Profile of diabetic ketoacidosis at a teaching hospital in Benghazi, Libyan Arab Jamahiriya

R. R. Elmehdawi and H. M. Elmagerhei

Abstract

This study described the profile of 100 cases of diabetic ketoacidosis (DKA) at a teaching hospital in Benghazi, Libyan Arab Jamahiriya. DKA was more frequent in young women with type 1 diabetes and mostly due to preventable causes, e.g. disrupted insulin treatment and/or infection. DKA also occurred in type 2 diabetics, with a higher mortality rate, as they were older patients with co-morbidity. Polyuria, fatigue, abdominal pain and vomiting were the most common clinical features, while coma was rarer. A high number of cases were first presentations of type 1 diabetes; hence this diagnosis should be considered in all patients with acute abdomen or decreased level of consciousness. The reasons for high mortality rate in this study (10%) were multifactorial.

Profil de l’acidocétose diabétique dans un hôpital universitaire de Benghazi (Jamahiriya arabe libyenne)

RÉSUMÉ Cette étude décrit le profil de 100 cas d’acidocétose diabétique dans un hôpital universitaire de Benghazi (Jamahiriya arabe libyenne). L’acidocétose diabétique était plus fréquente chez les jeunes femmes souffrant de diabète de type 1, et était essentiellement due à des causes telles qu’une interruption de l’insulinothérapie et/ou une infection. Elle a également été observée chez des personnes souffrant de diabète de type 2, avec un taux de mortalité plus élevé, les patients étant plus âgés et présentant une comorbidité. Les principales manifestations cliniques étaient une polyurie, un état de fatigue, des douleurs abdominales et des vomissements, le coma étant plus rare. Un grand nombre de cas étaient des premières présentations de diabète de type 1. C’est pourquoi ce diagnostic devrait être envisagé chez tous les patients présentant un abdomen aigu ou une altération de la conscience. Les causes du taux de mortalité élevé dans cette étude (10 %) étaient multifactorielles.

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Introduction

Type 1 diabetes mellitus (DM) is characterized by the development of a state of complete insulin deficiency which makes patients prone to ketoacidosis. Diabetic ketoacidosis (DKA) is a frequent cause of morbidity and mortality in type 1 diabetes patients. However, it also occurs occasionally in patients with type 2 DM during severe stress, for example sepsis and myocardial infarction [1–5].

About 12.8% of the diabetic adults in Benghazi have type 1 DM [6]. The incidence of type 1 DM in the Libyan population up to 34 years old is estimated to be approximately 9 per 100 000 per year [7]. DKA is the presenting feature of about 30% of Libyan children with type 1 DM [8]. However, the annual incidence of DKA in Libyan diabetics is not known. Even so, the disorder seems to contribute appreciably to the number of hospital admissions as it constitutes 9% of all diabetes-related admissions [9] and 3.2% of all acute admissions to the medical intensive care unit in Benghazi [10]. A report from Benghazi revealed that 1.6% of the adult diabetic patients had been admitted to hospital in the previous year because of DKA [6]. The overall mortality rate from DKA in the Libyan Arab Jamahiriya ranges from 2% to 9.4% of all DKA admissions according to different reports [1,2,11]. Although many DKA-associated deaths are due to concomitant illnesses (e.g. myocardial infarction, septicaemia), others are preventable and are due to delay in presentation, diagnosis and/or errors in management.

The aim of this study was to determine the pattern of DKA at a teaching hospital in Benghazi, Libyan Arab Jamahiriya, to assess the clinical and biochemical characteristics of the patients and the precipitating factors for DKA, and to correlate these parameters with the outcome.

Methods

A descriptive cross-sectional retrospective analysis was made of the records of adult patients admitted to the Seventh of October teaching hospital, Benghazi, and diagnosed with DKA between January 2003 and December 2006. During this 4-year period 200 suspected DKA cases were admitted to the medical ward and intensive care unit of the hospital. Out of these, we included only 100 episodes in this study because for the other 100 the records were missing important information.

The following variables were recorded: age, sex, nationality, duration of diabetes, precipitating factors for DKA, duration of symptoms before seeking medical advice, clinical features, laboratory findings at presentation with DKA (plasma glucose, serum blood urea nitrogen, serum creatinine, serum sodium and potassium, urine acetone, arterial blood pH, plasma bicarbonate and plasma osmolality), associated complications, duration of hospitalization and outcome. Patients were classified as having type 1 or type 2 diabetes based on their treatment history.

The criteria used to diagnose DKA in the patients included in the study were: typical clinical features such as hyperventilation, vomiting and dehydration; hyperglycaemia ≥ 250 mg/dL; arterial blood pH ≤ 7.3 and/or serum bicarbonate ≤ 18 mmol/L and presence of ketonuria (2+ on dipstick).

The severity of DKA was defined according to the American Diabetes Association (ADA) criteria [12,13] as mild (arterial blood pH 7.25–7.30), moderate (pH 7.00–7.24) or severe (pH < 7.00). Effective osmolality was calculated using the ADA formula: [(2 × sodium) + plasma glucose/18], with normal values being 290 mmol/kg water. Blood urea nitrogen was not included in this calculation because urea has less osmotic activity [14].

Results

We studied 100 episodes of DKA in 81 patients; 8 patients were responsible for 19 episodes (3 patients had 3 episodes and 5 patients had 2 episodes). These 100 admissions accounted for 769 medical and intensive care bed-days (2.4% of the total medical and intensive care bed-days). According to the ADA criteria, 29 of the episodes were mild, 37 were moderate and 34 were severe. Type 1 DM was the diagnosis in 90 of the episodes, while the other 10 had type 2. There were 19 episodes in newly diagnosed cases and 81 episodes in previously known cases of DM.

Patient and disease characteristics

A higher number of episodes were in females (71) than males (29) (female to male ratio 2.3:1) (Table 1). The age distribution is shown in Figure 1. The mean age of all patients was 29.2 years (range 15–68 years); males were significantly older than those with type 1 DM (mean age 52.6 versus 26.5 years) (P < 0.001) (Table 1). Previously diagnosed patients were also older on average than the new cases of DM (mean age 32.0 (SD 14.9) years versus 28.4 (SD 9.8) years), but this difference was not statistically significant.

Patients with type 2 DM were significantly older than those with type 1 DM (mean age 52.6 versus 26.5 years) (P < 0.001) (Table 1). Previously diagnosed patients were also older on average than the new cases of DM (mean age 30.1 versus 25.1 years), but the difference was not significant (Table 1).

Clinical features at admission

Disruption of insulin treatment (complete stoppage or reduction of insulin dose or frequency) was the commonest precipitating factor for the episode of DKA.
DKA in 38 cases. Infection was the next most common reason in 30 cases: urinary tract infection (13 cases), upper respiratory tract infection (8), lower respiratory tract infection (3), abscess (2) and gastroenteritis, tuberculosis, diabetic foot, peritonitis (1 case each). In 19 cases DKA was the first manifestation of diabetes. Other causes were rarer: myocardial infarction (2 cases), emotional stress (2) and trauma (1). In 3 cases no obvious precipitating factor could be identified and data were missing for 5 episodes.

The commonest presenting symptoms in this study were general weakness and fatigue (100 cases), polyuria and polydipsia (100), abdominal pain nausea and/or vomiting (64). Other symptoms were drowsiness (15 cases), dyspnoea (12), coma (5), headache (3) and haematemesis (2). Table 1 shows the haemodynamic features at admission.

The mean duration of symptoms before presentation to the hospital was 2.7 (SD 2.2) days (range 1–10 days) (Table 1), with 48% of the cases presenting within the same day of the onset of symptoms and 62% within 48 hours. The duration of symptoms was significantly longer in patients with type 2 DM as compared with type 1 DM ($P < 0.05$) (Table 1). Also the mean duration of symptoms was longer in new cases of DM as compared with previously diagnosed cases (Table 1). The mean duration of symptoms was significantly longer in males than females [4.0 (SD 3.7) days versus 2.8 (SD 2.3) days] ($P < 0.05$).

### Biochemical abnormalities at admission

Table 2 summarizes the biochemical parameters of DKA cases at presentation. Plasma glucose levels were higher, but not significantly so, in cases presenting for the first time than in those with a previous diagnosis (Table 2). Serum sodium was significantly higher in the new cases of DM than the previously diagnosed cases ($P < 0.05$) (Table 2). Sodium levels were also significantly higher in males than in females [mean 137.9 (SD 13) versus 136.9 (SD 8) mmol/L] ($P < 0.05$). Serum potassium at admission was significantly lower in patients who subsequently died than in the survivors ($P < 0.05$) (Table 2). Blood urea nitrogen was higher for those with type 2 DM than type 1 and in the new cases compared with previously diagnosed cases (Table 2) but these differences were not significant. Serum creatinine was raised in 91% of cases at admission.

### Complications and outcome

The mean hospital stay was 7.7 days, range 1–25 days (Table 1).

About 66% of the cases had some sort of complication. Some of these were due to the episode of DKA itself, e.g. coma (5 cases), hypokalaemia (serum potassium < 3.5 mmol/L) (13 cases). However, some complications developed due to improper therapeutic interventions,
DKA cases; none of the patients with mild DKA died. An important comorbidity was associated with 6 of the 10 deaths: myocardial infarction (2 cases), acute abdomen, pulmonary tuberculosis, acute renal failure or diabetic foot (1 case each). The following parameters were associated with a significantly increased mortality: age > 40 years, type 2 DM, depressed level of consciousness at presentation, comorbidity, pulse rate ≥ 115 beats/min, systolic blood pressure ≤ 105 mmHg, diastolic blood pressure ≤ 65 mmHg, plasma glucose ≥ 525 mg/dL, serum sodium ≥ 144 mmol/L, blood urea nitrogen ≥ 50 mg/dL, serum creatinine ≥ 4 mg/dL, arterial blood pH ≤ 7 and plasma osmolality ≥ 325 mOsm/kg water (Table 3).

**Discussion**

Despite the small sample size of this study, and the fact that it was a retrospective analysis conducted at a teaching hospital, all of which are important limitations, this study gives a basic profile of DKA in this part of the world where studies about DKA are few.

**Patient and disease characteristics**

While most of the episodes of DKA in this study were due to type 1 DM, 10% were due to type 2 DM; this compares with 15% reported by Roaeid from the same hospital between 1997 and 1999 [1] and 11.6% reported by El-Sharief in another Libyan study from Tripoli [2]. Although DKA is usually considered as a unique marker for type 1 DM these reports clearly demonstrate that it can occur among type 2 diabetic patients. This fact is increasingly recognized throughout the world [3–5].

Females were 70% of all DKA admissions. A female predominance was previously reported in Benghazi by Roaeid and Kablan [1], whereas El-Sharief reported a nearly equal ratio of sexes in Tripoli [2]. This discrepancy in the sex ratio between different cohorts was also observed in studies from Saudi Arabia [15] and Jordan [16]. We think that the cause of these variations is multifactorial, including environmental, genetic and social differences between the cohorts. However, the small study samples and errors in sampling could be important contributing factors. The female predominance was maintained...
in the group of known diabetics, among the new cases and in those with type 1 DM. However, this predominance was reversed in patients with type 2 DM, where males constituted 60% of the cases.

The mean age of all patients (29.2 years) is similar to that previously reported by Roaeid and Kablan (28.9 years) [1]. Males were slightly older than females, although this was not statistically significant. However, patients with type 2 DM were significantly older than those with type 1 (52.6 and 26.5 years respectively) presumably because type 2 DM tends to develop in adults older than 40 years, while type 1 usually occurs at a much younger age.

Clinical features at admission

Poor drug compliance was the major precipitating factor of DKA in our patients (38%); which is similar to El-Sharief's report from Tripoli (36.7%) [2], but lower than 54.4% from Saudi Arabia [15]. However, it is worth mentioning that the rate of DKA due to treatment disruption in the current study (from 2003–06) is much lower than in the previous study in Benghazi from the years 1997–99 (64%) [1]; this might indicate an improvement in patients’ compliance and education. Infections were the second most common precipitating factor (30%), similar to other reports from Benghazi (29.7%) [1], Tripoli (21.7%) [2] and Saudi Arabia (28%) [15]. In developed countries infection is the commonest precipitating factor of DKA, while insulin disruption ranks second, perhaps due to better patient education [17]. Cases of DKA caused by drug omission and infection are potentially preventable with good patient education and proper outpatient management. About 3% of our patients had no obvious precipitating factor, which is in concordance with 2%–10% reported from other parts of the world [18].

The mean duration of symptoms before presentation to the hospital was 2.7 days, with 48% of the patients presenting within the same day of the onset of symptoms, and this probably contributed to the low rate of serious clinical features at presentation. However, the duration was longer in those who were not known diabetics (5.8 versus 2.7 days), because patients may not realize what is happening at the first episode of DKA. The duration of symptoms...
Fatigue, polyuria, abdominal pain and vomiting were the most common presenting symptoms in our study, which is similar to the report from Tripoli [2]. Only 5% of our patients had coma at presentation compared with 25% reported from a study in Nairobi [19], perhaps due to ethnic differences in diabetes severity or better education among our patients and easier availability of immediate health care services in our country which could contribute to earlier presentation and hence less severe clinical features.

**Biochemical abnormalities**

The mean plasma glucose level was higher in the new cases of DM and in those with type 2 DM, probably because patients belonging to these groups presented 2 to 3 days later than the known cases of type 1 DM, allowing a higher degree of hyperglycaemia to develop. The same was true for the higher serum sodium and blood urea in these groups, which indicates a more severe dehydration due to longer duration of glucose-mediated osmotic diuresis and water loss in excess of electrolytes. The great majority of patients (75%) were eukalaemic at presentation, 13% were hypokalaemic, while another 3% developed hypokalaemia as a result of potassium under-replacement during management. Hyperkalaemia was nearly as common as hypokalaemia at admission. The raised serum creatinine seen in most of the DKA patients was likely a false elevation, as acetoacetate artificially raises measured creatinine in the standard colorimetric assay [20,21]. Metabolism of the acetoacetate following the administration of insulin will lower the measured serum creatinine concentration towards its true value.

**Outcome**

The mean hospital stay was 7.7 days, with some cases discharged on their

<table>
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<th>Variable</th>
<th>Mortality (%)</th>
<th>P-value</th>
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<td>Age (years)</td>
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<td>≥ 40</td>
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<td>&lt; 40</td>
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<tr>
<td>No</td>
<td>4.5</td>
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was significantly longer for those with type 2 DM than type 1 DM because these patients are not primarily ketosis-prone but ketoacidosis may develop slowly due to secondary insulin deficiency which builds up gradually as a result of glucose toxicity. The duration of symptoms was also significantly longer in males than in females, suggesting that males postpone medical consultation longer than females.
request as early as the first day of admission and a few others who stayed at hospital more than 2 weeks for treating the precipitating factors and complications or for social reasons. This is similar to the average length of stay in other reports from the Libyan Arab Jamahiriya [1,2]. However, it is longer than the average length of stay for DKA in the United States (3.6 days) [22] and also longer than in southern Jordan where the average length of stay was 3.4 days [16]. Our longer hospitalization will result in higher costs of DKA management.

Fortunately, despite the high rate of DKA-related complications (68%) most of the complications were not serious and were easy to treat, e.g. mild electrolyte disturbances and prerenal azotaemia. However, serious complications were encountered in some cases, e. g. severe electrolyte disturbances. Unfortunately, some of the complications were iatrogenic, e.g. such as pneumothorax due to insertion of a central venous line and hypokalaemia due to potassium under-correction. Despite the low rate of serious complications, the mortality rate of our DKA cases was high (10%). While this is similar to the report from Tripoli (9.4%) [2], it is much higher than the rate that was previously reported in Benghazi (3.8%) [1], which might indicate a deficiency in diagnostic and therapeutic facilities at hospitals or a decline in doctors’ and co-workers’ skills and experience in the management of DKA. The mortality rate was also higher than figures from Saudi Arabia [15] and Jordan [16] (2.9% and 4.8% respectively); however, it was better than from Nairobi, where the mortality rate was nearly 30% [19].

Other reports from the Libyan Arab Jamahiriya [1] and Jordan [16] and Saudi Arabia [15] had higher mortality rates. The high variation in the mortality rates may reflect variability in access to medical services and standards of inpatient management as well as patient education.

DKA patients with type 2 DM had a significantly higher mortality rate (40.0%) than patients with type 1 DM (6.6%), probably because type 2 DM patients were significantly older and more likely to have comorbidity. Overall, patients who died were significantly older, with more comorbidity, a lower level of consciousness at presentation, lower blood pressure, faster pulse rate, higher plasma glucose, higher serum sodium, higher serum creatinine, higher plasma osmolality and lower blood pH.

**Conclusion**

DKA was more common in Libyan females than in males. It was frequently seen in young women with type 1 DM, mostly caused by potentially preventable causes such as disruption of insulin treatment and/or infection. DKA also occurred in type 2 DM patients and when this happened it resulted in higher mortality as it occurred in older persons with coexisting morbidity.

Polyuria, fatigue, abdominal pain and vomiting were the most common clinical features in our patients, while coma was relatively uncommon. DKA as a first presentation of type 1 DM accounted for a considerable number of cases; hence this diagnosis should be considered in all patients with acute abdomen or decreased level of consciousness, even if they are not known diabetics.

The high mortality rate in this study (10% of episodes) was due to multifactorial reasons, partly patient-related factors such as old age, and comorbidity, and partly disease-related factors such as DKA severity. However some may have been due to therapy-related factors such as errors in management. Further studies are needed to clarify the factors behind this high mortality rate and steps to reduce the rate should be taken.

**References**


Mortality and burden of disease attributable to selected major risks

*Mortality and burden of disease attributable to selected major risks* uses a comprehensive framework for studying health risks that was developed for the World Health Report 2002, which presented estimates for the year 2000. The report provides an update for the year 2004 for 24 global risk factors. It uses updated information from WHO programmes and scientific studies for both exposure data and the causal associations of risk exposure to disease and injury outcomes. The burden of disease attributable to risk factors is measured in terms of lost years of healthy life using the metric of the disability-adjusted life year (DALY). The DALY combines years of life lost due to premature death with years of healthy life lost due to illness and disability.

Health risks are in transition: populations are ageing owing to successes against infectious diseases; at the same time, patterns of physical activity and food, alcohol and tobacco consumption are changing. Low- and middle-income countries now face a double burden of increasing chronic, noncommunicable conditions, as well as the communicable diseases that traditionally affect the poor.

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