Original Article

Correlation between the outcomes and severity of diabetic ketoacidosis: A retrospective pilot study

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Abstract

Introduction: Diabetic ketoacidosis (DKA) is a serious acute metabolic complication of diabetes mellitus (DM). It is classified into mild, moderate, and severe based on severity as per the American Diabetes Association (ADA) guidelines. There are limited data on the correlation between the severity of DKA and its outcomes using this classification system. The aim is to study the correlation between the outcomes and severity of DKA in a tertiary care center in India. **Methodology:** In this retrospective pilot study, 1527 patients with DM were identified over a span of 3 years, of which 63 had a discharge diagnosis of DKA and 37 fulfilled the ADA criteria for DKA. Following inclusion details on clinical parameters and outcomes of patients with mild, moderate, and severe DKA were compared. **Results:** Mild, moderate, and severe DKA accounted for 8%, 41%, and 51% of the patients, respectively. Intensive Care Unit (ICU) care was required in 6.7% and 47.4% of those with moderate and severe DKA, respectively. Invasive ventilation (IV) was required in 47% (9) of those with severe DKA only. The mortality rates were 13.3% and 26% among those with moderate and severe DKA. The mean expenditure was ₹29,000, ₹30,000, and ₹64,000 among those with mild, moderate, and severe DKA, respectively. **Conclusions:** The ADA classification of severity of DKA correlates well with the duration of inhospital stay, costs of care, requirement of ICU care, need for IV or non-IV, and mortality. This suggests that this classification system could be a valuable tool in predicting outcomes.

Keywords: Diabetic ketoacidosis, outcomes, severity

Introduction

Diabetic ketoacidosis (DKA) is a life-threatening acute metabolic complication in patients with diabetes mellitus (DM). Diagnosis of DKA consists of a triad of uncontrolled hyperglycemia (blood glucose >250 mg/dL), metabolic acidosis (pH <7.3), and increased total body ketone concentration. An absolute or relative insulin deficiency and an increase in counterregulatory hormones such as glucagon, catecholamines, cortisol, and growth hormone lead to DKA.[1] The prevalence of diabetes in Southeast Asia is 8.4%.[2] India is the diabetic capital of the world with 69.2 million people living with diabetes (8.7%) as per national surveillance data from 2015.[3] Most patients with DKA have type 1 diabetes; however, patients with type 2 diabetes are also at risk during an acute illness such as trauma, surgery, myocardial infarction, or infections. Among these patients, clinical presentation and outcome are diverse. DKA is classified as mild, moderate, and severe based on severity as per the American Diabetes Association (ADA) guidelines.[4] Although there is a severity-based classification of DKA, there are limited data on the correlation between the severity of DKA and its outcomes using this classification system. Studies done previously showed that the duration of Intensive Care Unit (ICU) and hospital stay was related to the precipitating cause of ketoacidosis and not to the disease severity scores such as Acute Physiology and Chronic Health Evaluation II (APACHE) and Therapeutic Intervention Scoring System.[5] The mortality rate in patients with DKA is reported as being <1% according to the western studies with higher rate of more than 5% has been reported in the elderly and those with associated life-threatening conditions.[1] A prospective study in a

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tertiary care center in Karnataka reported a inhospital mortality of 10% in DKA in the year 2015.[6] In this study, we aimed to study the correlation between the outcomes and severity of DKA in terms of morbidity, requirement of Intensive Care Unit stay, duration of inhospital stay, requirement of noninvasive ventilation (NIV)/(IV), and costs of care among inpatients with DKA.

Methodology

This retrospective observational pilot study was conducted among the inpatients seen in a single department of general medicine at a tertiary care health center in South India. Medical records of all patients with a discharge diagnosis of DKA from April 2014 to November 2017 were analyzed by an independent physician. Those fulfilling the diagnosis of DKA as per the ADA guidelines were included in the study. These were classified further into mild, moderate, and severe DKA as per the ADA guidelines based on the laboratory values and examination findings recorded at presentation [Figure 1].[4] Details of demographic parameters, clinical presentation, laboratory parameters, precipitators of DKA, and management were ascertained. Prespecified outcomes of disease severity in terms of duration of inpatient stay, requirement of invasive or NIV, ICU stay, and mortality were analyzed. An independent blinded physician performed statistical analysis with the Statistical Package for the Social Sciences (SPSS version 20, IBM Corp., Armonk, NY). Chi-square test was used for the comparison of categorical variables and Student's *t*-test was used for comparison of the continuous variables. A two-sided $P < 0.05$ was considered statistically significant.

Results

A total of 5023 patients were admitted for inpatient care over 3 years, of these 1527 patients had a diagnosis of DM. Among these, 63 had a discharge diagnosis of DKA. However, only 37 fulfilled the ADA criteria for DKA, as shown in Figure 2. DKA accounted for 0.74% of all admissions over a 3-year period. DKA was seen in 2.4% of all inpatients with diabetes. Mild, moderate, and severe DKA accounted for 8% (3), 41% (15), and 51% (19) of the patients, respectively. The mean age was 50.2 ± 17.4 years (mean ± standard deviation [SD]) in all the three groups combined, as showed in Table 1. Males accounted for 54.1% (20) of the patients in all the groups combined. Patients with Type 2 diabetes accounted for 67.6% (25) of all the patients, with 16.2% (6) having type 1 diabetes, and 16.2% (6) had other types of diabetes. Young-onset diabetes defined as patients diagnosed to have diabetes at ≤40 years of age accounted for 45.9% (17) of the patients. The mean duration of diabetes was 4.7 ± 5.4 years (mean ± SD) among all the groups. The mean HbA1c was 12.1 ± 2.7 (mean ± SD) among all the groups. Infections were the most common precipitating factor amounting for 58.1% (25) among those with DKA, as shown in Table 2.

ICU care was required in 6.7% (1) and 47.4% (9) of those with moderate and severe DKA, respectively ($P = 0.007$). Invasive ventilation was required in 47% (9) of those with severe DKA only ($P = 0.002$). NIV was needed in 27% (4) and 21% (4) of those with moderate and severe DKA. Duration of stay ≤7 days was 100%, 60%, and 46% among those with mild, moderate, and severe DKA, respectively. The overall mortality rate observed was 18.9% (7), with rates of 13% (2) and 26% (5) among those with moderate and severe DKA [Table 3]. The mean expenditure was ₹29,000, ₹30,000, and ₹64,000 among those with mild, moderate, and severe DKA, respectively.

Discussion

DKA is a life-threatening acute metabolic complication in patients with DM and is diagnosed with the presence of a triad of uncontrolled hyperglycemia (blood glucose >250 mg/dL), metabolic acidosis (pH <7.3), and increased total body ketone concentration. The rate of hospitalization for DKA was 7.7/1,000 persons with diabetes in the United States of America[7] as compared to a rate of 12.54/1000 persons with diabetes in our study. The incidence of DKA per 1000 admissions in our study was 7.3, as compared to a rate of 4.59 per 1000 admissions in a study conducted in Canada.[8] The requirement of invasive ventilation was 47% as compared to 39% in the previous study. Our study also demonstrated that the number of patients with severe DKA requiring ICU care was 48% as compared to 81% in the previous study,[9] which was significantly higher as compared to patients with moderate and mild DKA.[9] In our study, the

	DKA		
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10
Urine ketone*	Positive	Positive	Positive
Serum ketone*	Positive	Positive	Positive
Effective serum osmolality†	Variable	Variable	Variable
Anion gap‡	>10	>12	>12
Mental status	Alert	Alert/drowsy	Stupor/coma

Figure 1: American Diabetes Association classification of diabetic ketoacidosis

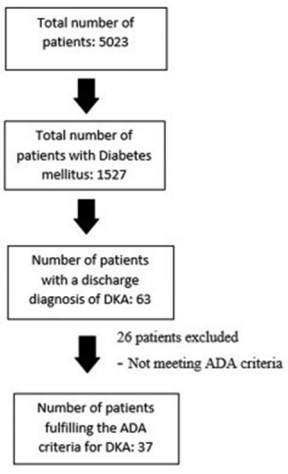

Figure 2: Strobe diagram

Table 1: Demographic, clinical and biochemical characteristics of DKA patients

Variables	Mild DKA	Moderate DKA	Severe DKA
Number of patients	3 (8%)	15 (41%)	19 (51%)
Mean Age (years)	49	52	49
Sex			
Male	1 (33%)	7 (47%)	12 (63%)
Female	2 (67%)	8 (53%)	7 (37%)
Mean Duration of stay (days)	6.3	6.1	8.7
Mean Plasma Glucose Levels (mg/dl)	455	446	533
Mean Arterial pH	7.27	7.19	7.04
Mean Serum Bicarbonate (meq/L)	16	10.3	7.4
Mental status	Alert - 100% (3) Drowsy - 0 Stupor - 0	Alert - 53.3% (8) Drowsy - 46.7% (7) Stupor - 0	Alert - 15.8% (3) Drowsy - 26.3% (5) Stupor - 57.9% (11)
Mean serum Creatinine (mg/dl)	1.45	1.75	1.58
Age at diagnosis of DM			
< 40 years	66.7% (2)	46.7% (7)	42.1% (8)
> 40 years	33.3% (1)	53.3% (8)	57.9% (11)
Type of DM			
Type I	0	20% (3)	15.8% (3)
Type 2	66.7% (2)	73.3% (11)	68.4% (13)
Others*	33.3% (1)	6.7% (1)	15.8% (3)
Duration of DM (Mean, in years)	7.8	6.3	3.1
Mean Sodium (Meq/dL)	115.3	121.2	130.5
Mean haemoglobin (g/L)	12.5	12.9	14.1
Mean potassium (Meq/dL)	4.5	4.7	4.7
Mean Calcium † (Meq/dL)	8.45	7.9	8.2
Mean phosphate‡ (Meq/dL)	2.6	2.4	2.6
Mean Serum Albumin § (g/L)	3.1	3.5	3.6
Mean Hba1c (%)[1]	10.8	11.6	12.8
Systemic Hypertension	33.3% (1)	33.3% (5)	15.8% (3)
Microvascular complications			
Retinopathy	33.3% (1)	33.3% (5)	21% (4)
Neuropathy	33.3% (1)	40% (6)	36.8% (7)
Nephropathy	33.3% (1)	40% (6)	42.1% (8)
Macro vascular complications			
Ischaemic heart disease	0	20% (3)	10.5% (2)
Cerebrovascular disease	0	0	15.8% (3)
Peripheral vascular disease	0	0	0

* Pancreatic diabetes, Latent autoimmune diabetes of adulthood, Maturity onset Diabetes of the young; † Calcium levels available only for 23 out of 37 patients; ‡ Phosphate levels available only for 28 out of 37 patients; § Serum albumin levels available only for 34 out of 37 patients; [1] Hba1c levels available only for 29 out of 37 patients

need for mechanical ventilation in severe DKA was significantly higher than in those with moderate and mild DKA. This was in concordance to other studies.[8,9] Baseline HbA1c levels were elevated (>10) in all the groups similar to previous studies. Duration of hospital stay in our study was similar to other studies. In a study conducted in a secondary health care center in Vellore, Tamil Nadu, the mean duration of stay in patients with mild and moderate DKA was 5.29 days,[10] which was similar to our study and other studies. Patients with moderate and severe DKA had longer duration of stay as compared to the patients with DKA. A previous study reported that disease severity scores did not predict prolonged hospital stay; however, in this study, the correlation of APACHE II score and Logistic Organ Dysfunction System was used.[5] The most common precipitating factor in our study was infections. Infections and poor access to health care were the most common factors precipitating DKA in studies from developing nations,[4,6,11-14] as compared to noncompliance, change of regimen, and newly detected DM in the United States of America and other developed nations.[5,8,9,13] Noncompliance was the second most common precipitating factor for DKA (20.9%) in our study. DKA precipitated by noncompliance was demonstrated to have the highest economic burden in a study.[15] Patients with type 2 diabetes accounted for 67.6% (25) of all the patients in our study, while in a similar study conducted in Israel, majority of the patients had type 1 diabetes.[9] However, other studies are in concordance with our findings.[6,14,16] In previous studies looking at outcomes in moderate and severe DKA, mortality rates were 3.4% and 11.4% in moderate and severe DKA, respectively;[9] however, in our study, the mortality rates were higher (13% and 26% in moderate and severe DKA, respectively). The increased mortality rates could be due to small sample size and a referral

Table 2: Precipitating factors of DKA

Precipitating Factor	Number of patients
Infection	25 (58.1%)
Non Compliance	9 (20.9%)
Intoxication	5 (11.6%)
Infarction	4 (9.3%)

Table 3: Outcomes in patients with DKA

Variables	Mild DKA	Moderate DKA	Severe DKA
Number of patients	3 (8.1%)	15 (40.5%)	19 (51%)
ICU stay	0	1 (6.7%)	9 (47.4%) [p - 0.007]
Invasive Ventilation	0	0	9 (47.4%) [p - 0.002]
Non Invasive ventilation	0	4 (26.7%)	4 (21%)
Shock	0	0	4 (21%)
Acute Kidney Injury (Serum Creatinine ≥1.4 mg/dl)	2 (66%)	5 (33%)	11 (58%)
≤ 7 days hospital stay	3 (100%)	9 (60%)	9 (47.4%)
Mortality	0	2 (13.3%)	5 (26.3%)
Mean Expenditure (Rs.)	29,000	30,000	64,000

bias. However, this was not statistically significant. The costs of care incurred in severe DKA were more than twice the costs incurred in the mild and moderate DKA group. This is of significance in a developing nation like India where most of the people are from a poor socioeconomic background. Hence, the role of patient education to prevent complications such as DKA cannot be overemphasized. The authors see a potential role of ADA severity classification of DKA in establishing clinical categorization, facilitating optimized treatment, and predicting prognosis and resource requirement among inpatients with DKA.

Limitations

Our study had several limitations. It was a pilot study; the sample size was small and was from a single medical unit. In view of the retrospective nature of the study, we did not have details on long-term outcome.

Conclusions

The ADA severity classification of DKA correlates well with the requirement of invasive ventilation and ICU care. An increasing trend in mortality and expenditure is also noted with the severity of DKA. This criterion though simple could serve as an effective tool in predicting outcomes.

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Conflicts of interest

There are no conflicts of interest.

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