid levels remain elevated longer25 and since urine levels may be positive even after resolution of serum levels of acetoacetate, the resolution of ketonuria would imply adequate resolution of ketonemia. Through our continuation of the insulin-glucose infusion protocol until the urine was ketone free, we have shown successful use of ketonuria as a marker of resolution of DKA in both type 1 and type 2 diabetes. Finally, given our results of the successful, almost uneventful management of DKA, we have shown that in adults the modern management of DKA with essentially no complications of treatment consists of effective intravenous insulin therapy with concomitant glucose administration when plasma glucose levels decrease below 300 mg/dL (16.7 mmol/L), sufficient volume and electrolyte replacement, and careful attention to identification and management of associated problems, such as acute pancreatitis and infection.

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Correspondence: Philip Raskin, MD, Department of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd, G5.238, Dallas, TX 75390-8858 (Philip.Raskin@UTSouthwestern.edu).

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