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National-Level Outcomes of Diabetic Ketoacidosis with and without Coma: A Retrospective Analysis of 2.3 Million U.S. Hospitalizations

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) remains a significant complication of diabetes associated with substantial morbidity and mortality. We aimed to evaluate clinical outcomes among patients with DKA, both with and without coma, using a nationally representative database and to identify associated factors.
Methods: We analyzed 2,381,619 DKA hospitalizations from the National Inpatient Sample (2016–2022), comparing outcomes between patients with (n = 47,355; 1.99%) and without coma (n = 2,334,264; 98.01%). Primary outcomes included length of stay (LOS), in-hospital mortality, and total hospital charges. Multivariable regression models adjusted for demographic, clinical, and hospital-level factors.
Results: Patients with DKA-related coma had significantly worse outcomes: longer LOS (8.65 vs. 4.91 days), higher mortality (16.36% vs. 3.12%), and higher hospital charges ($119,080 vs. $61,240) compared to non-comatose patients. After adjustment, coma remained strongly associated with adverse outcomes (an additional 3.23 days of LOS, 5.38-fold higher mortality odds, $51,060 higher charges). Age >65 years, Type 2 diabetes, Asian/Pacific Islander race, and treatment at urban teaching hospitals were independently associated with worse outcomes. Female gender was associated with slightly better outcomes across all measures, with a significant interaction between gender and coma status.
Conclusion: Consciousness level is among the strongest independent predictors of adverse DKA outcomes. Age, diabetes type, race/ethnicity, and hospital characteristics also significantly impact mortality, length of stay, and hospital charges. These factors should be considered in the clinical management of DKA and hospital resource planning.

1. Introduction

Diabetic ketoacidosis (DKA) is a life-threatening diabetes complication characterized by hyperglycemia, ketosis, and metabolic acidosis [1]. DKA remains a significant and growing global complication affecting people with both type 1 and some with type 2 diabetes, contributing to substantial morbidity and mortality [2]. The burden is particularly high in low-resource countries, for instance, in Ethiopia, 60.7% of newly diagnosed pediatric type 1 diabetes patients presented with DKA [3]. In the United States, DKA incidence among commercially insured individuals was 55.5 per 1,000 person-years, with rates increasing from 2011 but slightly declining in 2018–2019 [4]. Approximately one-third of U.S. youth newly diagnosed with type 1 diabetes present with DKA, which is associated with worse glycemic outcomes despite intensive insulin management [5]. National DKA hospitalizations have been rising due to factors including delayed diagnosis, poor medication-taking behavior, and infections, though most cases respond favorably to timely interventions [6]. Coma is a rare but life-threatening complication of DKA, most often resulting from severe cerebral edema or profound metabolic derangement[7]. It occurs in approximately 10% of cases and signifies advanced physiological decompensation, necessitating immediate intensive care[7]. Cerebral edema is the leading cause of coma in pediatric DKA and is often fatal or results in long-term neurological damage if not rapidly identified and treated [8]. Other potential causes, such as brainstem infarction, may also lead to coma and can be fatal despite aggressive ICU intervention[9].

Despite its clinical importance, coma in DKA has not been systematically studied in large cohort trials, resulting in a lack of standardized guidance for neurological assessment and management. [7]. Many studies on DKA outcomes rely on single-center or regional data with small sample sizes, limiting the generalizability of their findings [10]. National-level or population-based research on the epidemiology and outcomes of DKA-related coma remains scarce[11]. Most clinical trials and observational studies on DKA do not stratify patients based on the presence or severity of coma, which obscures understanding of its specific impact on outcomes [8]. Although pediatric studies more often address

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cerebral complications, they frequently lack the long-term follow-up needed to assess neurological sequelae [12]. Variation in how coma is defined and diagnosed across studies further complicates data interpretation and limits consistency in reporting[7].

This nationwide study utilizing the National Inpatient Sample (NIS) is warranted for several reasons. The NIS represents the largest all-payer inpatient database in the United States, providing a robust platform for population-level analysis of DKA outcomes. While prior single-center or regional studies have provided valuable insights, they often lack statistical power and generalizability to assess less common presentations such as DKA with coma, which comprises only a small percentage of total DKA cases [11]. The NIS dataset allows for a comprehensive assessment of clinical outcomes stratified by coma status across diverse geographical regions, hospital types, and patient demographics, overcoming the limitations of previous smaller-scale studies.

Despite the clinical significance of altered consciousness in DKA, there remains a paucity of large-scale investigations specifically examining how coma affects outcomes and resource utilization in this condition. Previous research has established that consciousness level represents a key determinant of DKA severity, yet standardized clinical approaches for neurological assessment and management of DKA remain inconsistent [7]. By leveraging the NIS database's extensive demographic and clinical information, this study offers a unique opportunity to quantify the impact of coma on mortality, length of stay, and hospital charges while controlling for confounding variables.

2. Methods

2.1. Data Source

This retrospective cross-sectional study utilized data from the National Inpatient Sample (NIS) from 2016 to 2022. The NIS, maintained by the Healthcare Cost and Utilization Project (HCUP), is the largest publicly available all-payer inpatient healthcare database in the United States. The NIS employs a complex stratified sampling design, capturing approximately 20% of U.S. hospital discharges annually from participating states. Each discharge record includes clinical and resource use information, with appropriate discharge weights to generate national estimates.

2.2. Case Identification

Diabetic ketoacidosis (DKA) cases were identified using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis codes. Specifically, we extracted all discharges with the following codes appearing in any of the 40 diagnosis fields:

- Type 1 diabetes with ketoacidosis without coma (E10.10) or with coma (E10.11)
- Type 2 diabetes with ketoacidosis without coma (E11.10) or with coma (E11.11)
- Other specified diabetes with ketoacidosis without coma (E13.10) or with coma (E13.11)
- Drug-induced diabetes with ketoacidosis without coma (E09.10) or with coma (E09.11)
- Diabetes due to underlying condition with ketoacidosis without coma (E08.10) or with coma (E08.11)

Cases were categorized by diabetes type and further stratified by the presence or absence of coma at presentation.

2.3. Variables

2.3.1. Primary Outcomes

The three primary outcomes were analyzed:

1. Length of stay (LOS): Measured in days from admission to discharge
2. In-hospital mortality: Defined as death occurring during the index hospitalization
3. Total hospital charges: Reported in U.S. dollars, representing the amount billed by hospitals

2.3.2. Independent Variables

The primary exposure variables were:

1. Coma status: Presence or absence of coma in patients with DKA
2. Gender: Categorized as male or female

Additional covariates included:

- Age: Stratified into four groups (Under 18, 18-34, 35-64, 65 and older)
- Race/ethnicity: Categorized as White, Black, Hispanic, Asian/Pacific Islander, Native American, or Other
- Diabetes type: Type 1, Type 2, Other, Drug-induced, or Due to underlying condition
- Expected payer: Medicare, Medicaid, Private insurance, Self-pay, No charge, or Other
- Median household income quartile: Based on the patient's ZIP code
- Hospital region: Northeast, Midwest, South, or West
- Hospital location/teaching status: Rural, Urban non-teaching, or Urban teaching
- Hospital bed size: Small, Medium, or Large (based on region-specific definitions)

2.4. Statistical Analysis

All analyses incorporated the complex survey design of the NIS, including sampling weights, stratification, and clustering, to produce nationally representative estimates. We used the "singleunit(certainty)" option to correct for single-unit strata.

Descriptive statistics were first generated for the study population, reporting weighted frequencies and percentages for categorical variables. Bivariate analyses were performed using survey-weighted cross-tabulations with Rao-Scott chi-square tests to compare demographic and clinical characteristics by coma status and gender.

For continuous outcomes (length of stay and total charges), we calculated survey-weighted means with 95% confidence intervals, stratified by key variables. We assessed differences using survey-weighted t-tests and ANOVA.

We developed multivariable regression models for each outcome:

1. Length of stay: Linear regression with survey adjustments
2. Mortality: Logistic regression with results presented as odds ratios
3. Total charges: Linear regression with values reported in thousands of dollars

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Table 1: Patient Characteristics of the Included Patients

Characteristic	Category	Overall (N=2,381,619)	Without Coma (N=2,334,264)	With Coma (N=47,355)	P-value	Male (N=1,217,869)	Female (N=1,163,749)	P-value
Gender	Male	1,217,869 (51.1%)	1,195,169 (51.2%)	22,700 (47.9%)	0.033*	–	–	–
	Female	1,163,749 (48.9%)	1,139,094 (48.8%)	24,655 (52.1%)		–	–	–
Age Group	Under 18	171,285 (7.2%)	169,540 (7.3%)	1,745 (3.7%)	<0.001***	84,130 (6.9%)	87,125 (7.5%)	<0.001***
	18–34	693,340 (29.1%)	683,930 (29.3%)	9,410 (19.9%)		341,485 (28.0%)	351,760 (30.2%)	
	35–64	1,125,059 (47.2%)	1,100,524 (47.1%)	24,535 (51.8%)		610,550 (50.1%)	514,325 (44.2%)	
	65 and older	392,310 (16.5%)	380,635 (16.3%)	11,675 (24.7%)		181,705 (14.9%)	210,540 (18.1%)	
Race/Ethnicity	White	1,290,019 (54.2%)	1,262,184 (54.1%)	27,835 (58.8%)	<0.001***	654,590 (53.8%)	635,240 (54.6%)	0.02*
	Black	576,045 (24.2%)	565,010 (24.2%)	11,035 (23.3%)		287,835 (23.6%)	288,105 (24.8%)	
	Hispanic	318,855 (13.4%)	314,620 (13.5%)	4,235 (8.9%)		171,835 (14.1%)	146,980 (12.6%)	
	Asian/Pacific Islander	37,855 (1.6%)	37,025 (1.6%)	830 (1.8%)		19,425 (1.6%)	18,425 (1.6%)	
	Native American	25,045 (1.1%)	24,500 (1.0%)	545 (1.2%)		12,680 (1.0%)	12,360 (1.1%)	
	Other	65,860 (2.8%)	64,545 (2.8%)	1,315 (2.8%)		35,535 (2.9%)	30,315 (2.6%)	
DKA Type	Type 1 DM	1,168,659 (49.1%)	1,146,684 (49.1%)	21,975 (46.4%)	<0.001***	567,960 (46.6%)	600,510 (51.6%)	<0.001***
	Type 2 DM	949,470 (39.9%)	929,300 (39.8%)	20,170 (42.6%)		512,515 (42.1%)	436,855 (37.5%)	
	Other DM	254,585 (10.7%)	249,770 (10.7%)	4,815 (10.2%)		132,500 (10.9%)	122,000 (10.5%)	
	Drug-induced DM	5,470 (0.2%)	5,360 (0.2%)	110 (0.2%)		2,695 (0.2%)	2,775 (0.2%)	
	DM due to underlying condition	3,810 (0.2%)	3,515 (0.2%)	295 (0.6%)		2,200 (0.2%)	1,610 (0.1%)	
Primary Expected Payer	Medicare	631,555 (26.5%)	614,570 (26.3%)	17,085 (36.1%)	<0.001***	298,235 (24.5%)	333,320 (28.6%)	<0.001***
	Medicaid	785,350 (33.0%)	771,030 (33.0%)	14,430 (30.5%)		382,745 (31.4%)	402,605 (34.6%)	
	Private	639,845 (26.9%)	629,920 (27.0%)	10,030 (21.2%)		335,060 (27.5%)	304,785 (26.2%)	
	Self-pay	231,475 (9.7%)	227,540 (9.7%)	3,980 (8.4%)		143,975 (11.8%)	87,500 (7.5%)	
	No charge	15,490 (0.7%)	15,350 (0.7%)	140 (0.3%)		10,115 (0.8%)	5,375 (0.5%)	
	Other	73,950 (3.1%)	72,365 (3.1%)	1,600 (3.4%)		45,510 (3.7%)	28,440 (2.4%)	
Median Household Income Quartile	1 (Lowest)	884,835 (37.2%)	867,685 (37.2%)	17,150 (36.2%)	0.3095	441,840 (36.3%)	442,840 (38.0%)	0.08
	2	633,335 (26.6%)	620,510 (26.6%)	12,825 (27.1%)		321,430 (26.4%)	311,860 (26.8%)	
	3	499,280 (21.0%)	489,065 (21.0%)	10,215 (21.6%)		258,540 (21.2%)	240,665 (20.7%)	
	4 (Highest)	319,730 (13.4%)	313,495 (13.4%)	6,235 (13.2%)		169,130 (13.9%)	150,515 (12.9%)	

Hospital Region	Northeast	345,285 (14.5%)	339,420 (14.5%)	5,900 (12.5%)	<0.001***	179,910 (14.8%)	165,375 (14.2%)	<0.001***
	Midwest	505,470 (21.2%)	494,610 (21.2%)	10,975 (23.2%)		256,370 (21.1%)	249,100 (21.4%)	
	South	1,040,200 (43.7%)	1,019,420 (43.7%)	20,945 (44.2%)		519,655 (42.7%)	520,545 (44.7%)	
	West	490,664 (20.6%)	481,179 (20.6%)	9,545 (20.2%)		261,935 (21.5%)	228,730 (19.7%)	
Hospital Location/Teaching Status	Rural	238,090 (10.0%)	233,750 (10.0%)	4,375 (9.2%)	<0.001***	118,980 (9.8%)	119,110 (10.2%)	0.01**
	Urban non-teaching	467,024 (19.6%)	456,894 (19.6%)	10,190 (21.5%)		238,635 (19.6%)	228,390 (19.6%)	
	Urban teaching	1,676,505 (70.4%)	1,643,985 (70.4%)	32,800 (69.3%)		860,255 (70.6%)	816,250 (70.1%)	
Hospital Bed Size Category	Small	547,789 (23.0%)	538,069 (23.1%)	9,850 (20.8%)	<0.001***	280,340 (23.0%)	267,449 (23.0%)	0.05*
	Medium	688,569 (28.9%)	674,689 (28.9%)	13,935 (29.4%)		352,460 (28.9%)	336,110 (28.9%)	
	Large	1,145,261 (48.1%)	1,121,871 (48.1%)	23,580 (49.8%)		585,070 (48.0%)	560,190 (48.1%)	

*P-value<0.05, **P-value<0.01, ***P-value<0.001.

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Table 2: Unadjusted Outcomes by Demographic and Clinical Factors

Variable	Category	Length of Stay (Days) Mean (95% CI)	P-value	Mortality (%) Mean (95% CI)	P-value	Total Charges Mean (95% CI)	P-value
Coma Status	Without Coma	4.91 (4.88, 4.94)	<0.001***	3.12 (3.05, 3.19)	<0.001***	$61.24K ($60.50K, $61.98K)	<0.001***
	With Coma	8.65 (8.41, 8.89)		16.36 (15.60, 17.12)		$119.08K ($115.14K, $123.03K)	
Gender	Male	5.01 (4.97, 5.05)	0.033*	3.59 (3.51, 3.68)	<0.001***	$64.21K ($63.33K, $65.09K)	<0.001***
	Female	4.96 (4.93, 5.00)		3.17 (3.09, 3.25)		$60.50K ($59.72K, $61.27K)	
Coma × Gender Interaction	Without Coma, Male	4.93 (4.89, 4.97)	<0.001***	3.54 (3.42, 3.66)	0.032*	$62.97K ($62.10K, $63.84K)	0.003**
	Without Coma, Female	4.89 (4.86, 4.93)		2.68 (2.58, 2.78)		$59.43K ($58.65K, $60.20K)	
	With Coma, Male	9.09 (8.73, 9.45)		17.80 (16.42, 19.18)		$129.33K ($123.32K, $135.33K)	
	With Coma, Female	8.25 (7.94, 8.57)		15.10 (13.88, 16.32)		$109.66K ($104.80K, $114.53K)	
Age Group	Under 18	2.45 (2.40, 2.49)	<0.001***	0.92 (0.76, 1.08)	<0.001***	$37.64K ($36.82K, $38.46K)	<0.001***
	18-34	3.29 (3.26, 3.32)		1.34 (1.25, 1.43)		$45.78K ($45.12K, $46.44K)	
	35-64	5.63 (5.59, 5.67)		3.48 (3.39, 3.57)		$66.92K ($66.08K, $67.76K)	
	65 and older	7.26 (7.19, 7.33)		7.69 (7.48, 7.90)		$83.44K ($82.33K, $84.55K)	
DKA Type	Type 1 DM	3.69 (3.66, 3.71)	<0.001***	2.06 (1.97, 2.15)	<0.001***	$50.64K ($49.96K, $51.32K)	<0.001***
	Type 2 DM	6.43 (6.38, 6.48)		4.75 (4.62, 4.88)		$73.58K ($72.64K, $74.52K)	
	Other DM	5.53 (5.45, 5.60)		4.23 (4.01, 4.45)		$68.97K ($67.26K, $70.68K)	
	Drug-induced DM	5.97 (5.52, 6.43)		2.85 (2.03, 3.67)		$64.14K ($58.87K, $69.41K)	
	DM due to underlying condition	6.97 (6.34, 7.61)		5.78 (4.62, 6.94)		$77.63K ($69.15K, $86.11K)	
Hospital Region	Northeast	5.69 (5.59, 5.78)	<0.001***	3.52 (3.35, 3.69)	0.004**	$80.72K ($79.02K, $82.42K)	<0.001***
	Midwest	4.63 (4.57, 4.69)		3.04 (2.92, 3.16)		$54.78K ($53.85K, $55.71K)	
	South	5.00 (4.95, 5.05)		3.42 (3.33, 3.51)		$58.62K ($57.89K, $59.35K)	
	West	4.84 (4.78, 4.91)		3.52 (3.39, 3.65)		$69.95K ($68.82K, $71.08K)	
Hospital Location/Teaching Status	Rural	3.67 (3.62, 3.73)	<0.001***	2.58 (2.42, 2.74)	<0.001***	$38.24K ($37.38K, $39.10K)	<0.001***
	Urban non-teaching	4.48 (4.43, 4.53)		3.15 (3.03, 3.27)		$52.86K ($52.04K, $53.68K)	
	Urban teaching	5.32 (5.27, 5.36)		3.63 (3.55, 3.71)		$68.78K ($68.05K, $69.51K)	

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Primary Expected Payer	Medicare	6.58 (6.53, 6.63)	<0.001***	6.35 (6.18, 6.52)	<0.001***	$74.86K ($73.92K, $75.80K)	<0.001***
	Medicaid	4.57 (4.52, 4.61)		2.47 (2.38, 2.56)		$57.94K ($57.13K, $58.75K)	
	Private	4.30 (4.26, 4.35)		2.30 (2.21, 2.39)		$60.35K ($59.52K, $61.18K)	
	Self-pay	4.09 (4.03, 4.16)		3.25 (3.09, 3.41)		$46.02K ($45.04K, $47.00K)	
	No charge	4.40 (4.13, 4.67)		2.42 (1.96, 2.88)		$42.34K ($39.32K, $45.36K)	
	Other	4.71 (4.58, 4.84)		3.06 (2.85, 3.27)		$57.32K ($55.29K, $59.35K)	
Race/Ethnicity	White	4.86 (4.82, 4.89)	<0.001***	3.40 (3.32, 3.48)	<0.001***	$58.19K ($57.49K, $58.89K)	<0.001***
	Black	5.08 (5.03, 5.14)		2.72 (2.62, 2.83)		$57.74K ($56.62K, $58.86K)	
	Hispanic	5.16 (5.09, 5.24)		3.77 (3.61, 3.95)		$80.67K ($78.82K, $82.52K)	
	Asian/Pacific Islander	6.46 (6.20, 6.71)		6.69 (6.13, 7.29)		$102.28K ($97.62K, $106.94K)	
	Native American	4.86 (4.65, 5.08)		2.86 (2.39, 3.41)		$55.39K ($51.66K, $59.11K)	
	Other	5.50 (5.34, 5.66)		4.82 (4.45, 5.23)		$85.16K ($81.11K, $89.21K)	

Notes: *P-value<0.05, **P-value<0.01, ***P-value<0.001; Total charges are presented in thousands of dollars.

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Table 3: Multivariable Regression Models for Primary Outcomes

Predictor Variable	Category	Length of Stay Model Coefficient (95% CI)	Mortality Model Odds Ratio (95% CI)	Total Charges Model Coefficient in $K (95% CI)
Coma Status (Ref: Without Coma)	With Coma	3.23 (2.98, 3.48)***	5.38 (5.04, 5.75)***	51.06 (47.20, 54.92)***
Gender (Ref: Male)	Female	-0.05 (-0.09, -0.01)*	0.84 (0.81, 0.87)***	-2.58 (-3.30, -1.86)***
Coma × Gender Interaction	With Coma × Female	-0.90 (-1.39, -0.41)***	0.87 (0.77, 0.99)*	-16.12 (-22.46, -9.79)**
Age Group (Ref: <18)	18-34	1.40 (1.32, 1.48)***	3.77 (2.84, 5.02)***	18.08 (16.69, 19.46)***
	35-64	3.58 (3.50, 3.66)***	22.13 (16.80, 29.17)***	47.72 (46.09, 49.36)***
	65 and older	4.76 (4.64, 4.88)***	67.45 (51.01, 89.21)***	63.55 (61.43, 65.67)***
Race/Ethnicity (Ref: White)	Black	0.18 (0.12, 0.24)***	0.91 (0.87, 0.96)***	0.36 (-0.73, 1.46)
	Hispanic	0.44 (0.36, 0.52)***	1.34 (1.27, 1.41)***	17.40 (15.76, 19.04)***
	Asian/Pacific Islander	1.19 (0.95, 1.43)***	1.62 (1.47, 1.80)***	26.60 (22.24, 30.96)***
	Native American	0.25 (0.03, 0.47)*	0.95 (0.78, 1.16)	-3.53 (-7.22, 0.16)
	Other	0.70 (0.54, 0.86)***	1.61 (1.47, 1.76)***	23.99 (20.28, 27.69)***
Hospital Region (Ref: Northeast)	Midwest	-0.73 (-0.83, -0.63)***	0.83 (0.78, 0.89)***	-17.53 (-20.01, -15.05)***
	South	-0.26 (-0.36, -0.16)***	0.92 (0.87, 0.97)**	-5.44 (-7.97, -2.92)***
	West	-0.75 (-0.85, -0.65)***	0.93 (0.88, 0.99)*	10.31 (7.35, 13.28)***
Hospital Location (Ref: Rural)	Urban	-0.66 (-0.76, -0.56)***	0.78 (0.73, 0.84)***	-4.50 (-6.10, -2.90)***
Hospital Teaching Status (Ref: Rural)	Urban non-teaching	1.48 (1.36, 1.60)***	1.80 (1.63, 1.98)***	26.65 (24.71, 28.58)***
	Urban teaching	2.42 (2.30, 2.54)***	2.27 (2.07, 2.48)***	38.15 (36.24, 40.06)***
Hospital Bed Size (Ref: Small)	Medium	0.62 (0.56, 0.68)***	1.25 (1.19, 1.32)***	10.08 (8.60, 11.56)***
	Large	1.35 (1.29, 1.41)***	1.45 (1.38, 1.52)***	19.74 (18.12, 21.36)***
Primary Expected Payer (Ref: Medicare)	Medicaid	-0.28 (-0.36, -0.20)***	0.81 (0.77, 0.86)***	-5.86 (-7.13, -4.59)***
	Private	-0.78 (-0.86, -0.70)***	0.89 (0.85, 0.94)***	-6.34 (-7.62, -5.07)***
	Self-pay	-1.06 (-1.16, -0.96)***	0.82 (0.75, 0.89)***	-13.05 (-14.50, -11.60)***
	No charge	-0.89 (-1.17, -0.61)***	0.57 (0.43, 0.78)***	-0.36 (-4.70, 3.99)
	Other	-0.52 (-0.66, -0.38)***	1.24 (1.12, 1.36)***	-5.99 (-8.47, -3.52)***
Income Quartile (Ref: 1-Lowest)	2	-0.05 (-0.11, 0.01)	0.95 (0.91, 0.99)*	-0.24 (-1.30, 0.82)
	3	-0.06 (-0.12, 0.00)	0.86 (0.82, 0.90)***	-0.62 (-1.87, 0.62)
	4 (Highest)	-0.04 (-0.12, 0.04)	0.81 (0.76, 0.86)***	3.32 (1.57, 5.08)***

*P-value<0.05, **P-value<0.01, ***P-value<0.001; All models are adjusted for all variables listed in the table plus year (2016-2022, not shown); Length of Stay model coefficients represent additional days compared to reference group; Total Charges model coefficients are in thousands of dollars ($K); Mortality model presents odds ratios (OR).

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For each outcome, we constructed models with progressive adjustment: (1) coma status only; (2) coma status and gender; (3) addition of demographic variables; (4) addition of hospital characteristics; and (5) full model including all covariates. We assessed the interaction effects between coma status and gender for all outcomes. Additional stratified analyses were conducted to examine the differential effects of coma status by gender and vice versa. All statistical analyses were performed using Stata version 17 (StataCorp, College Station, TX), with significance defined as p<0.05.

3. Results

3.1. Patient Characteristics

A total of 2,381,619 DKA admissions were identified in the NIS from 2016 to 2022. Among these admissions, 47,355 (1.99%) presented with coma, while the remaining 2,334,264 (98.01%) did not have coma on presentation. The sample had a relatively balanced gender distribution with 51.1% male (n=1,217,869) and 48.9% female (n=1,163,749) patients (Table 1).

3.1.1. Age and Gender Distribution

The largest proportion of DKA admissions occurred in patients aged 35–64 years (47.2%), followed by those aged 18–34 years (29.1%). Elderly patients (≥65 years) accounted for 16.5% of admissions, while pediatric patients (<18 years) represented 7.2%. Notably, patients with coma had significantly different age distributions compared to those without coma ($p < 0.001$), with higher proportions in the 35–64 (51.8% vs. 47.1%) and ≥65 (24.7% vs. 16.3%) age groups, and lower proportions in the younger age categories.

Gender distribution also varied significantly by age group ($p < 0.001$). Males had higher representation in the 35–64 age group (50.1% vs. 44.2% for females), while females had higher proportions in the 18–34 (30.2% vs. 28.0%) and ≥65 (18.1% vs. 14.9%) age categories (Table 1).

3.1.2. Race/Ethnicity

White patients constituted the majority (54.2%) of DKA admissions, followed by Black (24.2%) and Hispanic (13.4%) patients. Race/ethnicity distribution differed significantly between patients with and without coma (p<0.001). Notably, White patients had higher representation among those with coma (58.8% vs. 54.1%), while Hispanic patients had lower representation (8.9% vs. 13.5%). Small but statistically significant differences were also observed in race/ethnicity distribution by gender (p=0.02) (Table 1).

3.1.3. DKA Type

Type 1 diabetes mellitus was the most common etiology (49.1%), followed by Type 2 diabetes mellitus (39.9%). Other diabetes mellitus types accounted for 10.7% of cases, while drug-induced diabetes and diabetes due to underlying conditions were rare (0.2% each). DKA type distribution differed significantly between patients with and without coma (p<0.001), with Type 2 diabetes more common among coma patients (42.6% vs. 39.8%). Gender differences in DKA type were also significant (p<0.001), with Type 1 diabetes more prevalent among females (51.6% vs. 46.6%) and Type 2 diabetes more common among males (42.1% vs. 37.5%) (Table 1).

3.1.4. Insurance and Socioeconomic Status

Medicaid was the most common primary payer (33.0%), followed by private insurance (26.9%) and Medicare (26.5%). Self-pay patients accounted for 9.7% of admissions. Insurance status differed significantly between coma and non-coma patients (p<0.001), with Medicare more prevalent among those with coma (36.1% vs. 26.3%). Gender differences in insurance status were also significant (p<0.001), with higher proportions of females covered by Medicare (28.6% vs. 24.5%) and Medicaid (34.6% vs. 31.4%), while more males were self-pay (11.8% vs. 7.5%) (Table 1). Regarding socioeconomic status, 37.2% of patients were from the lowest income quartile, while only 13.4% were from the highest income quartile. Income distribution did not differ significantly between patients with and without coma (p=0.3095) or between genders (p=0.08) (Table 1).

3.1.5. Hospital Characteristics

The largest proportion of DKA admissions occurred in Southern hospitals (43.7%), followed by Midwestern (21.2%), Western (20.6%), and Northeastern (14.5%) facilities. Most patients were treated at urban teaching hospitals (70.4%), with 19.6% at urban non-teaching hospitals and 10.0% at rural hospitals. Nearly half (48.1%) of admissions were to large hospitals, with 28.9% to medium and 23.0% to small hospitals. All hospital characteristic distributions showed statistically significant differences between coma and non-coma patients (p<0.001) and between genders (p<0.01 or p<0.001) (Table 1).

3.2. Outcomes by DKA Presentation and Patient Characteristics

3.2.1. Coma Status and Outcomes

Coma at presentation was associated with markedly worse outcomes. The mean length of stay for patients with coma was 8.65 days (95% CI: 8.41-8.89) versus 4.91 days (95% CI: 4.88-4.94) for those without coma (p<0.001). Most notably, mortality was more than five times higher in patients with coma (16.36%, 95% CI: 15.60-17.12%) compared to those without coma (3.12%, 95% CI: 3.05-3.19%) (p<0.001). Total hospital charges were also substantially higher for coma patients, averaging $119,080 versus $61,240 for non-coma patients (p<0.001) (Table 2).

3.2.2. Gender Differences in Outcomes

Male patients experienced slightly longer hospital stays (5.01 vs. 4.96 days, p=0.033) and significantly higher mortality rates (3.59% vs. 3.17%, p<0.001) compared to females. Male patients also incurred higher total charges ($64,210 vs. $60,500, p<0.001). When examining the interaction between coma status and gender, males with coma had the worst outcomes with the longest hospital stays (9.09 days), highest mortality (17.80%), and highest charges ($129,330), while females without coma had the best outcomes with the shortest stays (4.89 days), lowest mortality (2.68%), and lowest charges ($59,430) (all interaction p-values <0.01) (Table 2).

3.2.3. Age-Related Outcomes

A strong age gradient was observed across all outcome measures. Pediatric patients (<18 years) had the most favorable outcomes with the shortest length of stay (2.45 days), lowest mortality (0.92%), and lowest charges ($37,640). In contrast, elderly patients (≥65 years) had the poorest outcomes with the longest stays (7.26 days), highest mortality (7.69%), and highest charges ($83,440). Middle-aged adults (35–64 years) had intermediate outcomes. All age-related differences were highly significant ($p < 0.001$) (Table 2).

3.2.4. Outcomes by DKA Type

Type 1 DM patients had significantly better outcomes compared to other DKA types, with the shortest hospital stays (3.69 days), lowest mortality (2.06%), and lowest charges ($50,640). Patients with

Type 2 DM experienced longer stays (6.43 days), higher mortality (4.75%), and higher charges ($73,580). Patients with diabetes due to underlying conditions had the worst outcomes, with the longest stays (6.97 days), highest mortality (5.78%), and highest charges ($77,630). All differences by DKA type were highly significant (p<0.001) (Table 2).

3.2.5. Hospital Characteristics and Outcomes

Regional variations in outcomes were observed, with the Northeast having the longest length of stay (5.69 days) and the highest charges ($80,720), while the Midwest had the shortest stays (4.63 days) and the lowest charges ($54,780). Mortality rates were relatively similar across regions (range: 3.04-3.52%, p=0.004). Urban teaching hospitals had longer stays (5.32 days), higher mortality (3.63%), and substantially higher charges ($68,780) compared to rural hospitals (3.67 days, 2.58%, and $38,240, respectively). All differences were highly significant (p<0.001) (Table 2).

3.2.6. Insurance Status and Outcomes

Medicare beneficiaries had the poorest outcomes with the longest hospital stays (6.58 days), highest mortality (6.35%), and highest charges ($74,860). Private insurance and Medicaid patients had intermediate outcomes, while self-pay patients had relatively short stays (4.09 days), low charges ($46,020), and moderately high mortality (3.25%). All outcome differences by payer were highly significant (p<0.001) (Table 2).

3.2.7. Race/Ethnicity and Outcomes

Significant disparities in outcomes were observed across racial/ethnic groups. Asian/Pacific Islander patients had the longest hospital stays (6.46 days), highest mortality (6.69%), and highest charges ($102,280). Hispanic patients also had high charges ($80,670) and relatively high mortality (3.77%). Black patients had an intermediate length of stay (5.08 days) but the lowest mortality rate (2.72%). White and Native American patients had comparable length of stay (4.86 days for both), with mortality rates of 3.40% and 2.86%, respectively. All outcome differences by race/ethnicity were highly significant (p<0.001) (Table 2).

3.3. Multivariable Regression Analyses of DKA Outcomes

3.3.1. Impact of Coma on Outcomes After Adjustment

After adjusting for demographic, clinical, and hospital factors, DKA-related coma remained strongly associated with worse outcomes. Patients with coma stayed an additional 3.23 days (95% CI: 2.98-3.48, p<0.001), had 5.38 times higher odds of mortality (95% CI: 5.04-5.75, p<0.001), and incurred $51,060 higher charges (95% CI: $47,200-$54,920, p<0.001) compared to patients without coma (Table 3).

3.3.2. Gender and Gender-Coma Interaction

Female gender was associated with slightly better outcomes across all measures: shorter length of stay (-0.05 days, 95% CI: -0.09 to -0.01, p<0.05), 16% lower odds of mortality (OR 0.84, 95% CI: 0.81-0.87, p<0.001), and $2,580 lower charges (95% CI: -$3,300 to -$1,860, p<0.001) compared to males. Notably, a significant interaction was observed between gender and coma status, with female patients with coma having better outcomes than expected: shorter stays (-0.90 days, 95% CI: -1.39 to -0.41, p<0.001), lower mortality (OR 0.87, 95% CI: 0.77-0.99, p<0.05), and substantially lower charges (-$16,120, 95% CI: -$22,460 to -$9,790, p<0.01) compared to male patients with coma (Table 3).

3.3.3. Age Effects

A strong age gradient was evident in all outcome models. Compared to pediatric patients (<18 years), adults aged 65 and older had significantly longer stays (4.76 additional days, 95% CI: 4.64-4.88, p<0.001), dramatically higher odds of mortality (OR 67.45, 95% CI: 51.01-89.21, p<0.001), and $63,550 higher charges (95% CI: $61,430-$65,670, p<0.001). Even young adults (18-34 years) had worse outcomes than pediatric patients, with longer stays (1.40 additional days), higher mortality risk (OR 3.77), and higher charges ($18,080 higher), all statistically significant at p<0.001 (Table 3).

3.3.4. Racial/Ethnic Disparities

After adjusting for other factors, significant racial/ethnic disparities persisted. Compared to White patients, Asian/Pacific Islander patients had the worst outcomes with longer stays (1.19 additional days, 95% CI: 0.95-1.43, p<0.001), higher mortality risk (OR 1.62, 95% CI: 1.47-1.80, p<0.001), and higher charges ($26,600 higher, 95% CI: $22,240-$30,960, p<0.001). Hispanic patients also had worse outcomes, while Black patients had slightly longer stays (0.18 days, p<0.001) but lower mortality risk (OR 0.91, 95% CI: 0.87-0.96, p<0.001) and similar charges compared to White patients (Table 3).

3.3.5. Hospital Characteristics

The Northeast region was associated with longer stays and higher mortality compared to other regions, while the West had the highest charges after adjusting for other factors. Hospital teaching status had a strong impact on outcomes, with urban teaching hospitals having longer stays (2.42 additional days, 95% CI: 2.30-2.54, p<0.001), higher mortality risk (OR 2.27, 95% CI: 2.07-2.48, p<0.001), and higher charges ($38,150 higher, 95% CI: $36,240-$40,060, p<0.001) compared to rural hospitals. Larger hospital bed size was also associated with worse outcomes across all measures (Table 3).

3.3.6. Insurance Status and Socioeconomic Factors

Medicare beneficiaries had the worst outcomes after adjustment, with all other payer types showing shorter stays, generally lower mortality (except for "Other" payers), and lower charges. Self-pay patients had the shortest stays (-1.06 days, 95% CI: -0.96 to -1.16, p<0.001) and lowest charges (-$13,050, 95% CI: -$14,500 to -$11,600, p<0.001) compared to Medicare patients (Table 3). While the neighborhood income quartile was not significantly associated with length of stay, higher income quartiles had progressively lower odds of mortality, with the highest quartile having 19% lower odds (OR 0.81, 95% CI: 0.76-0.86, p<0.001) compared to the lowest quartile. Paradoxically, patients from the highest income quartile incurred significantly higher charges ($3,320 higher, 95% CI: $1,570-$5,080, p<0.001) compared to those from the lowest quartile (Table 3).

4. Discussion

To our knowledge, this is the most comprehensive retrospective cohort study that addressed patients with DKA in the USA over the last decade. Using multivariable regression analyses on more than 2.3 million DKA admissions from 2016 to 2022, we identified significant disparities in clinical outcomes by age, diabetes type, coma status, payer source, and hospital characteristics.

Previous studies have identified several factors associated with increased mortality in DKA, including advanced age, infections, impaired consciousness, and the presence of severe comorbidities

[13, 14, 15, 16]. In our study, the highest in-hospital mortality, longest hospital stays, and greatest hospital charges were observed among patients aged ≥65 years, those with type 2 diabetes, Asian or Pacific Islander patients, and those presenting with coma. Older adults often have multiple comorbid conditions that contribute to clinical complexity and may prolong hospitalization for reasons beyond DKA itself. Their higher acuity and increased need for medical interventions likely account for both the extended length of stay and the elevated healthcare costs.

Older adults in the United States face a heightened risk of DKA-related coma due to atypical presentations that delay diagnosis., Unlike younger individuals, older adults are more likely to present with altered mental status rather than classic DKA symptoms [17]. Infections, particularly respiratory and urinary tract infections, are the primary precipitating factors for approximately 70.1% of DKA cases in this age group, rapidly accelerating metabolic decompensation[17]. Comorbidities, including renal dysfunction and hypoalbuminemia, diminish physiological reserves, increasing vulnerability to severe acidosis and coma [17]. These factors likely explain the significantly higher in-hospital mortality observed of 7.69% in older adults with DKA, compared to 3.48% and 1.34% in the age groups 35-64 and 18-34, respectively, as in our study.

Prevention strategies for older adults with diabetes in the USA must address their unique DKA risk factors. Structured diabetes self-management education (DSME) tailored for cognitive decline and complex medication regimens can significantly improve medication-taking behavior and symptom recognition [18]. Because infections are the most common DKA trigger in elderly patients, early detection and treatment are essential components of prevention [19]. Healthcare systems should also implement 24-hour telehealth services and clear sick-day protocols to prevent DKA during acute illnesses or missed insulin doses [20]. Regular medication reviews and caregiver engagement can prevent unintentional insulin omissions that commonly precipitate DKA in older patients [20]. Clinicians should maintain a low threshold for ketone testing in elderly individuals with hyperglycemia, even in the absence of classic DKA symptoms, given the atypical presentations common in this population (Anupama et al., 2018). Finally, prevention efforts should be personalized, incorporating socioeconomic status, mental health, and prior history of DKA into individualized risk mitigation strategies [18].

In our study, individuals with type 2 diabetes accounted for 39.9% of DKA admissions—fewer than those with type 1 diabetes, who comprised 49.1%. This distribution is consistent with previous studies from the United States and England, where the proportion of DKA admissions among patients with type 2 diabetes has ranged from 20% to 30% [21, 22]. Regardless of whether multivariable regression was used, prior studies consistently concluded that people with type 2 diabetes experience higher in-hospital mortality and longer hospital stays compared to those with type 1 diabetes [23, 24, 25].

This difference is likely attributable to the older age distribution of individuals with T2DM, who often have a clustering of metabolic risk factors such as hypertension, dyslipidemia, and obesity [26]. Moreover, patients with T2DM are more likely to have established cardiovascular comorbidities and other complications that exacerbate clinical severity [26]. Greater insulin resistance and the presence of a concurrent hyperosmolar state further complicate management and contribute to prolonged hospitalization. Together, these factors also lead to higher total hospital charges among patients with DKA and type 2 diabetes.

Consciousness level is a clinical symptom that must be evaluated in patients diagnosed with DKA. Altered consciousness may result from various factors, including acidosis, elevated osmolality, the direct impact of ketone bodies, diminished cerebral blood flow, reduced glucose uptake and utilization by neuronal cells, as well as other contributing elements such as severe infections and strokes [24, 16]. Altered consciousness can occur from brain edema, a complication of fluid therapy in DKA [26]. Altered consciousness is considered one of the parameters for evaluating the severity of DKA and is frequently linked to mortality rates. Our findings detected that comatose patients have a higher in-hospital mortality rate compared to non-comatose patients. This result was further supported by findings from Sato et al., who reported that the in-hospital mortality rate was 4.33 times higher in the alert patients' group compared to the control group. Also, Venkatesh et al. revealed that the average GCS score was significantly higher in DKA survivors compared with non-survivors [27].

Our study revealed that Medicare beneficiaries experienced the poorest outcomes among all payer groups, characterized by the longest hospital stays (6.58 days), the highest in-hospital mortality (6.35%), and the highest charges ($74,860). Prior research analysis reveals Medicare beneficiaries face a 3.3-fold higher adjusted risk of recurrent DKA hospitalizations compared to privately insured individuals, even after controlling for socioeconomic variables [28]. This heightened vulnerability is partly attributable to demographic characteristics, as Medicare patients typically present with advanced age and multiple comorbidities, including cardiovascular and renal disease, significantly increasing DKA episode severity and mortality rates [23]. Systemic healthcare delivery issues further compound these challenges, including fragmented care, insufficient diabetes education, and limited access to specialist endocrinology services [28]. Notably, younger individuals qualifying for Medicare through disability represent a particularly high-risk group, as they often face both socioeconomic disadvantages and complex medical needs that exacerbate DKA vulnerability [28]. Our findings further support these disparities, as Medicare patients required more intensive care, longer hospitalizations, and incurred higher total costs, consistent with more complex clinical presentations and greater resource needs. After adjustment for sex, multivariate regression analysis showed that females were associated with significantly shorter hospital stays, lower in-hospital mortality rates, and fewer hospital charges. However, the difference in length of stay, while statistically significant, was minimal and likely not clinically meaningful. Although the effect sizes for mortality and hospital charges were statistically significant, they were relatively small; however, the differences in hospital charges may still be meaningful from a health system and cost-management perspective. Previous studies evaluated that females with DKA and females with decompensated diabetes had lower in-hospital mortality and lower mortality, respectively [13, 29]. Conversely, another study concluded no significant differences in in-hospital mortality between males and females hospitalized with DKA [30]. Our study was aligned with the analysis of the large-scale Japanese dataset; both concluded that there was a difference among sexes as a factor that affects the mortality rate, but it was still less clinically important when compared to other factors like coma, age, or DM type [25].

For adjustment for hospital teaching status and hospital bed size, we found that urban teaching hospitals and hospitals with large hospital bed sizes had the highest mortality rates, hospital stays, and total charges. More complicated cases come to teaching hospitals; thus, they carried the highest mortality rate as they were admitted to teaching hospitals due to more supported resources and more frequent intensive care [31]. Thus, patients who were hospitalized in teaching hospitals had a longer hospital stay and total charges because of the complexity of the admitted cases and ICU utilization. Either hospital stay may be prolonged due to the nature of the educational process.

For adjustment for hospital regions, our findings suggest that Midwest hospitals carried a lower risk for developing mortality, but these results also had less clinical importance, which concluded that this is a less clinically important factor when compared to other factors. But total charges for Midwest hospitals carried the best results compared to other regions, as they carried the least total charges. The hospital stay results were fewer for Midwest and West hospitals compared to South and Northeast hospitals.

Additionally, our results revealed that self-payers carried the shortest hospital stay period and the fewest total charges compared to other Primary Expected Payer groups, despite still carrying no remarkable difference according to mortality. Finally, hospital location and income quartile appear to be the least important factors affecting outcomes in this study.

Strengths and limitations: This retrospective cohort study contains a huge number of patients, which exceeded 2 million in the last decade; thus, the data can be validated through a wider portion of patients than previous studies in the USA. Also, this retrospective cohort study is favorable because it contains three outcomes: in-hospital mortality, hospital stay, and total charges. Also, it contains a multivariate regression model for each outcome, which will give an insight into the hospital stay and total charges that are more important outcomes for the decision-making process among hospitals, patients, and physicians. However, our study had some limitations. We were unable to address the severity of DKA in this study, as the database didn't contain laboratory data (e.g., levels of plasma glucose, glycated hemoglobin, insulin, ketone bodies, electrolytes, anti-glutamic acid decarboxylase antibodies, and c-peptide). As we addressed comatose patients as severe cases, we couldn't address the severity of DKA among non-comatose patients. There are other confounders we could access through our analysis (e.g., BMI, infection status, Charlson Comorbidity Index, or scores for daily activity). HHS may not have been fully excluded from our study population, as there is a clear distinction between DKA and HHS in clinical settings.

5. Conclusion

We found that age (>65 years), consciousness level (comatose patients), race (Asian or Pacific Islander), and hospital teaching status (urban teaching) are the strongest independent factors associated with increased in-hospital mortality, hospital stay length, and total charges using multivariate regression models through a large dataset of hospitals in the USA. All these factors should be considered for treatment, controlling hospital resources, and the decision-making process.

Conflicts of Interest

The authors declare no competing interests that could have influenced the objectivity or outcome of this research

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Institutional Review Board (IRB)

IRB review was not required. This study analyzed the HCUP National Inpatient Sample (NIS), a HIPAA-defined limited data set released under a Data Use Agreement that excludes direct patient identifiers. The research involved only secondary analysis of de-identified data with no interaction or intervention with individuals. The study complied with all HCUP Data Use Agreement requirements.

Large Language Model

The authors used a generative AI tool (ChatGPT, and Grammarly) solely to improve grammar, spelling, and clarity of the manuscript text. The tool did not generate scientific content, conduct data analysis, create tables/figures, or interpret results. All AI-assisted edits were reviewed and verified by the authors, who accept full responsibility for the content.

Authors Contribution

MN conceptualized the study. MHE, MRM, and ON performed the data analyses and formatted the tables. MN, MHE, MRM, and NE drafted the manuscript. All authors critically revised the work for important intellectual content, approved the final version, and agree to be accountable for all aspects of the work.

Data Availability

The data used in this study were obtained from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS), which is a restricted-access, proprietary database. Due to HCUP's data use agreement, the dataset cannot be shared publicly or redistributed by the authors. Researchers may obtain the NIS directly from HCUP after completing the required data use training and purchasing the dataset through the HCUP Central Distributor (`https://www.hcup-us.ahrq.gov/tech_assist/centdist.jsp`). All Stata code and analytic procedures used in this study are available from the corresponding author upon reasonable request; however, the underlying NIS data must be obtained independently through HCUP.

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