The occurrence of diabetic ketoacidosis (DKA), a serious but largely preventable acute complication of diabetes mellitus, has been declining in recent years. However, empiric observations indicate that DKA continues to have a major effect on ethnic minority patients in inner-city settings. In this study, we conducted a retrospective analysis of five-year hospital admission data for DKA at a single inner-city hospital that serves a largely uninsured adult African American population. A computer-assisted search of the International Classification of Diseases. Ninth Revision, Clinical Modification codes for DKA revealed 847 admissions for confirmed DKA in 630 patients. Of these, 592 (94%) were African Americans, 22 (3.5%) were Whites, and 16 (2.5%) were Hispanics. The mean age was  $43.4 \pm .4$  years. Five hundred seventy-one (90.6%) of the patients had type 1 diabetes, and 59 (9.4%) had type 2 diabetes. One hundred forty-five patients (23%) were newly diagnosed with diabetes. Ninety-four (14.9%) of the patients had multiple admissions, ranging from 2 to 23 admissions per patient during the five-year period, while the remaining 391 (62.1%) patients were single admissions. Half of the patients (52%) did not have health insurance. Major precipitating factors for DKA included discontinuation of insulin, infection, and other medical illness in 501 (59.1%), 136 (16.1%), and 30 (3.5%) of the admissions, respectively. In conclusion, these data demonstrate that DKA continues to have a major effect in urban African American patients with diabetes. Therefore, multiple targeted interventions are needed in this population to improve diabetes care and thereby decrease the frequency of DKA. (Ethn Dis. 2007;17:234-237)

**Key Words:** Admissions, Diabetes Mellitus, Diabetic Ketoacidosis (DKA)

From the Division of Endocrinology, Diabetes, and Metabolism, Wayne State University School of Medicine, Detroit, Michigan.

Address correspondence and reprint requests to Berhane Seyoum, MD; Division of Endocrinology, Diabetes, and Metabolism; Wayne State University School of Medicine; 4201 St. Antoine, UHC-4H; Detroit, MI 48201; 313-595-2830; 313-993-0903 (fax); bseyoum@med.wayne. edu INTRODUCTION

Diabetic ketoacidosis (DKA) is a common and serious acute complication of diabetes caused by a relative or absolute lack of insulin. Diabetic ketoacidosis (DKA) is one of the preventable acute complications of diabetes mellitus through appropriate outpatient diabetes management. Although the management of DKA has been markedly improved in recent years in association with the general healthcare improvements, it is still a public health problem. In 1983, the incidence of DKA was reported to be 46 per 10,000 patients with diabetes.<sup>1</sup> During the last two decades the trend of DKA admissions has been increased.<sup>2</sup> Part of this increased frequency of admissions may be related to the increased prevalence of diabetes mellitus. Moreover, multiple episodes of DKA have also contributed to the increase of admissions,<sup>3</sup> but the age-adjusted mortality rate has been improving over the last two decades.<sup>2</sup>

In earlier reports, infection was the major precipitating factor in 33%-56% of cases, followed by noncompliance with therapy, including discontinuation of insulin and oral medications and nonadherence to diet, in 4%-25% of the cases.<sup>4-11</sup> Most of these studies were done on White populations, the results of which may not apply to African American populations. Contrary to these reports, a study by Musey et al<sup>12</sup> in a largely African American population showed that the major cause of DKA was discontinuation of insulin therapy in up to 67% of the cases. More than 50% of the patients discontinued or reduced the insulin dose; 21% did not know how to manage their insulin dosage with change of diet and physical activity; 14% discontinued insulin because of behavioral or psychological

Berhane Seyoum, MD; Paulos Berhanu, MD

Diabetic ketoacidosis (DKA) is one of the preventable acute complications of diabetes mellitus through appropriate outpatient diabetes management.

reasons; and 14% stopped insulin because they did not know what to do when they became sick.

Empiric observations in our city indicate that DKA continues to have a considerable effect on ethnic minority patients in an inner-city hospital that serves disproportionately large uninsured adult African American population. This study was intended to expand previous empiric observations by investigating the causes of DKA and its complications during a five-year period and to suggest preventive measures to reduce the impact of the problem.

# Methods

# **Patient Population**

This study is a retrospective analysis of confirmed DKA admission to one inner-city hospital in Detroit during the five-year period from January 1, 1999, to December 30, 2003. The hospital is a teaching facility associated with a medical school. It serves a largely indigent urban population that is >90% African American. Many of the patients are under- or uninsured for health care.

# Diabetic Ketoacidosis Admissions: Criteria and Confirmation

A computer assisted search of the International Classification of Diseases,

Table 1. Patterns of diabetic ketoacidosis (DKA) and diabetes-related admissions toDetroit Regional Hospital from 1999 to 2003

N	%
13,068	6.5*
847	1.3†
391	62.1‡
94	14.9‡
145	23.0‡
	N 13,068 847 391 94 145

 $\ast$  Out of the total 66,317 admission during the study period.

† Out of the total 13,068 patients with diabetes.

‡ Out of the total 630 patients admitted to the hospital.

Ninth Revision, Clinical Modification (ICD-9-CM) codes 250.1 (DKA in type 1 diabetes) and 250.11 (DKA in type 2 diabetes) were used to identify patients from the computer records of the hospital. After cases were identified in the computer data center, the medical records of the patients were retrieved, and the diagnosis of DKA was confirmed by detailed review of the records according to clinical criteria that indicated DKA along with one or all of the following laboratory data: 1) serum bicarbonate  $\leq 15 \text{ mg/L}$ ; 2) anion gap  $\geq$ 14; 3) arterial pH  $\leq$ 7.3; or 4) positive serum or urine ketones at any dilution level.

After confirming the diagnosis, patient age, sex, ethnicity, insurance coverage, length of hospital stay, type and duration of diabetes, medications, previous episodes of DKA, physical examination findings, and outcome of DKA were recorded in a database.



Fig 1. Frequency of admissions among 702 patients with known diabetes

### **Statistical Analysis**

SAS software JMP version 6 (SAS Institute Inc, Cary, NC) was used for all statistical analyses. Data were analyzed as means plus or minus standard errors of mean (SEM) for continuous variables and as frequency and percentage of study population for categorical variables. Nonparametric binomial test was used to evaluate the statistical significance of the different precipitating factors for DKA among the patients with and without insurance coverage. Chi-square tests were used to explore the univariate relationships among categorical variables. Statistical significance was set at  $P \leq .05$  for all tests.

### RESULTS

During the five-year period from January 1, 1999, to December 30,

2003, we noted 66,317 medical, surgical, and other admissions to the hospital under study. Of these, 13,068 were related to diabetes and 847 were for DKA admissions; DKA made up 1.3% of total admissions and 6.5% of diabetes-related admissions. Using the ICD codes for DKA, we originally found that the total number of DKA admissions was 971. However, when the medical records were identified and reviewed, 124 cases were excluded because they did not meet the criteria for DKA. Data analysis was then performed on the 847 confirmed admissions for DKA and included 630 patients with diabetes (Table 1).

Of the 847 admissions for DKA, 145 (17.1%) admissions were for newly diagnosed patients and the rest were admission for known patients with diabetes. Of the 702 admissions for previously diagnosed patients, 311 (36.9%) were multiple admissions during the study period, while the remaining 391 (46.2%) were single admissions (Fig. 1). Several characteristics are described in Table 2. The newly diagnosed patients were significantly younger than the known patients with diabetes admitted for DKA (P < .05). Males were seen twice as frequently as females in the known patients but nearly four times as frequently among the newly diagnosed

Table 2. Patient characteristics of newly diagnosed and previously diagnosed patients with diabetes who were admitted with diabetic ketoacidosis (DKA) during the five-year period

	Newly Diagnosed Patients with Diabetes Mellitus <i>n</i> =145	Patients with Previously Diagnosed Diabetes Mellitus <i>n</i> =702*
Mean age (years)	36.2 ± .1	43.4 ± .5†
Sex: M/F	114/31	468/234
Hospital stay (days) Ethnicity	5.1 ± .2	6.8 ± .2
African Americans	142	658
Hispanics	2	27
Whites	1	17

\* Based on the total number of admissions. Some patients had multiple admissions.

† P<.05.



Fig 2. Precipitating factors for DKA in 847 admissions during the 5-year period

patients. Most of the patients were African Americans.

The precipitating factors for DKA among all the patients are shown in Figure 2. In 59% of the admissions, patients discontinued insulin either because of lack of insulin or for reasons related to noncompliance. Patients who stopped taking insulin for various reasons while they have it were labeled as noncompliant. The second common precipitating factor was infection. Figure 3 shows the precipitating factors according to the insurance coverage. Lack of insulin and infection were the main causes of precipitating factors for DKA in patients without insurance (P<.001). The overall mean hospital stay was  $6.7 \pm .2$  days. No difference was observed in hospital stay among the new and the known patients. The major complications observed were anoxic brain damage in four patients, and one patient developed respiratory distress that eventually required permanent tracheostomy. Two patients (.3%) died, one secondary to myocardial infarction and the other secondary to sepsis.

### DISCUSSION

Diabetic ketoacidosis (DKA) remains one of the most commonly seen



Fig 3. Precipitating factors for DKA according to insurance status of patients with known diabetes

acute complications of diabetes mellitus. Diabetic ketoacidosis (DKA) is a preventable complication in educated patients who are compliant with their treatment regimens, including diet, insulin, or other diabetic medications. The incidence of DKA is reported to be 30–46 per 10,000 patients with diabetes.<sup>1,13</sup>

However, in spite of the preventable nature of the complication and the growing availability of health education for patients with diabetes, DKA still occurs among the underprivileged, underinsured, or uninsured segments of the population. Our study hospital is a major tertiary inner-city hospital that serves primarily poor and uninsured African Americans throughout Detroit. During the study period, DKA made up 1.3% of the total admissions and 6.5% of diabetes-related admissions. Of the total DKA patients, 23% were newly diagnosed individuals admitted for the first time. The occurrence of DKA admissions is consistent with several other reports.<sup>12,14</sup> Most patients (90.6%) in this study were African Americans, of whom >50% had no insurance. This pattern reflects the population served by our urban innercity hospital. A similar pattern was seen in other inner-city hospitals that provide medical care primarily to uninsured patients.12

As described in Figure 2, among most of the admissions (59%) for DKA, the main precipitating factor was discontinuation of insulin. Of those who discontinued insulin, 51.7% were noncompliant-they discontinued the insulin for no apparent reason-whereas in 48.3%, the patients discontinued insulin treatment because they were not able to afford or obtain the medication. Again, similar data were reported from other centers that serve largely indigenous patients with diabetes who had no insurance. Musey et al<sup>12</sup> reported that among their largely African America patients, 67% of them developed DKA after discontinuation of insulin therapy. More than 50% of those who discontinued their insulin did so because they could not afford to purchase insulin.

Despite all the progress in diabetes care and continuing increase in health care budget, some patients who depend on insulin for survival are unable to obtain insulin until they develop DKA and get admitted to the hospital. Insulin, which is one of the essential life saving drugs, has to be accessible to the people who depend on it, in order to avoid serious and potentially life-threatening complications such as DKA. Patients who are non-compliant and discontinue insulin until they develop DKA need to go through intensive diabetes education programs. They have to be educated by a health professional and must understand the consequences of discontinuing insulin. It is economically much cheaper for the hospital or any healthcare provider to identify these patients and provide them with the necessary diabetes education. In addition, healthcare providers need to allocate appropriate resources and provisions for these patients in order to ensure reliable access to insulin. In this study, more than 50% of the patients indicated that they stopped the insulin because they could not get insulin and they were not able to afford it, even though, they knew the consequences of discontinuing insulin. The issue of lack of an insulin prescription to purchase insulin was not a factor since the commonly used insulins are readily available in pharmacies without prescription. For the healthcare system, it would be cost-effective to provide insulin to patients who cannot afford it, rather than face the cost of managing DKA in the inpatient setting. Providing patients with insulin as outpatients and preventing the occurrence of DKA would reduce hospital admissions and limit the direct and indirect costs from DKA-related morbidities and mortalities.

The major precipitating factor for DKA in a number of earlier reports was

In our study, infection was the second most common cause of DKA.

infection rather than discontinuation of insulin.4-11 In our study, infection was the second most common cause of DKA. Those studies that showed infection to be the main precipitating cause were probably done in an economically more privileged population where financial resources and diabetes education are not a major problem, thus the social environment did not adversely contribute to DKA. In the inner-city setting, where there are larger number of indigent population and the health delivery status is meager, the main precipitating factor of DKA continues to be discontinuation of insulin, and infection comes in second.<sup>12</sup> The different trends seen among the economically privileged and indigent population can be improved if appropriate measures are undertaken to improve the services of diabetic management to these patients. It is intriguing that the main precipitating factors for DKA did not change in the last two decades in spite of major advances in the healthcare delivery system. While medical advances and modernization are important, health education and access to appropriate diabetes education remain the core issue in managing diabetes mellitus and preventing DKA. Consistent with this view, some large employers are beginning to provide diabetes medications and supplies to their employees with diabetes by waiving the patient's components of the cost.<sup>15</sup> Such approaches should, hopefully become more common.

### References

 Faich GA, Fishbein HA, Ellis SE. The epidemiology of diabetic acidosis: a population based study. *Am J Epidemiol.* 1983;117(5): 551–558.

- Center for Disease Control, Division of Diabetes Translations. National diabetes surveillance system. Available at: http:// www.cdc.gov/diabetes/statistics/dkafirst/index. htm.
- Cefalu WT. Diabetic ketoacidosis. Crit Care Clin. 1991;7(1):89–108.
- 4. Lebovitz HE. Diabetic ketoacidosis. *Lancet*. 1995;345(8952):767–772.
- Taft P, Stockigt JR, Harrison JW, Cameron DP. Diabetic ketoacidosis: its causes and their prevention. *Med J Aust.* 1968;2(19):825–829.
- Umpierrez GE, Kitabchi AE. Diabetic ketoacidosis: risk factors and management strategies. *Treat Endocrinol.* 2003;2(2):95–108.
- Gale EA, Dornan TL, Tattersall RB. Severely uncontrolled diabetes in the over fifties. *Diabetologia*. 1981;21(1):25–28.
- Hockaday TD, Alberti KG. Diabetic coma. Clinical Endocrinol Metab. 1972;1(3):750–788.
- Davoren PM, Bowen KM. Precipitating factors in diabetic ketoacidosis. *Med J Aust.* 1991;154(12):855–856.
- Johnson DD, Palumbo PJ, Chu CP. Diabetic ketoacidosis in a community based population. *Mayo Clin Proc.* 1980;55(2):83–88.
- Wachtel TJ, Tetu-Mouradjian LM, Goldman DL, Ellis SE, O'Sullivan PS. Hyperosmolarity and acidosis in diabetes mellitus: a three year experience in Rhode island. *J Gen Intern Med.* 1991;6(6):495–502.
- Musey VC, Lee JK, Crawford R, Klatka MA, McAdams D, Phillips L. Diabetes in urban African Americans. I. Cessation of insulin therapy is the major precipitating cause of diabetic ketoacidosis. *Diabetes Care*. 1995;18(4):483–489.
- Fishbein HA. Diabetic ketoacidosis, hyperosmolar nonketotic coma, lactic acidoisis, and hypoglycemia. In Harris MI, Hamman RF, eds. *Diabetes in America* (National Diabetes Data Group). Washington, DC: US Dept Health and Human Sciences, 1985;XII-1–XII-16.
- Ellemann K, Soerrensen JV, Pedersen L, Edsberg B, Sndersen OO. Epidemiology and treatment of diabetic acidosis in a community population. *Diabetes Care*. 1984;7(6):528–532.
- 15. University of Michigan will cut drug costs in 2 year test. *Detroit Free Press*. April 26, 2006.

#### AUTHOR CONTRIBUTIONS

Design concept of study: Seyoum, Berhanu Acquisition of data: Seyoum, Berhanu Data analysis and interpretation: Seyoum,

- Berhanu Manuscript draft: Seyoum, Berhanu
- Statistical expertise: Seyoum, Berhanu
- Acquisition of funding: Berhanu
- Administrative, technical, or material assistance: Berhanu

Supervision: Berhanu