Predictors and treatment outcome of hyperglycemic emergencies: a one-center experience

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Background
Hyperglycemic emergencies (HEs) are serious acute complications of uncontrolled diabetes, which can be life threatening. In spite of major advances in diagnosis and treatment, it still is an important cause of morbidity and mortality.
Aims
To evaluate treatment outcomes among diabetic patients presented with HEs and to ascertain the determinants and factors associated with the outcome.
Patients and methods
This prospective, longitudinal study was conducted on 240 diabetic patients presented with HEs at Specialized Medical Hospital, Mansoura University. They were subjected to full history, physical examination, laboratory assessment, and follow-up. According to the laboratory results, patients were divided into three groups: diabetic ketoacidosis (DKA); hyperglycemic hyperosmolar nonketotic state (HHS); and normo-osmolar nonketotic hyperglycemic state.
Results
The study included 82 men and 158 women. The most common HE was DKA. Nonadherence to medications was the most common cause of DKA and normo-osmolar nonketotic hyperglycemic state (52.1 and 47.8%, respectively). The overall hospital mortality due to HEs was 12.5%. The highest mortality was recorded in the HHS group (51.7%). Mortality was higher in old-aged, nonobese patients, and in those without education. Nonsurvivors had longer duration of ICU stay than survivors, with no difference in total hospital stay. No hypoglycemic episodes detected in the nonsurvived group versus 37 episodes in the survived one. There were significant associations between mortality and Glasgow coma scale, the presenting and the highest random plasma glucose, serum sodium, osmolarity, creatinine, white blood cells, and glycated hemoglobin.
Conclusion
DKA is the most common HE, while HHS has the highest mortality rate. The strongest predictors of mortality of HEs are HHS, DKA in type 2 diabetes, old age, chronic kidney disease, coronary artery disease, highest random plasma glucose, glycated hemoglobin, and length of ICU stay.

Keywords:
diabetic ketoacidosis, hyperglycemic emergencies, hyperosmolar hyperglycemic state, mortality, risk factors

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Introduction

Hyperglycemic emergencies (HEs) are serious acute complications of uncontrolled diabetes associated with metabolic derangement, which can be life threatening. It includes diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar nonketotic state (HHS), and normo-osmolar nonketotic hyperglycemic state (NNHS); of these, DKA and HHS are two of the most serious acute complications of diabetes [1].

DKA and HHS are HEs with overlapping features. In DKA, ketoacidosis is prominent, while in HHS, the main features are extracellular fluid volume depletion and hyperosmolarity [2]. NNHS is seen in a group of patients who present with hyperglycemia, normal osmolality with symptoms of metabolic decompensation, and insignificant ketonuria. These patients do not fit into DKA or HHS criteria [3].

The true incidence of HEs is difficult to establish. DKA occurs in 4–9% of all hospital discharge summaries among patients with diabetes. The rate of hospital admissions due to HHS is lower than that of DKA and accounts for less than 1% of all primary diabetic admissions [4].

In spite of major advances in understanding their pathogenesis and uniform agreement about their diagnosis and treatment, these HEs are still being important causes of morbidity and mortality among diabetic patients.

United States mortality rates, 2–5% in DKA and up to 15% in HHS, increase substantially with aging and the presence of concomitant life-threatening illness [5–7]. In Spain, a study aimed to determine the outcome of 132 patients with HHS, and reported a mortality rate of 16.9% [8].

In Nigeria, HEs are a leading cause of morbidity and mortality due to many causes: ignorance, poor health education, poverty, infection, delayed diagnosis, and management [9,10]. Olugbemide *et al.* [11] reported 23 and 38% mortality rate of DKA and HHS, respectively. In Ethiopia, DKA was a leading cause for diabetic admission in about 71.1% of diabetic admissions with a mortality rate of 5.8% [12].

Despite all the challenges and costs of diabetes and its complications, studies are limited on the treatment complications, determinants, length of hospital stay, and mortality of acute diabetes complications in our country. Hence, this study was designed to describe the clinical and laboratory scenarios associated with HEs plus the predictors of mortality in our setting in order to suggest measures that may reduce their occurrence and subsequent mortality rates.

Patients and methods

Patients

This is a prospective, descriptive, longitudinal study that was conducted on all diabetic patients admitted to the ICU of the Diabetes Unit, Specialized Medical Hospital, Mansoura University, in the period between December 2016 and December 2017, presented with HEs (DKA, HHS, or NNHS). All participants were aged more than or equal to 18 years; type 1 or type 2 diabetes. The exclusion criteria included: patients diagnosed as end-stage renal disease, congestive heart failure, hepatic failure, and anasarca due to their fluid overload as these conditions affect rapid intravenous fluid administration. Pregnant women and those using SGLT 2 inhibitors were also excluded.

Recruited individuals met the following criteria: random plasma glucose (RPG) more than 300 mg/dl, ketonuria of 2+ or more, and serum bicarbonate less than 18 mmol/l for DKA; RPG more than 450 mg/dl and serum osmolarity of more than 320 mOsmol/l with insignificant ketonuria for HHS; RPG more than 300 mg/dl, serum osmolarity less than 320 mOsmol/l, and absent or (1+) ketonuria for NNHS [13–15].

According to laboratory results, patients were classified into three groups. Group 1: DKA and group 2: HHS and group 3: NNHS. All patients were subjected to medical history taking, physical examination, laboratory assessment, and work follow-up.

Medical history taking

Name, age, sex, diabetes mellitus (DM) duration, type of diabetic emergency, line of treatment (insulin or oral hypoglycemic drugs), adherence to medication, precipitants, associated comorbidities [neuropathy, chronic kidney disease (CKD), retinopathy, hypertension (HTN), coronary artery disease (CAD), diabetic foot ulcers (DFUs), and chronic liver disease].

Physical examination

Physical examination was to determine the cause of HE, infection or myocardial infarction, other comorbidities, and to report the clinical presentation of HEs, consciousness level by Glasgow coma scale (GCS), abdominal pain, nausea, vomiting, and the level of dehydration.

Laboratory assessment

Admission RPG, glycated hemoglobin (HbA1c), serum osmolarity, arterial blood gases, serum electrolytes, ketone bodies in urine, complete blood count, liver enzymes, and serum creatinine.

Work follow-up

Monitoring the protocol of therapy, daily needed laboratory investigations (arterial blood gases, serum osmolarity, frequent blood glucose monitoring), recording any episodes of hypoglycemia, time of cure of HEs, and time of discharge from ICU and from hospital. Fundus examination was done for all cases.

Statistical analysis

Data were entered and statistically analyzed with SPSS, version 21 (SPSS Inc., Chicago, Illinois, USA). The normality of data was first tested with one-sample Kolmogorov–Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using c^2 test. Continuous variables were presented as mean±SD for parametric data or median and range for nonparametric data. The two groups were compared with Student's t test for parametric data and Mann–Whitney test for nonparametric data. Analysis of variance test was used

to compare more than two means while Kruskal–Wallis test was used to compare more than two medians. Multivariable logistic regression analysis was used for the prediction of independent variables of mortality. *P* value less than or equal to 0.05 was considered to be statistically significant.

Ethics

The approval by Mansoura Medical Ethics Committee of Faculty of Medicine was obtained and written consents from patients participated in the study or from their family were also obtained.

Results

The study included 240 diabetic patients with HEs: 158 (65.8%) were women, with a wide age range of 18 to 83 years. More than half (62.1%) of the patients were from rural areas. Of these patients, 25 (10.42%) were newly diagnosed with diabetes; type 1 DM represents 75 (31.2%) of participants and all presented with DKA. The most common HE was DKA, accounting for 119 (49.5%) patients (Table 1). The clinical features and comorbidities of the studied group are shown in Table 1.

Nonadherence to medications was the most common cause of DKA and NNHS (52.1, 47.8%, respectively), while infection was the most common for HHS (41.4%). Urinary tract infection 52% (50) was the most common infection that precipitated HEs, followed by community-acquired pneumonia 26% (25). Disturbed consciousness level was more evident in the HHS group. Abdominal pain was the most common presentation in all types of HEs (Table 2).

The presenting RPG, HbA1c, serum osmolarity, sodium, and creatinine measurements were significantly higher in HHS versus DKA and NNHS ($P<0.001$). There was no statistically significant difference between the three types of HEs as regards episodes of hypoglycemic during the hospital stay ($P=0.245$) (Table 3). The median length of hospital stay was not significantly different among the three groups ($P=0.287$). The overall in-hospital mortality rate due to HEs was 12.5% (30). The highest mortality rate was found in the HHS group (51.7%) (Table 4).

Table 1 Admission characteristics of the studied patients

Admission characteristics	Study group (*N*=240) [*n* (%)]
Sex (male/female)	82/158 (34.2/65.8)
Age (years)	
Mean±SD	48.97±19.21
Range	18–83
Level of education (No/primary/secondary)[a]	84/71/85 (35/29.6/35.4)
Location (rural/urban)	149/91 (62.1/37.9)
BMI	29.8±1.09
Obesity (nonobese/obese)	147/93 (61.2/38.8)
DM duration (days) median (minimum–maximum)	132 (0–600)
Treatment (oral/insulin)	27/213 (11.2/88.8)
Type of diabetic emergency	
DKA (type1 DM)	75 (31.2)
DKA (type2 DM)	44 (18.3)
HHS (type2 DM)	29 (12.1)
NNHS (type2 DM)	92 (38.3)
Hypertension	119 (49.6)
Neuropathy	163 (67.9)
Retinopathy	68 (28.3)
Chronic kidney disease	12 (5.0)
Coronary artery disease	50 (20.8)
Diabetic foot ulcers	36 (15.0)
Chronic liver disease	35 (14.6)

Primary, less than university education; secondary, university education. DKA, diabetic ketoacidosis; DM, diabetes mellitus; HHS, hyperosmolar nonketotic state; NNHS, normo-osmolar nonketotic hyperglycemic state. [a]No, illiterate.

Table 2 Chief complaints and precipitants of hyperglycemic emergencies

	DKA (*N*=119) [*n* (%)]	HHS (*N*=29) [*n* (%)]	NNHS (*N*=92) [*n* (%)]	Test of significance	*P* value
Abdominal pain	103 (86.6)	13 (44.8)[a]	35 (38)[a]	χ^2	<0.001*
Dehydration	101 (84.9)	6 (20.7)[a]	11 (12)[a],b	χ^2	<0.001*
Level of consciousness					
GCS=15	94	12[a]	81[b]	χ^2	<0.001*
GCS<15	25	17	11		
Precipitants of HEs					
Newly onset DM	12 (10.1)	6 (20.7)	7 (7.6)	χ^2	0.131
Infection	45 (37.8)	12 (41.4)	39 (42.4)	χ^2	0.787
Myocardial infarction	0	2 (6.9)[a]	2 (2.2)[a]	MC	0.030*
Nonadherence to medication	62 (52.1)	9 (31)	44 (47.8)	χ^2	0.126

χ^2, c^2 test; DKA, diabetic ketoacidosis; DM, diabetes mellitus; GCS, Glasgow coma scale; HE, hyperglycemic emergency; HHS, hyperosmolar nonketotic state; MC, Monte Carlo test; NNHS, normo-osmolar nonketotic hyperglycemic state. [a]There is a statistical significance with DKA group. [b]There is a statistical significance with HHS group. **P* value is significant.

Table 3 Laboratory parameters among hyperglycemic emergencies

Laboratory parameters	DKA (*N*=119)	HHS (*N*=29)	NNHS (*N*=92)	Test of significance	*P* value
Blood glucose (mg/dl) (on admission)	539.10±185	752.07±303.1[a]	428.98±178[a],b	F	<0.001*
Highest blood glucose (mg/dl)	575.24±187	783.07±311[a]	480.59±168[a],b	F	<0.001*
Lowest blood glucose (mg/dl)	98.41±32.2	128.55±50.8[a]	110.32±38.9[a],b	F	<0.001*
pH	7.23±0.15	7.33±0.09[a]	7.35±0.12[a]	F	0.001*
HCO_3 (mmol/l)	15.54±6.46	18.63±3.61[a]	19.81±5.28[a],b	F	<0.001*
K+ (mmol/l)	4.58±1.07	4.50±1.36	4.20±0.81[a],b	F	0.025*
Na+ (mmol/l)	133.26±8.85	152.49±28.9[a]	130.67±8.79[b]	F	<0.001*
Arterial PCO_2 (mmHg)	31.75±12.23	34.10±8.20	34.09±8.33	F	0.224
Serum osmolarity (mosmol/l)	305.77±19.57	353.52±60.51[a]	290.41±32.79[a],b	F	<0.001*
Ketonuria (2+)	117 (98.3)	0[a]	0[a]	χ^2	<0.001*
ALT (IU/l)	18 (10–342)	27 (11–106)	21 (10–87)	KW	0.033
Serum creatinine (mg/dl)	0.9 (0.6–6.8)	2.0 (0.7–6.4)[a]	1.0 (0.4–8.3)[b]	KW	<0.001*
Hemoglobin (g %)	11.53±1.98	11.38±2.61	10.95±2.45	F	0.182
WBCs (10^3)	10.70 (2.7–38)	10.8 (3.2–18.8)	8.8 (3.2–89)	KW	0.441
Platelets (10^3)	259 (34–793)	232 (21–487)	222.5 (21–601)	KW	0.058
HbA1c (%)	9.83±2.27	11.83±2.70[a]	9.74±2.24[b]	F	<0.001*
Episodes of hypoglycemia	23 (19.3)	3 (10.3)	11 (12)	χ^2	0.245

Data are presented as mean±SD and *n* (%). χ^2, χ^2 test; ALT, alanine aminotransferase; DKA, diabetic ketoacidosis; F, analysis of variance test; HbA1c, glycated hemoglobin; HCO_3, serum bicarbonate; HHS, hyperosmolar nonketotic state; K+, serum potassium; KW, Kruskal–Wallis test; Na+, serum sodium; NNHS, normo-osmolar nonketotic hyperglycemic state; PCO_2, partial pressure of carbon dioxide; WBC, white blood cells. [a]There is a statistical significance with DKA group. [b]There is a statistical significance with HHS group. **P* value is significant.

Table 4 Outcome of hyperglycemic emergencies

Outcome	DKA (*N*=119)	HHS (*N*=29)	NNHS (*N*=92)	Test of significance	*P* value
ICU stay (days)	3 (0–19)	4 (0–10)[a]	0 (0–10)[a]	KW	<0.001*
Ward stay (days)	3 (0–30)	0 (0–18)[a]	5 (0–24)[a], b	KW	<0.001*
Total hospital stay (days)	6 (2–36)	7 (1–26)	6 (1–24)	KW	0.287
Discharge to home	109 (91.6)	14 (48.3)[a]	87 (94.6)[b]	χ^2	<0.001*
Mortality	10 (8.4)	15 (51.7)[a]	5 (5.4)[b]	χ^2	<0.001*

Data are presented as median (range) and *n* (%). χ^2, χ^2 test; DKA, diabetic ketoacidosis; HHS, hyperosmolar nonketotic state; KW, Kruskal–Wallis test; NNHS, normo-osmolar nonketotic hyperglycemic state. [a]There is a statistical significance with DKA group. [b]There is a statistical significance with HHS group. **P* value is significant.

Mortality rate was higher in men than women (14.6 vs. 11.4%); however, it was not statistically significant (*P*=0.471). Mortality was higher in old-aged, nonobese patients, and in those with no education (all *P*<0.001). Type of antidiabetic medications, diabetes duration, and patient locality were not significantly associated with the outcome (Table 5). The prevalence of HTN, CKD, and CAD were significantly higher in the nonsurvived group compared with the survived group (*P*=0.017, *P*=0.025 and *P*<0.001, respectively) (Table 6).

The precipitating causes of HEs were not significantly associated with the outcome. Nonsurvivors had a longer duration of stay in ICU than survivors (*P*<0.001), with no significant difference in total hospital stay (*P*=0.248) (Table 7). No hypoglycemic episodes (during the hospital admission) were detected in the nonsurvived group versus 37 episodes in the survived one (*P*=0.012). The associations between outcome and laboratory parameters are shown in Table 8.

On multivariable logistic regression analysis, the strongest independent predictors of mortality were age, HHS, DKA in type 2 diabetes, CKD, CAD, GCS values, the highest RPG detected during the admission period, HbA1c %, and length of ICU stay (Table 9).

Discussion

HE remains an important acute metabolic complication of diabetes, especially for those living in developing countries where resources are scarce. The results of this unique study may aid emergency physicians in making follow-up and disposition decisions for patients presenting with hyperglycemia.

The data of the current study demonstrated that the overall mortality rate of HEs was 12.5% which is higher than the rate of 9.8, 4.8, and 3.57% reported by previous studies [16–18], respectively, and lower than the rate of 34% reported in a previous study in Nigeria [19], and 16% reported by Adesina *et al.* [20]. Comparing the mortality rates in diabetic emergencies

Table 5 Relation between demographic data and outcome

Demographic data	Nonsurvivors (*N*=30) [*n* (%)]	Survivors (*N*=210) [*n* (%)]	Test of significance	*P* value
Sex				
Male	12 (40.0)	70 (33.3)	χ^2=0.519	0.471
Female	18 (60.0)	140 (66.7)		
Age (years) (mean±SD)	69.30±11.66	46.06±18.31	*t*=6.74	<0.001*
Level of education[a]				
No	22 (73.3)	62 (29.5)	χ^2=23.46	<0.001*
Primary	6 (20.0)	65 (31.0)		
Secondary	2 (6.7)	83 (39.5)		
Location				
Rural	23 (76.7)	126 (60)	χ^2=3.09	0.078
Urban	7 (23.3)	84 (40)		
BMI	26.82±3.96	29.52±5.53	*t*=1.61	0.023*
DM duration (days)				
Median (minimum–maximum)	180 (0–600)	120 (0–600)	*Z*=0.903	0.367
Treatment				
Oral	2 (6.7)	25 (11.9)	χ^2=0.721	0.396
Insulin	28 (93.3)	185 (88.1)		
GCS=15	6 (20)	181 (86.2)	*t*=12.70	<0.001*
GCS<15	24 (80)	29 (13.8)		

χ^2, χ^2 test; primary, less than university education; secondary, university education; DM, diabetes mellitus; GCS, Glasgow coma scale; *t*, Student's *t* test; *Z*, Mann–Whitney test. [a]No, illiterate. **P* value is significant.

Table 6 Relation between associated comorbidities and outcome

Comorbidities	Nonsurvivors (*N*=30) [*n* (%)]	Survivors (*N*=210) [*n* (%)]	χ^2	*P* value
Hypertension	21 (70.0)	98 (46.7)	5.71	0.017*
Neuropathy	24 (80.0)	139 (66.2)	2.29	0.130
Retinopathy	8 (26.7)	60 (28.6)	0.047	0.829
Chronic kidney disease	4 (13.3)	8 (3.8)	5.01	0.025*
Coronary artery disease	15 (50.0)	35 (16.7)	17.68	<0.001*
Diabetic foot ulcers	4 (13.3)	32 (15.2)	0.075	0.785
Chronic liver disease	7 (23.3)	28 (13.3)	2.11	0.147

χ^2, χ^2 test. **P* value is significant.

Table 7 Relation of mortality with precipitants and length of stay of hyperglycemic emergencies

	Nonsurvivor (*N*=30) [*n* (%)]	Survivors (*N*=210) [*n* (%)]	Test of significance	*P* value
Newly onset DM	5 (16.7)	20 (9.5)	χ^2=1.435	0.231
Infection	14 (46.7)	82 (39)	χ^2=0.635	0.426
Myocardial infarction	0	4 (1.9)	χ^2=0.581	0.446
Nonadherence to medication	11 (36.7)	104 (49.5)	χ^2=1.739	0.187
ICU stay (days)	6 (1–19)	3 (1–10)	*Z*=5.03	<0.001*
Ward stay (days)	4 (2–6)	4 (1–30)	*Z*=0.44	0.660
Total hospital stay (days)	7.5 (1–21)	6 (2–36)	*Z*=1.15	0.248

χ^2, c^2 test; DM, diabetes mellitus; *Z*, Mann–Whitney test. **P* value is significant.

is difficult because the presenting syndromes vary according to clinical and biochemical criteria [21]. Most recorded mortality rates are not adjusted for age and many studies have grouped all acidotic presentations together, regardless of the degree of hyperosmolarity [21].

The higher morbidity and mortality rates that occur in patients with HEs in developing countries are as a result of paucity of medical facilities and personnel, late hospital presentation, and prevalent socioeconomic distress [22,23]. The lower mortality rates depend on successful treatment of HEs which depend on the commitment of the house officers, resident doctors, and nurses in administering the intravenous fluids and insulin therapy with close monitoring of the patients [18].

Okoro *et al.* [24] reported that the mortality rate was 22 and 25% for DKA and HHS, respectively. Eregie and Unadike [25] reported a mortality rate of 27.7% among DKA patients in Benin. In our study, mortality rates of DKA and HHS were 8.4 and 51.7%, respectively. Our high mortality rate among HHS patients may be explained by the fact that most of them were of old age, with associated comorbidities and late presentation. In agreement with recent studies [26,27], our study also found that older age was one of the nonmodifiable factors

Table 8 Relation between outcome and laboratory parameters

Laboratory parameters	Nonsurvivor (*N*=30)	Survivors (*N*=210)	Test of significance	*P* value
Blood glucose (mg/dl) (on admission)	637.80 ±279.94	506.17 ±209.28	*t*=3.07	0.002*
Highest blood glucose (mg/dl)	704.97 ±317.09	543.94 ±194.58	*t*=3.86	<0.001*
pH	7.27±0.16	7.28±0.14	*t*=0.297	0.767
HCO_3 (mmol/l)	16.30 (5.7–26.7)	18.48 ±13.72	*t*=0.650	0.516
K+ (mmol/l)	4.53±1.51	4.41±0.95	*t*=0.627	0.531
Na+ (mmol/l)	144.50±29.6	133.18 ±10.21	*t*=4.119	<0.001*
Arterial PCO_2 (mmHg)	33.30±6.48	32.88 ±10.93	*t*=0.205	0.838
Serum osmolarity (mosmol/l)	333.29 ±65.24	301.70 ±29.65	*t*=4.503	<0.001*
Ketonuria (2+) [*n* (%)]	10 (33.3)	107 (51)	χ^2=3.26	0.071
Serum creatinine (mg/dl)	2.40 (0.6–6.8)	0.90 (0.4–8.3)	*Z*=5.91	<0.001*
Hemoglobin (g %)	10.70±2.15	11.37 ±2.26	*t*=1.54	0.125
WBCs (10^3)	13.90 (3.2–38)	9.75 (2.7–2812)	*Z*=3.16	0.002*
Platelets (10^3)	215 (21–793)	248.50 (21–689)	*Z*=1.04	0.299
HbA1c (%)	11.61±2.47	9.81±2.3	*t*=3.96	0.001*
Hypoglycemia [*n* (%)]	0	37 (17.6)	χ^2=6.24	0.012*

χ^2, χ^2 test; HbA1c, glycated hemoglobin; HCO_3, serum bicarbonate; K+, serum potassium; Na+, serum sodium; PCO_2, partial pressure of carbon dioxide; *t*, Student's *t* test; WBC, white blood cells; *Z*, Mann–Whitney test. **P* value is significant.

associated with death in diabetic patients presented with HEs.

In our study, the mortality rate was higher in men than in women. This runs parallel to multiple previous studies [17,19,27,28], who concluded that being a male is predictive of fatal diabetic outcome. The reasons for high mortality in admitted male diabetic patients were not clear and may be related to the pattern of presentation and associated comorbidities. The point that may be taken into consideration that cardiovascular diseases, the most common cause of death in DM, are more common in men than women who are protected against cardiovascular diseases with their sex hormone levels [29]. In contrast to our study, Ojobi *et al.* [30] reported mild higher mortality in women.

The most common HE in our study was DKA (49.5%), while HHS occurred in 12.1%. This is in agreement with Elangovan *et al.* [31] and Desse *et al.* [16] who reported that DKA was seen predominantly in 66.2 and 92.6%, respectively. This is in contrast to a previous study which reported that HHS accounted for 53% of HE admissions, while DKA accounted for 39% [11]. Higher proportion of DKA in our finding may be due to the fact that the majority of our patients were known diabetics and were noncompliant to medications (115 out of 215 patients that were on treatment were noncompliant). Umpierrez and Kitabchi [32] reported that DKA is common in known diabetics.

Nonadherence to antidiabetic drugs was the leading precipitating factor of DKA (52.1%) and NNHS (47.8%) in our study. This is in agreement with a previous study in Saudi Arabia [33] (51.2%) and another Brazilian study [34] (39%). In contrast, some studies [35–37] reported that the most common cause of DKA was infection. Most of our patients presented with DKA were of type 1 DM, and discontinuation of antidiabetic drugs easily causes DKA. Lack of patient education, accessibility of health facilities that provide medical care for diabetics, and economic burden of antidiabetic medications are common problems that contributed to noncompliance. High rate of infection in other studies may be due to poor infection prevention approaches by the patients either due to poverty or poor awareness.

Demba *et al.* [27] reported that HTN was associated in 38.5% of patients and mortality rate among hypertensive patients with HEs was 19.5%. This is in agreement with our study which reported that HTN was associated in 49.6% and the mortality rate was 17.6%. The mean age of our study patients (48.97 ±19.21) may explain the high prevalence of HTN as aging is associated with HTN. A previous study reported that CAD was associated in 13.7% with a mortality rate of 37.2% [27]. Our study reported higher percentage (20.8%) with 30% mortality rate.

In our study, DFUs occurred in 15% with a mortality rate of 11.1%. Demba *et al.* [27] reported a higher percent of DFUs (19.9%) with a mortality rate of 28.1%. Higher mortality rate in Demba's study was explained by late presentation and occurrence of sepsis. In contrast, most of our patients were not having infected DFUs.

In our study, abdominal pain was the most common presentation in all types of HEs. The high rate of abdominal pain may be due to hyperglycemia and severe metabolic disturbances. In agreement to our study, Anumah [9] concluded that the presenting

Table 9 Multivariate logistic regression analysis for independent predictors of mortality

Independent predictors	β	*P* value	OR (95% CI)
Age (years)	0.164	0.012*	1.18 (1.04–1.34)
Level of education[a]			
No (*r*)	1.699	0.243	5.47 (0.31–94)
Primary and secondary			
BMI	–0.167	0.082	0.847 (0.7–1.02)
Diabetic emergency			
DKA (type1 DM) (*r*)	–	–	1
DKA (type2 DM)	1.95	0.023*	7.02 (1.3–37)
HHS (type2 DM)	3.48	<0.001*	32.5 (5.7–83)
NNHS (type2 DM)	0.524	0.560	1.68 (0.29–9.8)
Hypertension	2.433	0.073	11.39 (0.8–62)
Chronic kidney disease	1.517	0.032*	4.5 (1.1–18.2)
Coronary artery disease	1.578	0.001*	4.8 (1.9–12.3)
Glasgow coma scale	–0.601	<0.001*	0.61 (0.48–0.77)
Blood glucose (mg/dl) (on admission)	–0.003	0.142	0.997 (0.993–1.0)
Highest blood glucose (mg/dl)	0.005	0.012*	1.005 (1.001–1.01)
Serum Na+ (mmol/l)	–0.162	0.194	0.851 (0.67–1.08)
Serum osmolarity (mosmol/l)	0.068	0.281	1.07 (0.94–1.21)
Serum creatinine (mg/dl)	0.386	0.172	1.471 (0.84–2.5)
WBCs (10^3)	0.001	0.858	1.001 (0.99–1.01)
HbA1c (%)	0.285	0.042*	1.33 (1.01–1.75)
ICU length of stay (days)	0.520	0.003*	1.681 (1.19–2.36)

CI, confidence interval; DKA, diabetic ketoacidosis; DM, diabetes mellitus; HbA1c, glycated hemoglobin; HHS, hyperosmolar nonketotic state; Na+, sodium; NNHS, normo-osmolar nonketotic hyperglycemic state; OR, odds ratio; primary, less than university education; secondary, university education; WBC, white blood cells. [a]No, illiterate. **P* value is significant.

first RPG was significantly higher in HHS than DKA patients. In our study, nonsurvivors had higher plasma glucose and plasma osmolarity levels. This may explain the higher mortality rate among HHS patients (51.7%). Olugbemide *et al.* [11] reported higher plasma osmolarity in nonsurvivors.

Although serum sodium levels might be expected to be increased in a dehydrated state, the osmotic effect of glucose that draws water into the extracellular space and the urinary loss of Na tend to reduce the sodium concentration [38]. In our study, hyponatremia occurred more in patients with DKA (133.26 ±8.85 mmol/l) while HHS patients presented more with hypernatremia (152.49±28.9 mmol/l). This was in contrast to a previous study that reported normal serum sodium in all patients [11].

In agreement to our study, two studies [11,38] reported that serum potassium was within normal limits in most patients. In metabolic acidosis and insulin deficiency states, it is expected that the potassium levels will be elevated or within the normal range due to physiological compensation, although it is known that total body stores of potassium are depleted in DKA [39].

High levels of HbA1c seen among the majority of our patients indicate the chronicity of poor glycemic control. HbA1c in our study was highly elevated in HHS (11.83±2.7%) than DKA (9.83±2.27%), the finding that was also reported by Sivakumar *et al.* [40].

Hypoglycemia is a serious complication of treatment in patients with diabetes. Episodes of hypoglycemia in our study occurred in 15.4% of patients, which was similar to a previous study [41] in Thailand (15.7%), and lower than a study [16] in Ethiopia (20.9%). In our study, hypoglycemic episodes occurred in 19.3% of patients with DKA versus 10.3% in HHS. The higher hypoglycemic episodes may be related to infrequent blood glucose monitoring to adjust insulin doses based on patient need that may lead to inadequate use of insulin resulting in hypoglycemia. Previous studies found that hypoglycemia was a cause of death in 3% of cases [42] and 10.2% of the total deaths reported among diabetic patients [43]. In our study, no mortality occurred in patients with hypoglycemia. Mild hypoglycemic episodes and rapid correction of hypoglycemia in ICU by the medical staff may be an explanation.In our study, the median length of hospital stay was 6 days for DKA and NNHS patients, and 7 days for HHS ones. The same duration was reported also by Desse *et al.* [16] In contrast, Ezeani *et al.* [17] reported a mean duration of 24.2 days (range, 0.5–88). The reason for this long hospital stay was the associated advanced stages of foot ulcers that usually require a longer time

for wound healing with multidisciplinary care. Only 15% of our patients were associated with superficial noninfected DFUs.

In our study, it was logical that nonsurvivors had a longer duration of ICU stay than survivors (median duration, 6 vs. 3 days) ($P \leq 0.001$). The median duration of hospitalization in the nonsurvived group was 7.5 (1–21) days. This was much longer than what was reported in Nigeria [24], where all recorded deaths occurred within 2 days, but similar to what was reported by Nkpozi *et al.* [44] who reported 9 days as a mean duration of hospital stay. The explanation for long duration of hospitalization in the nonsurvived group could be due to deaths from comorbid conditions or precipitating factors and not necessarily from the metabolic abnormalities of HEs [45].

Conclusion

DKA is the most common HE, while HHS has the highest mortality rate. Nonadherence to antidiabetic medications is the most common precipitating factor for DKA and NNHS, while infection was the most common cause of HHS. Women are most commonly affected with higher mortality among men. Abdominal pain and HTN are the most common presentation and comorbidity among HEs. The strongest independent predictors of mortality were old age, HHS, DKA in type 2 diabetes, CKD, CAD, GCS values, highest RPG detected during admission, HbA1c %, and length of ICU stay.

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Conflicts of interest

There are no conflicts of interest.

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