Health Care Utilization and Burden of Diabetic Ketoacidosis in the U.S. Over the Past Decade: A Nationwide Analysis

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EPIDEMIOLOGY/HEALTH SERVICES RESEARCH

OBJECTIVE

Diabetes is one of the most common chronic diseases and a leading cause of morbidity and mortality in the U.S. Although our ability to treat diabetes and its associated complications has significantly improved, presentation with uncontrolled diabetes leading to ketoacidosis remains a significant problem.

RESEARCH DESIGN AND METHODS

We aimed to determine the incidence and costs of hospital admissions associated with diabetic ketoacidosis (DKA). We reviewed the National Inpatient Sample Database for all hospitalizations in which DKA (ICD-9 codes 250.10, 250.11, 250.12, and 250.13) was the principal discharge diagnosis during 2003–2014 and calculated the population incidence by using U.S. census data. Patients with ICD-9 codes for diabetic coma were excluded because the codes do not distinguish between hypoglycemic and DKA-related coma. We then analyzed changes in temporal trends of incidence, length of stay, costs, and in-hospital mortality by using the Cochrane-Armitage test.

RESULTS

There were 1,760,101 primary admissions for DKA during the study period. In-hospital mortality for the cohort was 0.4% (n = 7,031). The total number of hospital discharges with the principal diagnosis of DKA increased from 118,808 in 2003 to 188,965 in 2014 ($P < 0.001$). The length of stay significantly decreased from an average of 3.64 days in 2003 to 3.24 days in 2014 ($P < 0.01$). During this period, the mean hospital charges increased significantly from $18,987 (after adjusting for inflation) per admission in 2003 to $26,566 per admission in 2014. The resulting aggregate charges (i.e., national bill) for diabetes with ketoacidosis increased dramatically from $2.2 billion (after adjusting for inflation) in 2003 to $ 5.1 billion in 2014 ($P < 0.001$). However, there was a significant reduction in mortality from 611 (0.51%) in 2003 to 620 (0.3%) in 2014 ($P < 0.01$).

CONCLUSIONS

Our analysis shows that the population incidence for DKA hospitalizations in the U.S. continues to increase, but the mortality of this condition has significantly decreased, indicating advances in early diagnosis and better inpatient care. Despite decreases in the length of stay, the costs of hospitalizations have increased significantly, indicating opportunities for value-based care intervention in this vulnerable population.

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Diabetic ketoacidosis (DKA) is a potentially fatal metabolic complication of uncontrolled diabetes. Although characteristically associated with type 1 diabetes, DKA also can occur in type 2 diabetes under conditions of catabolic stress, especially in patients of African or Hispanic descent (1). DKA is the presenting manifestation in almost 25–30% of patients with type 1 diabetes (2–4) and in 4–29% of younger patients with type 2 diabetes (5–7). A study describing the clinical presentation of type 2 diabetes in the pediatric and adolescent population observed that 11% of this age-group presents with DKA (8). Hyperglycemic emergencies continue to be an important cause of morbidity and mortality among patients with diabetes, despite current advances in both diagnosis and treatment.

Recent epidemiological studies have suggested that the number of patients hospitalized with DKA in the U.S. is increasing. A 35% increase was found in the number of patients from 1996 to 2006, a rate of increase perhaps more rapid than the overall increase in diabetes (9). According to the Centers for Disease Control and Prevention (CDC), the number of hospital discharges with DKA as the first-listed diagnosis increased from 80,000 in 1988 to ~140,000 in 2009. In 2011, there were 175,000 emergency department visits for patients of all ages who experienced hyperglycemic crises. DKA results in >500,000 hospital days per year, with a total estimated potential hospital cost of $2.4 billion (10).

Diabetic hyperglycemic crises were invariably fatal until the discovery of insulin, after which mortality has decreased significantly. According to the CDC, the number of deaths caused by hyperglycemic crises was stable in the 1980s and then began to decrease in the 1990s. In 2009, hyperglycemic crises caused 2,417 deaths, 19.8% lower than the 3,012 deaths in 1980 (11).

Although our ability to manage diabetes and its associated complications has significantly improved, DKA remains a significant health burden. A paucity of epidemiological data exists on the effect of DKA on the U.S. health care system. The last update was provided by the CDC in 2014 (12). Hence, the aim of the current study was to use the largest national inpatient database to analyze the trends in hospitalization for DKA from 2003 to 2014.

RESEARCH DESIGN AND METHODS

The National Inpatient Sample (NIS) database was the main source used to determine a national population-based estimate of hospitalization trends. The NIS is part of the Healthcare Cost and Utilization Project through a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality (Rockville, MD) (13).

NIS is the largest publicly available all-payer inpatient health care data set in the U.S. and represents an ~20% stratified sample of discharges from community (nonfederal) hospitals. The 2003 NIS data were collected from 994 hospitals in 37 states, with information on all inpatient stays totaling ~8 million records. The 2014 NIS entails discharge data from >4,000 hospitals in 45 states and totals ~7 million records.

Owing to its to exceptional database size, the NIS comprehensively represents >95% of the U.S. population and is used for analyzing health care utilization, access, charges, quality, and outcomes. In addition, it promotes comparative studies of health care services and supports health care policy research. This database provides only administrative data for analysis. Patient-specific clinical data are lacking.

We identified cases of DKA by querying the NIS database for hospital data on all discharge diagnoses with a primary ICD-9 Clinical Modification diagnosis code of 250.10, 250.11, 250.12, and 250.13 (DKA) from 2003 to 2014. We excluded patients with ICD-9 codes for diabetic coma (250.3) because the codes do not distinguish between hypoglycemic and DKA-related coma.

Patient demographics, including age, sex, and insurance status, was obtained from the NIS database. We recorded various hospital characteristics, including location (Northeast, Midwest, South, and West and metropolitan vs. nonmetropolitan area), type (teaching vs. nonteaching), and size (small, medium, and large). Metropolitan areas were defined as those with a population of at least 50,000 people. A teaching hospital was defined as one designated as an American Medical Association–approved residency program by the American Hospital Association Annual Survey, a member of the Council of Teaching Hospitals, or that has a ratio of full-time-equivalent interns and residents to beds of ≥0.25. The definition of bedsize varied according to hospital location and teaching status; hence, a large overlap exists in the definition of hospital size. For small hospitals, bedsize ranged from 1 to 299, for medium hospitals the range was 50–499, and for large hospitals the range was 100 to ≥500. We also obtained the payer status for all admissions. Length of stay was defined as the number of nights the patient remained in the hospital for this inpatient visit.

The trends for the annual point estimates of frequency of DKA for the sample were analyzed. The annual frequency of discharges with a diagnosis of DKA was computed by dividing the annual number of discharges with DKA listed in the NIS database in each year by the total number of all discharges listed in the NIS for the same year. The temporal trend in frequencies of discharges, lengths of stay, hospital charges, and frequencies of deaths in patients with DKA was estimated by linear and polynomial regression. The most appropriate functional form for the trend was assessed by examination of regression diagnostic plots. Linear shape was determined for hospital charges and in-hospital deaths: a quadratic shape for length of stay and a cubic shape for number of discharges and discharge rate. $P < 0.05$ was considered statistically significant. All analyses were performed using SAS 9.4 statistical software (SAS Institute, Cary, NC).

In addition to the percentages available adjacent to the data in the tables, the frequency per 10,000 admissions was calculated for each categorical variable. These numbers represent the density of patients diagnosed with DKA compared with the total number of hospital discharges per category. Each frequency was calculated by dividing the number of patients with DKA by the total discharges in a specific categorical variable for each year and multiplying that number by 10,000. We viewed the counts as arising from a Poisson distribution and the total discharges as an offset, yielding Poisson rates that were compared over time through Poisson regression and yielded relative rates (RRs) and 95% CIs that expressed the ratio of rate per 10,000 in 2014 to that of 2003. These values differed from the percentages, which describe each category exclusively for either patients with DKA or for total discharges. The percentages distinguished differences among the variables for each specific year, whereas the frequencies were vital for comparing trends from 2003 to 2014, especially for age-group and region.

RESULTS

Number and Costs of DKA Discharges

There was a 59% increase in the total number of hospital discharges with the principal diagnosis of DKA from 118,808 in 2003 to 188,965 in 2014, which was statistically significant ($P < 0.0001$). A statistically significant increase was found in the frequency of hospital discharges for DKA as the principal diagnosis from 32.04 per 10,000 discharges in 2003 to 53.4 per 10,000 discharges in 2014 (RR 1.66 [95% confidence limits (CL) 1.65–1.67]; $P < 0.0001$) (Fig. 1). The average length of hospital stay for patients with DKA decreased from 3.64 in 2003 to 3.24 in 2014 ($P < 0.01$) (Fig. 2). Despite the decrease in the average length of hospital stay, the mean total charges for DKA-related hospital admissions increased considerably between 2003 and 2014. After adjusting for inflation, mean hospital charges per patient increased by 40% in a statistically significant linear fashion from $18,987 in 2003 to $26,566 in 2014 ($P < 0.001$). The total aggregate cost for hospitalizations with DKA as the discharge diagnosis increased from $2.2 billion in 2003 to $5.1 billion in 2014 (inflation adjusted). Although there was a dramatic increase in the number of hospital discharges from 2003 to 2014, there was a significant reduction in mortality from 611 (0.51%) in 2003 to 620 (0.33%) in 2014 ($P < 0.01$) (Fig. 3).

Patient Characteristics by Age

The highest rate of discharges with the principal diagnosis of DKA was seen in the 18–44-year age-group in 2003 as well as in 2014. A twofold increase was found in the frequency of discharge rates in the 65–84-year age-group from 6,638 in 2003 to 12,975 in 2014 (RR 2.08 [95% CL 2.02–2.15]; $P < 0.0001$). The increase in the frequency of discharge rates was very similar in the 45–64-year age-group (1.8 [95% CL 1.77–1.82]; $P < 0.0001$), ≥85-year age-group (1.8 [95% CL 1.62–1.98]; $P < 0.0001$), and 18–44-year age-group (1.73 [95% CL 1.71–1.75]; $P < 0.0001$). In the 1–17-year age-group, the frequency of discharge rates increased from 18,763 in 2003 to 20,705 in 2014. Although the increase in DKA discharge rates of the 1–17-year age-group (1.43 [1.40–1.46]; $P < 0.0001$) and <1-year age-group (0.7 [95% CL 0.5–0.98]; $P < 0.05$) were lower, they also reached statistical significance (Table 1).

Patient Characteristics by Sex

The frequency of DKA discharges was higher in males in 2003 and 2014; however, the increase in the frequency of DKA from 2003 to 2014 was slightly higher in females (Table 1). The increase in females went up from 27.7 per 10,000 admissions in 2003 to 46.6 per 10,000 admissions in 2014 (RR 1.67 [95% CL 1.65–1.7]; $P < 0.0001$). The frequency of discharges in men increased from 38.1 per 10,000 admissions in 2003 to 62.6 per 10,000 admissions in 2014 (1.63 [95% CL 1.62–1.66]; $P < 0.0001$) (Table 1).

Patient Characteristics by Payer Group

Between 2003 and 2014, the relative frequency of DKA discharges increased for all types of payer groups. Although in 2003, the highest absolute number of DKA discharges was seen in private insurance groups (36.82%), the absolute number of DKA discharges in 2014 was highest in the Medicaid group (34.33%). The increase in the relative frequency of DKA discharges was greatest in patients with Medicare, increasing by 117% from 12.5 per 10,000 admissions in 2003 to 27.1 per 10,000 admissions in 2014 (RR 2.16 [95% CL 2.12–2.2]; $P < 0.0001$), followed by patients with Medicaid (in whom the relative frequency of DKA increased by 70.3%) from 47.6 per 10,000 admissions to 81.1 per 10,000 admissions (1.7 [95% CL 1.67–1.72]; $P < 0.0001$). Patients with private insurance (32.3 per 10,000 to 49.9 per 10,000 [RR 1.54]) and uninsured groups (104.8 per 10,000 to 159.8 per 10,000 [RR 1.5]) showed the least increase (Table 1).

Patient Discharges by Hospital Characteristics and Region

During both 2003 and 2014, metropolitan areas had a higher absolute number of DKA discharges than the nonmetropolitan areas. However, the relative frequencies of discharges were higher in

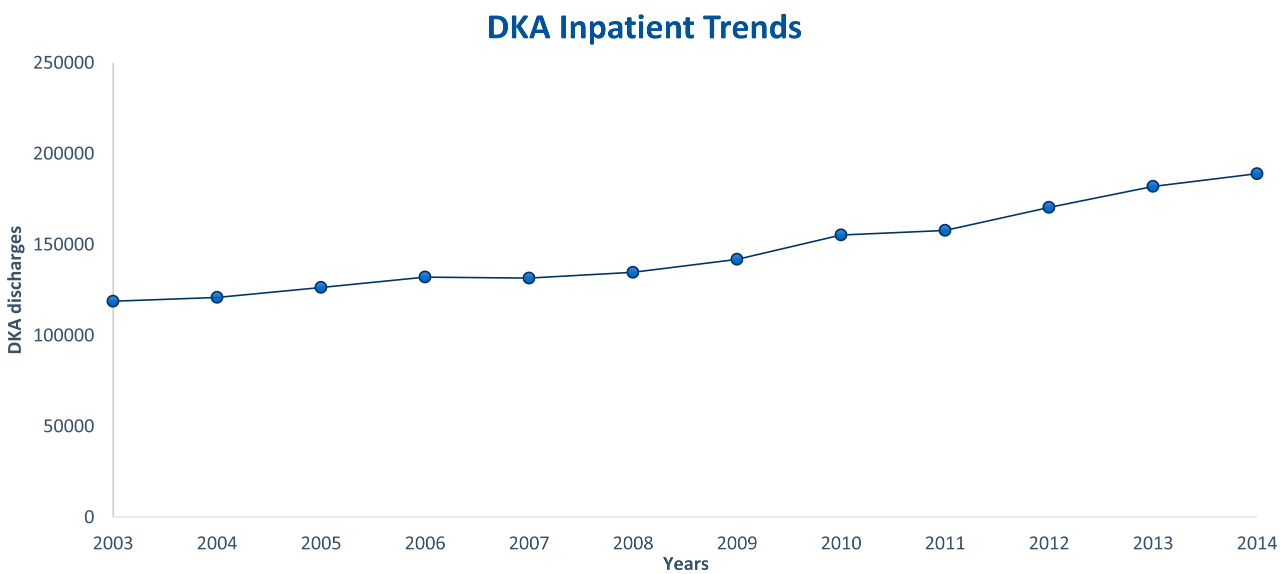

Figure 1—Trend of DKA in inpatient population. (A high-quality color representation of this figure is available in the online issue.)

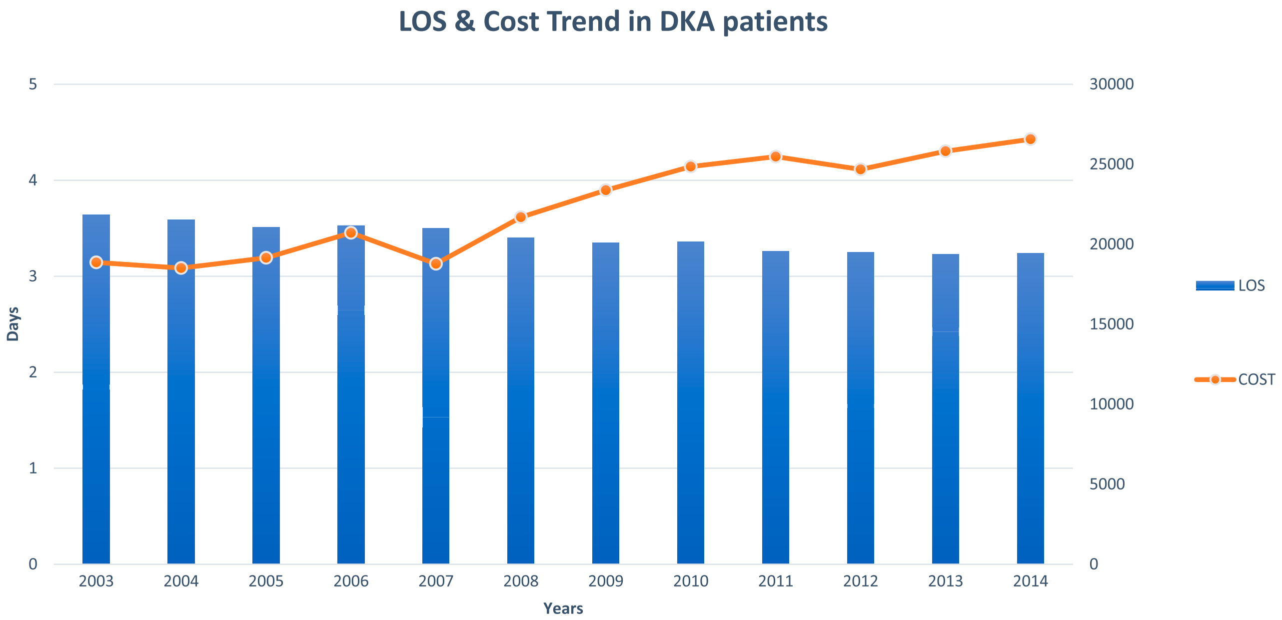

Figure 2—Length of stay (LOS) and mean cost of each hospitalization for patients with DKA. (A high-quality color representation of this figure is available in the online issue.)

nonmetropolitan areas in 2003 as well as in 2014. In metropolitan areas, the frequency of discharges increased from 31.4 per 10,000 in 2003 to 51.8 per 10,000 in 2014 (RR 1.64 [95% CL 1.62–1.66]; $P < 0.0001$). The frequency of discharges in nonmetropolitan areas increased from 35.8 per 10,000 in 2003 to 69.1 per 10,000 in 2014 (1.92 [95% CL 1.88–1.96]; $P < 0.0001$).

The South had the highest absolute number of DKA discharges as well as the highest relative frequency of DKA discharges during both 2003 and 2014 (Table 1). The frequency of discharges in the South increased from 34.7 per 10,000 in 2003 to 59.4 per 10,000 in 2014 (RR 1.7 [95% CL 1.68–1.72]; $P < 0.0001$). For the Midwest, the frequency of discharges increased from 30.3 per 10,000 in 2003 to 49.8 per 10,000 in 2014 (1.75 [95% CL 1.73–1.78]; $P < 0.0001$), which was followed by the West from 32.8 per 10,000 in 2003 to 53 per 10,000 in 2014 (1.6 [95% CL 1.58–1.63]; $P < 0.0001$) (Table 1).

During both 2003 and 2014, patients with DKA were more likely to be diagnosed in a hospital with a small number of beds (Table 1). There was a significant increase in the relative frequency of DKA discharges in these hospitals with a small number of beds from 34.6 per 10,000 discharges in 2003 to 57.6 per 10,000 discharges in 2014 (RR 1.66 [95% CL 1.63–1.69]; $P < 0.0001$) (Table 1).

CONCLUSIONS

This study suggests that the number of DKA-related hospitalizations in the U.S. continues to increase. With the total health care cost related to these hospitalizations being ∼$5.1 billion in 2014, DKA

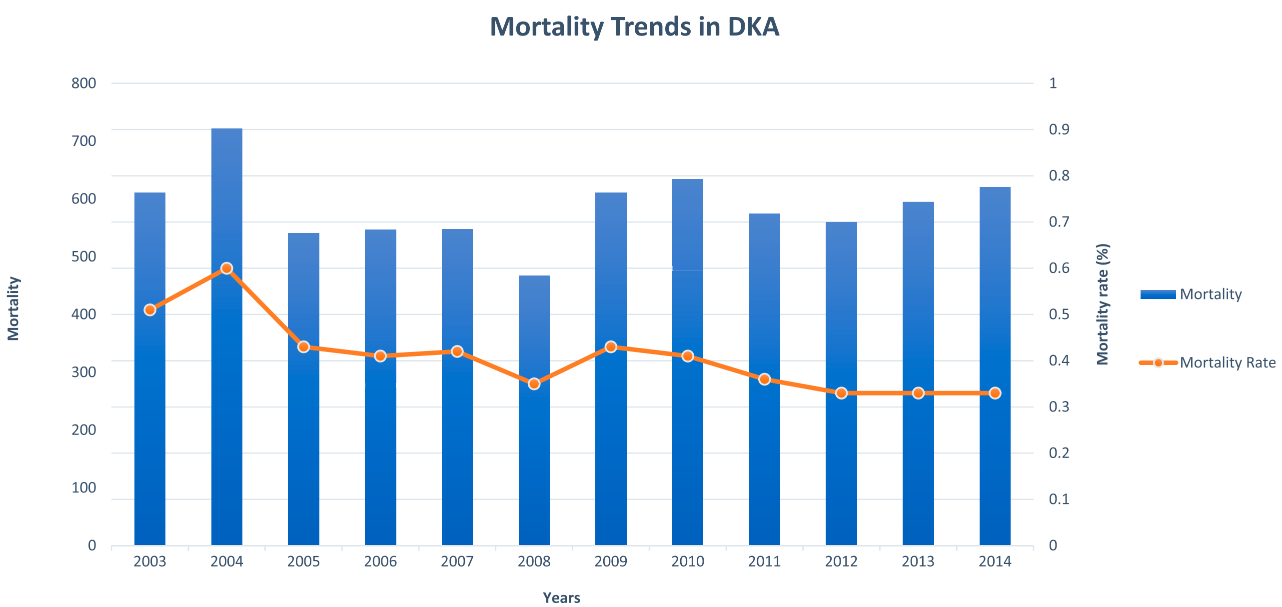

Figure 3—Mortality trend of patients with DKA. (A high-quality color representation of this figure is available in the online issue.)

Table 1—Patient characteristics for inpatient DKA primary discharges

Categorical variable	DKA		Total		DKA per 10,000 admissions			
	2003	2014	2003	2014	2003	2014	RR (95% CL)	*P* value
All discharges	118,808 (100.00)	188,965 (100.00)	37,074,605 (100.00)	35,358,818 (100.00)	32.04	53.4	1.66 (1.65–1.67)	<0.0001
Mean age (years)								
Age-group (years)								
<1	91 (0.08)	60 (0.03)	4,581,417 (12.36)	4,247,755 (12.01)	0.2	0.14	0.7 (0.5–0.98)	<0.05
1–17	18,763 (15.79)	20,705 (10.96)	1,762,383 (4.75)	1,347,359 (3.81)	106.5	153.6	1.43 (1.40–1.46)	<0.0001
18–44	66,110 (55.64)	102,775 (54.39)	9,772,014 (26.36)	8,714,895 (24.65)	67.65	117.9	1.73 (1.71–1.75)	<0.0001
45–64	26,407 (22.23)	51,330 (27.16)	8,086,876 (21.81)	8,709,298 (24.63)	32.65	58.9	1.8 (1.77–1.82)	<0.0001
65–84	6,638 (5.59)	12,975 (6.87)	10,150,753 (27.38)	9,490,054 (26.84)	6.54	13.67	2.08 (2.02–2.15)	<0.0001
≥85	577 (0.49)	1,105 (0.58)	2,666,613 (7.19)	2,837,716 (8.03)	2.16	3.9	1.8 (1.62–1.98)	<0.0001
Sex								
Male	57,394 (48.31)	94,470 (49.99)	15,064,915 (40.63)	15,095,708 (42.69)	38.1	62.6	1.63 (1.62–1.66)	<0.0001
Female	60,618 (51.02)	94,445 (49.98)	21,861,583 (58.97)	20,255,555 (57.29)	27.7	46.6	1.67 (1.65–1.7)	<0.0001
Payer								
Medicare	17,221 (14.49)	37,480 (19.83)	13,761,829 (37.12)	13,795,116 (39.01)	12.5	27.1	2.16 (2.12–2.2)	<0.0001
Medicaid	32,504 (27.36)	64,870 (34.33)	6,828,282 (18.42)	7,993,545 (22.61)	47.6	81.1	1.7 (1.67–1.72)	<0.0001
Private insurance	43,746 (36.82)	54,095 (28.63)	13,555,962 (36.56)	10,833,048 (30.64)	32.3	49.9	1.54 (1.52–1.56)	<0.0001
Uninsured	17,901 (15.07)	26,370 (13.95)	1,707,382 (4.61)	1,650,461 (4.67)	104.8	159.8	1.5 (1.48–1.54)	<0.0001
Other	7,102 (5.98)	5,700 (3.02)	1,147,219 (3.09)	1,019,269 (2.88)	61.9	55.9	0.9 (0.87–0.93)	<0.001
Median income for zip code								
Low ($0–$35,999)	39,536 (33.28)	70,115 (37.10)	10,061,048 (27.14)	10,244,655 (28.97)	39.3	68.4	1.73 (1.71–1.75)	<0.0001
Not low (≥$36,000)	75,865 (63.86)	114,550 (60.62)	26,173,832 (70.60)	24,344,858 (68.85)	28.98	47.05	1.62 (1.6–1.63)	<0.0001
Missing	3,407 (2.87)	4,300 (2.28)	839,725 (2.26)	769,305 (2.18)	40.6	55.9	*	
Owner								
Government	21,584 (18.17)	25,410 (13.45)	5,172,217 (13.95)	4,310,458 (12.19)	41.7	58.9	1.4 (1.3801.44)	<0.0001
Private, not-for-profit	83,374 (70.18)	135,940 (71.94)	26,964,496 (72.73	25,831,562 (73.06)	30.9	52.6	1.69 (1.68–1.71)	<0.0001
Private, for-profit	13,850 (11.66)	27,615 (14.61)	4,937,891 (13.32)	5,216,798 (14.75)	28	52.9	1.88 (1.84–192)	<0.0001
Location								
Nonmetropolitan	19,986 (16.82)	23,245 (12.30)	5,583,485 (15.06)	3,360,976 (9.51)	35.8	69.1	1.92 (1.88–1.96)	<0.0001
Metropolitan	98,753 (83.12)	165,720 (87.7)	31,471,911 (84.89)	31,997,842 (90.49)	31.4	51.8	1.64 (1.62–1.66)	<0.0001
Bedsize								
Small	14,955 (12.59)	37,730 (19.97)	4,327,304 (11.67)	6,553,063 (18.53)	34.6	57.6	1.66 (1.63–1.69)	<0.0001
Medium	32,742 (27.56)	57,080 (30.21)	9,613,451 (25.93)	10,398,925 (29.41)	34.05	54.9	1.6 (1.58–1.63)	<0.0001
Large	71,041 (59.80)	94,155 (49.83)	23,114,641 (62.35)	18,406,830 (52.06)	30.7	51.1	1.66 (1.64–1.67)	<0.0001
Region								
Northeast	20,468 (17.23)	27,725 (14.67)	7,264,150 (19.59)	6,623,697 (18.73)	28.2	41.9	1.48 (1.45–1.51)	<0.0001
Midwest	25,812 (21.73)	42,430 (22.45)	8,520,023 (22.98)	7,942,913 (22.46)	30.3	49.8	1.75 (1.73–1.78)	<0.0001
South	49,307 (41.50)	81,630 (43.20)	14,205,434 (38.32)	13,774,248 (38.96)	34.7	59.4	1.7 (1.68–1.72)	<0.0001
West	23,221 (19.54)	37,180 (19.68)	7,084,998 (19.11)	7,017,960 (19.85)	32.8	53	1.6 (1.58–1.63)	<0.0001

Data are *n* (%) unless indicated. Sociodemographic and patient characteristics for inpatient DKA primary discharges. *Missing data for median income. RR not calculated.

is a significant burden on the U.S. health care system.

From 2003 to 2014, the number of discharges with DKA as the primary diagnosis rose by 59%, which possibly was influenced by several factors. A fourfold increase has been seen in the incidence of diagnosed diabetes in the U.S., from 5.5 million in 1980 to 22 million in 2014, with ~1.4 million new patients diagnosed every year. In 2012, the prevalence of type 1 diabetes was 1.25 million, with close to 20,000 patients being young (<20 years old) and the rest adult (12).

Although traditionally described in type 1 diabetes, an increasing number of patients with type 2 diabetes now present with DKA, which accounted for 35% of total DKA cases in 2003 (9). Among this subset has been a rise in an entity described as ketosis-prone diabetes. Characterized by obesity, patients with ketosis-prone diabetes present with DKA in the absence of precipitating factors (14). Although these patients experience an impairment in insulin secretion, they tend to recover after ketoacidosis resolves and often are able to discontinue insulin therapy within a few months (1). Even so, 60% of these patients, especially those treated with lifestyle modifications alone, have a recurrence of DKA after discontinuation of insulin therapy (15). We postulate that the rising prevalence of ketosis-prone diabetes could contribute to the increasing number of DKA hospitalizations. In patients with latent autoimmune diabetes of adulthood

(LADA), insulin dependency develops earlier than in patients with type 2 diabetes, and individuals in this insulinopenic stage are at risk for DKA (16). Individual patients with LADA who present with ketoacidosis have been reported, but not enough evidence exists to conclude what proportion of patients with DKA are attributable to LADA (17).

Medication nonadherence is a major factor that results in DKA, and the growing cost of insulin contributes significantly (18). Despite insulin's introduction more than a century ago, no generic form is available. The mean price of insulin has increased from $4.34 per milliliter in 2002 to $12.92 per milliliter in 2013 (19). The past several years have seen an evolution of newer insulins that have offered better glycemic control, albeit at a higher cost. Both short-acting insulin analogs (e.g., insulin lispro, insulin aspart) and long-acting analogs (e.g., insulin glargine, insulin determir) offer better glycemic control with a reduced rate of hypoglycemia and less weight gain compared with regular human insulin and NPH insulin but, again, at a higher cost. More recently, newer basal insulins, such as insulin degludec, pegylated insulin lispro, and glargine U300, have provided the advantage of a longer duration of action than insulin glargine with a further reduction of risk of hypoglycemia and improved quality of life, although at an even higher price (20). The economic burden that insulin usage imposes may have led to poorer adherence and increased rates of DKA over the past decade. With the advent of biosimilar insulin, patients are expected to have access to cheaper insulin (21).

Another major reason for poor medication adherence is the lack of knowledge about diabetes, which is particularly the case in inner city areas where diabetes education is lacking likely secondary to a low literacy rate and poor access to outpatient health care (22). In a prospective randomized study, youth with type 1 diabetes randomized to the arm receiving multisystem therapy, including home-based psychotherapy, were observed to have increased medication adherence and decreased hospitalization rates for DKA compared with the control group (23). We also speculate that diabetes care managed by primary care physicians rather than by endocrinologists might be one of the reasons the led to the rise of DKA. However, more studies are needed in this area to compare outcomes of diabetes managed by primary care physicians versus endocrinologists.

The costs associated with DKA hospitalizations have increased by 56% from 2003 to 2014, with a 40% increase in mean hospital charges per admission. In most institutions, patients with DKA are admitted to the intensive care unit (ICU), as recommended by the American Diabetes Association (24,25). However, more-recent studies have failed to demonstrate differences in outcome of uncomplicated DKA (i.e., without any precipitating factors except for insulin treatment cessation or new onset of diabetes in a patient without any major comorbidities) managed in the ICU, the general medical ward, or even the emergency department (26). A retrospective cohort study that compared costs in lower versus higher ICU utilization groups among 94 acute care hospitals concluded that hospitals that used ICU care for managing DKA were likely to have more-invasive procedures and incur higher hospital costs with no difference in mortality (27). Costs related to DKA hospitalizations can be reduced by careful assessment of the severity of DKA and the avoidance of unnecessary ICU admissions for uncomplicated DKA.

The current analysis revealed that the average hospital length of stay for DKA decreased during our study period. Mortality related to DKA also decreased from 0.51% in 2003 to 0.33% in 2014. The use of standardized DKA treatment protocols likely is partly responsible (24). Treatment outcomes of patients with DKA are similar in community and teaching hospitals and independent of whether the treating physician is a family physician, internist, house staff with supervision, or an endocrinologist if standardized guidelines are followed (25). Thus, a simple protocol-based treatment regimen has improved outcomes, decreased the length of stay, and reduced mortality of this significant problem.

Prevention of this disease remains the crux of the problem. The current study shows that the highest number of DKA discharges were in the 18–44-year age-group in 2003 as well as in 2014, which is consistent with results seen in epidemiological data in 2006 (9). Nonadherence to insulin in this age-group may be attributed to several factors, including the constant burden of having a chronic disease, psychological factors that lead to eating disorders, fear of hypoglycemia, and fear of weight gain (28). Furthermore, increasing use of cocaine, alcohol, and cannabis in this age-group has been observed to be responsible for the recurrence of DKA episodes (29). Patients with ketosis-prone diabetes also belong to this age-group. We also observed a twofold increase in the frequency of DKA discharges in the 65–84-year age-group from 2003 to 2014. Infections, cerebrovascular accidents, myocardial infarction, trauma, drugs, and pancreatitis, well-known precipitating factors of DKA (30), are increasingly prevalent in elderly patients, which may have contributed to the increased rates of DKA hospitalizations.

Few data exist about sex-related differences in the risk and outcomes of patients hospitalized for DKA. We found that the rate of hospitalizations for DKA was significantly higher in men than in women in 2003 and 2014, which could be due to the absolute increase in the number of newly diagnosed cases of diabetes in males, which grew by 177% (from 2.6 to 7.2 age-adjusted rate per 100 population) from 1980 to 2010, whereas in females, the age-adjusted rates increased by only 114% (from 2.8 to 6.0 per 100 population) from 1990 to 2009 (12). However, the current study also shows that the rate of increase of DKA discharges from 2003 to 2014 was slightly higher in females. Prior studies have shown that women with diabetes are offered less-aggressive treatment and interventions than men and that with their increased familial responsibility, they often prioritize caring for their family members' disease management over that of their own (31). A study by Polonsky et al. (28) found that 31% of their female population reported intentional omission of administering insulin, which was associated with higher rates of eating disorders, psychological stressors, fear of hypoglycemia, poorer medication adherence, and increased worry about weight gain.

Access to adequate insurance coverage is a powerful determinant in the management of patients with diabetes. We found that in both 2003 and 2014, the relative frequency of DKA discharges increased in all payer groups. Of note, the absolute number of DKA discharges in 2014 was highest in the Medicaid group

(34.33%) than in 2003, when it was highest in the privately insured group (36.82%). The expansion of Medicaid coverage after the initiation of the Affordable Care Act in 2014 led to higher detection rates of DKA in this population group, which could be a contributory factor. Furthermore, the relative frequency of DKA rose by 117% from 2003 to 2014 in patients with Medicare and by 70.3% in the patients with Medicaid, which was higher than the difference observed in privately insured patients. We consider two possible explanations. Medicaid- and Medicare-insured patients face significant barriers to seeking appropriate care and often wait until a health concern becomes debilitating enough to warrant a hospital admission (32). In addition, privately insured groups have far more access to advanced treatment modalities and the newer drugs available for diabetes. They also tend to have less-severe diabetes and are younger with fewer comorbidities (33).

Hospital characteristics, such as metropolitan/nonmetropolitan areas, region, and hospital bedsize, were studied. Metropolitan areas had a higher absolute number of DKA discharges than nonmetropolitan areas throughout the study period. More densely populated metropolitan areas have higher DKA discharge detection rates possibly as a result of easier access to medical attention in emergent situations compared with nonmetropolitan areas.

In terms of regional distribution, the South had the highest absolute number and relative frequency of DKA discharges in both 2003 and 2014. According to the CDC, a diabetes belt exists that is located in the southern portion of the U.S. and consists of 644 counties in 15 mostly southern states. The population in the diabetes belt comprises a higher number of African Americans than the rest of the country (23.8% vs. 8.6%) who are known to be at a higher risk of developing DKA. The prevalence of obesity also is higher because of a sedentary lifestyle compared with the rest of the U.S., conferring a greater risk of metabolic syndrome and development of diabetes (34).

Advancement of newer technologies for the control of diabetes, including continuous glucose monitoring and continuous subcutaneous insulin infusion, has facilitated improvement in glycemic control along with a reduction in health care utilization (35,36). A greater number of patients who adhere to these newer technologies might be a potential solution to help to reverse the increasing incidence of DKA.

With regard to the design and use of the NIS database, this study has several limitations. We relied on national hospital discharge data, which reflect the coding practices different health care institutions use; thus, the findings may have underestimated the actual incidence of DKA discharges because the discharges may have been coded with an alternative diagnosis, such as hyperglycemia or hyperglycemic emergency. Also possible is that patient discharges may have been coded incorrectly as hyperglycemic hyperosmolar state or hyperglycemic hyperosmolar nonketotic coma when in fact the actual discharge diagnosis was DKA because considerable overlap exists between the two hyperglycemic conditions. An additional limitation of the study is that the data could not be normalized for the increase in the prevalence of diabetes, and hence, whether the increase in the number of DKA discharges was due to an overall increase in the prevalence of diabetes is difficult to correlate. Furthermore, the study does not distinguish between DKA as a presentation of new-onset diabetes from DKA in a patient with established diabetes. The NIS database does not control for errors made during data entry. Individual patient-specific clinical variables (e.g., ethnicity, medication use, duration of diabetes) was not obtained, limiting demographic analysis. Future studies that analyze patient-specific trends and individual hospital coding practices may provide additional information.

In conclusion, this nationwide study shows that hospitalizations with a primary discharge diagnosis of DKA increased by 59% over an 11-year period. The burden that this finding poses is a major concern for physicians and the U.S. health care system. The mortality associated with DKA, however, has significantly decreased. We aim to draw attention to the magnitude of the problem and stress the importance of focusing on preventive measures to reduce the burden of DKA and diabetes-related emergencies.

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References

1. Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: ketosis-prone type 2 diabetes mellitus. Ann Intern Med 2006;144:350–357

2. Rewers A, Klingensmith G, Davis C, et al. Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the Search for Diabetes in Youth Study. Pediatrics 2008;121: e1258–e1266

3. Lawrence JM, Mayer-Davis EJ, Reynolds K, et al.; SEARCH for Diabetes in Youth Study Group. Diabetes in Hispanic American youth: prevalence, incidence, demographics, and clinical characteristics: the SEARCH for Diabetes in Youth Study. Diabetes Care 2009;32(Suppl. 2):S123–S132

4. Liu LL, Yi JP, Beyer J, et al.; SEARCH for Diabetes in Youth Study Group. Type 1 and type 2 diabetes in Asian and Pacific Islander U.S. youth: the SEARCH for Diabetes in Youth Study. Diabetes Care 2009;32(Suppl. 2):S133–S140

5. Zdravkovic V, Daneman D, Hamilton J. Presentation and course of type 2 diabetes in youth in a large multi-ethnic city. Diabet Med 2004; 21:1144–1148

6. Sellers EA, Dean HJ. Diabetic ketoacidosis: a complication of type 2 diabetes in Canadian aboriginal youth. Diabetes Care 2000;23:1202–1204

7. Pinhas-Hamiel O, Dolan LM, Zeitler PS. Diabetic ketoacidosis among obese African-American adolescents with NIDDM. Diabetes Care 1997;20:484–486

8. Klingensmith GJ, Connor CG, Ruedy KJ, et al.; Pediatric Diabetes Consortium. Presentation of youth with type 2 diabetes in the Pediatric Diabetes Consortium. Pediatr Diabetes 2016; 17:266–273

9. Centers for Disease Control and Prevention. *National Hospital Discharge Survey*. Atlanta, GA, Centers for Disease Control and Prevention, 2006

10. Department of Health and Human Services; Centers for Disease Control and Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States. Washington, DC, Department of Health and Human Services, 2015

11. Centers for Disease Control and Prevention. National diabetes statistics report [Internet], 2014. Atlanta, GA, Centers for Disease Control and Prevention. Available from https://www.cdc.gov/diabetes/data/statistics/statistics-report.html. Accessed 13 May 2018

12. Centers for Disease Control and Prevention, National Diabetes Statistics Report, 2014: estimates of diabetes and its burden in the United States. Atlanta, GA, Centers for Disease Control and Prevention, 2014

13. Healthcare cost and Utilization Project (HCUP). Rockville, MD, Agency for Healthcare Research and Quality, 2013

14. Nyenwe EA, Kitabchi AE. The evolution of diabetic ketoacidosis: an update of its etiology,

pathogenesis and management. Metabolism 2016;65:507–521
15. Smiley D, Chandra P, Umpierrez GE. Update on diagnosis, pathogenesis and management of ketosis-prone type 2 diabetes mellitus. Diabetes Manag (Lond) 2011;1:589–600
16. Nabhan F, Emanuele MA, Emanuele N. Latent autoimmune diabetes of adulthood. Unique features that distinguish it from types 1 and 2. Postgrad Med 2005;117:7–12
17. Nadhem O, Nakhla E, Smalligan RD. Diabetic ketoacidosis as first presentation of latent autoimmune diabetes in adult. Case Rep Med 2015; 2015:821397
18. Maldonado MR, Chong ER, Oehl MA, Balasubramanyam A. Economic impact of diabetic ketoacidosis in a multiethnic indigent population: analysis of costs based on the precipitating cause. Diabetes Care 2003;26:1265–1269
19. Hawkes N. The travesty of expensive insulin. BMJ 2016;353:i2933
20. Standl E, Owen DR. New long-acting basal insulins: does benefit outweigh cost? Diabetes Care 2016;39(Suppl. 2):S172–S179
21. Heinemann L, Carter AW. Will biosimilar insulins be cheaper? Diabetes Technol Ther 2017;19:513–515
22. Anderson RM, Herman WH, Davis JM, Freedman RP, Funnell MM, Neighbors HW. Barriers to improving diabetes care for blacks. Diabetes Care 1991;14:605–609
23. Ellis D, Naar-King S, Templin T, et al. Multisystemic therapy for adolescents with poorly controlled type 1 diabetes: reduced diabetic ketoacidosis admissions and related costs over 24 months. Diabetes Care 2008;31:1746–1747
24. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009;32:1335–1343
25. Kitabchi AE, Umpierrez GE, Murphy MB, et al. Management of hyperglycemic crises in patients with diabetes. Diabetes Care 2001;24: 131–153
26. Cohn BG, Keim SM, Watkins JW, Camargo CA. Does management of diabetic ketoacidosis with subcutaneous rapid-acting insulin reduce the need for intensive care unit admission? J Emerg Med 2015;49:530–538
27. Chang DW, Shapiro MF. Association between intensive care unit utilization during hospitalization and costs, use of invasive procedures, and mortality. JAMA Intern Med 2016;176:1492–1499
28. Polonsky WH, Anderson BJ, Lohrer PA, Aponte JE, Jacobson AM, Cole CF. Insulin omission in women with IDDM. Diabetes Care 1994; 17:1178–1185
29. Isidro ML, Jorge S. Recreational drug abuse in patients hospitalized for diabetic ketosis or diabetic ketoacidosis. Acta Diabetol 2013;50:183–187
30. Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin North Am 2006;35:725–751, viii
31. Brugel L, Laurent M, Caillet P, et al. Impact of comprehensive geriatric assessment on survival, function, and nutritional status in elderly patients with head and neck cancer: protocol for a multicentre randomised controlled trial (EGeSOR). BMC Cancer 2014;14:427
32. Temkin-Greener H. Medicaid families under managed care. Anticipated behavior. Med Care 1986;24:721–732
33. Garfield SS, Xenakis JJ, Bastian A, McBride M. Experiences of people with diabetes by payer type: an analysis of the Roper Diabetes Data Set. Diabetes Ther 2015;6:113–125
34. Barker LE, Kirtland KA, Gregg EW, Geiss LS, Thompson TJ. Geographic distribution of diagnosed diabetes in the U.S.: a diabetes belt. Am J Prev Med 2011;40:434–439
35. Parkin CG, Graham C, Smolskis J. Continuous glucose monitoring use in type 1 diabetes: longitudinal analysis demonstrates meaningful improvements in HbA1c and reductions in health care utilization. J Diabetes Sci Technol 2017;11: 522–528
36. Floyd B, Chandra P, Hall S, et al. Comparative analysis of the efficacy of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes mellitus. J Diabetes Sci Technol 2012;6:1094–1102