Treatment Outcome Of Hyperglycemic Emergency And Predictors In Ethiopia

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Abstract

Background: Hyperglycemic Emergency (HE) denotes critical cases of decompensated diabetes mellitus (DM). Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the extreme cases of HE. This study aims to assess the treatment outcome of HE and predictors in Ethiopia.

Method: Four-year medical records of DM patients admitted for HE at Hiwot Fana Specialized University Hospital (HFSUH) were reviewed retrospectively. Data were entered into and cleaned by Epi-Info^{TM}7 software. The statistical analysis was executed using the statistical package for social sciences software (SPSS) version 24. Chi-square test and student's t-test were done to compare categorical and continuous variables. Logistic regression with the level of α set at 0.05 and AOR of 95% CI was done to determine the predictors. Statistical significance was established at AOR ≠1 within a 95% CI and P-value < 0.05. The model was verified using the Hosmer-Lemeshow goodness of fit test (P = 0.392).

Results: This study included 321 eligible patients. The median duration of hospital stay was 7 days. The pooled HE mortality was 16.5%; 21.4% of HHS and 11.1% of DKA died. Infection (AOR = 3.74, 95% CI: 1.85-7.57, P <0.001), comorbidity (AOR = 2.95, 95% CI: 1.34-6.48, P = 0.007), and lower admission Glasgow Coma Scale score ≤ 8 (AOR = 2.58, 95% CI: 1.17-5.71, P = 0.019) were the independent predictors of HE mortality.

Conclusion: Mortality and duration of hospital stay stand high among DM patients admitted with HE. Infection, comorbidity, and lower admission GCS ≤ 8 are the independent predictors of HE mortality.

Background

Hyperglycemic Emergency (HE) denotes critical cases of decompensated diabetes mellitus (DM). Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the extreme cases of HE (1). DKA usually occurs in type 1 DM; HHS often rises in type 2 DM. However, each case can appear in any of the two DM types (2). Patient's admission features comprise a varying degree of hyperglycemia, dehydration, electrolyte imbalance, acidosis, altered mentation. The treatment entails fluid and electrolyte and insulin therapy alongside vigilant assessment and management of the precipitating conditions (3, 4).

HE remains one of the most important causes of global morbidity and mortality among individuals living with DM. Studies from various countries had accentuated this connotation (5-8). The fatality rate for HHS is unsurpassed in contrast to DKA (8-12). The significant predictors of mortality in adult DM patients hospitalized for HE include infection, comorbidities, coma, age extremes, cardiac arrhythmias (13).

Immensely augmented by the detrimental meddling of the extensive socioeconomic glitches in the effective deterrence and management, the HE morbidity and mortality reside even more pronounced in Africa. A study by Ogbera et al in 2009 reported a 20% collective DKA and HHS mortality rate from an urban hospital in Nigeria (14). Later in 2017, Olugbemide et al reported a pooled DKA and HHS mortality

rate of 34% from a specialist teaching hospital in Nigeria (15). Correspondingly, Mbugua et al described a 30% mortality rate of DKA from Kenyatta National Hospital (KNH), Nairobi, Kenya (16).

HE stands the domineering why and wherefore of hospitalizations among DM patients in Ethiopia (17, 18). The treatment outcome of HE among DM patients in Ethiopia is yet to be assessed. There are few studies on patients with DKA (19-21). However, a single study assessed DKA and HHS pooled mortality and patient's hospital stay duration (22). Thus, our study aims to assess the treatment outcome of HE and predictors among DM patients hospitalized with DKA and HHS at Hiwot Fana Specialized University Hospital (HFSUH), Ethiopia. This study is keen to reveal the actual HE incurred woes and losses of DM patients and to call attention to the predictors.

Methods

Medical records of DM patients admitted with HE at Hiwot Fana Specialized University Hospital (HFSUH) from 01 January 2016 to 31 December 2019 were reviewed retrospectively. This study included all DM patients admitted with HE at age ≥15 years whose medical records comprised of complete relevant data. Overall, 613 DM patients were admitted with HE over the four-year period. However, medical records comprised of complete relevant information were available only for 321 patients and included in this study.

The data abstraction tool was developed as per the study objectives and the literature searches. The extracted data comprised sociodemographic characteristics (age, sex, and residence); morbidity features (HE type, DM type, DM history, DM duration, and comorbidities); admission clinical features (the vital signs); admission biochemical features (blood glucose level, serum electrolytes, blood urea nitrogen, and serum creatinine); precipitants; and treatment outcome. The data was collected by trained clinical pharmacists working in the hospital. The primary outcome was all-cause in-hospital mortality once the HE was diagnosis (DKA: random blood glucose > 300mg/dl and urine ketones > 2+ and HHS: random blood glucose > 600mg/dl and urine ketones < 2+). and treatment was started based on the national treatment guideline (23).

Statistical analysis

Data were entered into and cleaned by Epi-Info^{TM}7 software. The statistical analysis was executed using the statistical package for social sciences software (SPSS) version 24. Chi-square test and student's t-test were done to compare categorical and continuous variables, respectively. Logistic regression with the level of α set at 0.05 and AOR of 95% CI was fitted to determine the predictors. Variables with p-values ≤ 0.2 on a bivariable binary logistic regression analysis were considered in a multivariable binary logistic regression model. Statistical significance was established at AOR ≠1 within a 95% CI and P-value < 0.05. The model was verified using the Hosmer-Lemeshow goodness of fit test (P = 0.392).

This study was conducted after ethical clearance was obtained from the Research and Ethics Review Committee of the College of Medicine and Health Sciences, University of Gondar. To access the patient medical records for data abstraction, HFSUH was requested with a formal letter of cooperation from the College of Medicine and Health Sciences, University of Gondar. Patient data were kept confidential and used only for the purpose of this study.

Results

From a total of 613 HE admissions, 321 patients were eligible and included in this study.

Sociodemographic and morbidity features

The participants were comprised of 129 (40.2%) males and 192 (59.8%) females, with a sex ratio of 1:1.5. The mean age of the patients was 43.3 ± 18.4 years. Their age ranged from 15 - 85 years. There were 153 (47.7%) DKA and 168 (52.3%) HHS cases. HHS patients were significantly older than DKA patients (57.3 ± 12.7 vs. 28.0 ± 9.2 years, $P < 0.001$). Patients with T1DM and T2DM were 143 (44.5%) and 178 (55.5%). At admission, 117 (36.4%) patients had no prior DM history and the rest 204 (63.6%) were known DM patients on treatment for a 4-year median duration. Hundred-four (32.4%) patients had comorbidities, of whom 46 (44.2%) had hypertension.

Table 1: Sociodemographic and morbidity features of hyperglycemic emergency patients

Variables	DKA (n = 153)	HHS (n = 168)	P-value
Age (years), mean ± SD	28.0 ± 9.2	57.3 ± 12.7	<0.001
Sex, male (%)	59 (38.6)	70 (41.7)	0.571
Residence, urban (%)	62 (40.5)	101 (60.1)	<0.001
Type 1 diabetes	143 (93.5)	0	
Type 2 diabetes	10 (6.5)	168 (100)	
known diabetes	88 (57.5)	125 (74.4)	
Hypertension	7 (4.6)	39 (23.2)	<0.001
Congestive heart failure	0	12 (7.1)	
Ischemic heart disease	2 (1.3)	5 (3.0)	
Chronic kidney disease	2 (1.3)	8 (4.8)	
Chronic liver disease	4 (2.6)	6 (3.6)	
Stroke	0	12 (7.1)	
Asthma	1 (0.7)	1 (0.6)	
COPD	0	2 (1.2)	
Epilepsy	4 (2.6)	0	

COPD: Chronic Obstructive Pulmonary Disease; SD: Standard Deviation

Clinical admission features

Compared with DKA, both admission systolic and diastolic blood pressure records stood significantly higher while admission Glasgow Coma Scale (GCS) score remained significantly lower among DM patients hospitalized with HHS. The clinical admission features of the study participants as DKA compared to HHS are displayed in Table 2.

Table 2: Clinical admission features of hyperglycemic emergency patients

Variables	DKA (Mean ± SD)	HHS (Mean ± SD)	P-value
SBP (mmHg)	107.4 ± 12.0	110.0 ± 20.6	<0.001
DBP (mmHg)	69.7 ± 5.6	70.2 ± 10.1	<0.001
Pulse rate (bpm)	97.2 ± 12.4	93.4 ± 11.4	0.317
Respiratory rate (bpm)	25.9 ± 3.3	20.5 ± 3.7	0.615
Temperature (^{0}C)	36.7 ± 0.9	36.6 ± 0.9	0.705
GCS score	12.4 ± 2.0	10.5 ± 2.9	<0.001

DBP: Diastolic Blood Pressure; DKA: Diabetic Ketoacidosis; GCS: Glasgow Coma Scale; HHS: Hyperosmolar Hyperglycemic State; SBP: Systolic Blood Pressure; SD: Standard Deviation

Biochemical admission features

The mean admission blood glucose level (BGL) of the study participants was 544.5 ± 123.1 mg/dL. Admission BGL, serum creatinine (SCr.) and blood urea nitrogen (BUN) were significantly higher in patients admitted with HHS than DKA. The biochemical admission features of the study participants as DKA compared to HHS are displayed in Table 3.

Table 3: Biochemical admission features of hyperglycemic emergency patients

Variable	DKA (Mean ± SD)	HHS (Mean ± SD)	P-value
BGL (mg/dL)	421.2 ± 34.5	656.8 ± 36.3	<0.001
Serum potassium (mEq/L)	3.7 ± 0.6	4.2 ± 0.5	0.075
Serum sodium (mEq/L)	135.8 ± 3.5	137.2 ± 3.9	0.052
Serum chloride (mEq/L)	106.4 ± 5.6	105.9 ± 6.2	0.324
Serum creatinine (mg/dL)	1.1 ± 0.5	1.4 ± 0.8	<0.001
BUN (mg/dL)	18.6 ± 8.5	22.8 ± 10.6	<0.001

BGL: Blood Glucose Level; BUN: Blood Urea Nitrogen; DKA: Diabetic Ketoacidosis; HHS: Hyperosmolar Hyperglycemic State; SD: Standard Deviation

Hyperglycemic emergency precipitating conditions

Infection was documented in 154 (48.0%) of the study participants. Fifty-eight (37.7%) of the infection cases were pneumonia. Treatment noncompliance was recorded in 124 (38.6%) of the patients. The noncompliance type in 83 (66.9%) of the patients was medication discontinuation.

Table 4: Hyperglycemic emergency precipitating conditions

Precipitating conditions	Frequency (%)
Infection	154 (48.0)
Pneumonia	58 (37.7)
Urinary tract infection	39 (25.3)
Sepsis	29 (18.8)
Diabetic foot ulcer	11 (7.2)
Others	17 (11.0)
Noncompliance	124 (38.6)
Medication discontinuation	83 (66.9)
Missed insulin doses	41 (33.1)
Newly diagnosed diabetes	63 (19.6)
Cardiovascular events	18 (5.6)
Physical traumatic injury	3 (0.9)

Treatment outcome of HE

The median duration of hospital stay of the study participants was 7-day. The total number of the study participants registered dead was 53 (16.5%); 36 (21.4%) of the patients admitted with HHS and 17 (11.1%) of the patients hospitalized with DKA.

Predictors of mortality among DM patients admitted with HE

As per the multivariable binary logistic regression analysis of the variables significantly associated ($P \leq 0.2$) with the mortality on the bivariable analysis, infection (AOR = 3.74, 95% CI: 1.85-7.57, $P < 0.001$), comorbidity (AOR = 2.95, 95% CI: 1.34-6.48, P = 0.007), and lower admission GCS $\leq$ 8 (AOR = 2.58, 95% CI: 1.17-5.71, P = 0.019) were the independent predictors of mortality among DM patients hospitalized with HE. Table 5 illustrates the predictors of mortality among DM patients hospitalized with HE.

Table 5: Predictors of mortality among hospitalized hyperglycemic emergency patients

Variable	Died		COR (95% CI)	P-value	AOR (95% CI)	P-value
	Yes (%)	No (%)				
Age						
15-24	5 (8.8)	52 (91.2)	1.00		1.00	
25-34	8 (11.3)	63 (88.7)	1.32 (0.41-4.28)	0.643	1.22 (0.36-4.14)	0.751
35-44	9 (20.0)	36 (80.0)	2.60 (0.81-8.40)	0.110	1.42 (0.40-5.07)	0.592
45-54	6 (11.1)	48 (88.9)	1.30 (0.37-4.54)	0.681	0.47 (0.12-1.88)	0.287
55-64	9 (18.8)	39 (81.2)	2.40 (0.75-7.73)	0.142	0.98 (0.26-3.70)	0.971
≥65	16 (34.8)	30 (65.2)	5.55 (1.85-16.67)	0.002	1.45 (0.37-5.70)	0.595
GCS						
3 – 8	24 (29.6)	57 (70.4)	3.06 (1.66 – 5.67)	<0.001	**2.58 (1.17 – 5.71)**	**0.019**
9 – 15	29 (12.1)	211 (87.9)	1.00		1.00	
SCr. (mg/dL)						
≤ 1.2	33 (13.6)	209 (86.4)	1.00		1.00	
> 1.2	20 (25.3)	59 (74.7)	2.15 (1.15 – 4.02)	0.017	1.48 (0.69 – 3.18)	0.316
Comorbidity						
Yes	30 (28.8)	74 (71.2)	3.42 (1.87 – 6.27)	<0.001	**2.95 (1.34 – 6.48)**	**0.007**
No	23 (10.6)	194 (89.4)	1.00		1.00	
Infection						
Yes	37 (24.0)	117 (76.0)	2.99 (1.58 – 5.63)	0.001	**3.74 (1.85 – 7.57)**	**<0.001**
No	16 (9.6)	151 (90.4)	1.00		1.00	

AOR: Adjusted Odds Ratio; COR: Crude Odds Ratio; GCS: Glasgow Coma Scale; SCr.: Serum Creatinine

Discussion

The findings of this study depicted that HHS was the major diagnosis of DM patients hospitalized for HE. The majority of the participants were known DM patients on treatment. Comorbidities were common. Infection was the foremost precipitant of HE, followed by noncompliance followed by newly diagnosed DM. Mortality and duration of hospital stay were high. Infection, comorbidity, and lower admission GCS score ≤ 8 were the independent predictors of mortality.

HHS was the major HE case. This finding goes in line with studies from Nigeria and Taiwan (15, 24-27) but stands against a study reported that DKA was the commonest HE (22). The higher prevalence of HHS in our study might be explained by the fact that the majority of the study participants were T2DM patients, and that HHS often raids patients with uncontrolled T2DM (28). Furthermore, the higher percentage of known DM patients in our study might also have lifted the prevalence of HHS as it was reported that HHS is common in patients with a prior history of DM (26). This implies that HHS is on the rise and demands great attention.

The rate of comorbidity in our study was 32.4%. This rate is higher than the 22.1% reported by a study from Jimma (22). The relatively higher proportion of known DM patients in our study might justify this higher prevalence of comorbidity. Comorbidities are more likely to be diagnosed and controlled in known DM patients on follow up than in newly diagnosed DM patients at admission with HE as they may be masked by the resultant HE complications. HTN, for instance, can be obscured by the hypotension from the HE. The substandard DM care has obfuscated the effort to control the morbidity and mortality among DM patients in Ethiopia (29). Therefore, works need to be done to standardize DM care.

The infection rate documented in our study was 48%. This is higher than the infection rates reported from South Africa, Saudi Arabia, and Colombia that ranged from 23% to 32% (5, 30, 31). The reason for the upstretched infection rate documented among our study participants might be the incapacitating poverty restraining the healthcare systems in Sub-Saharan Africa (32). Comprehensive health promotion and infection prevention strategies need to be implemented to control infection and its lethal complications.

The noncompliance rate in our study was 38.6%. This is higher than the 32.3% and 34% rate reported respectively from Jimma and Kenya (16, 22). The comparatively higher percentage of known DM patients on treatment in our study might explain this disparity. The financial hitches and unjust traditional tenets have been linked with missed insulin doses and antidiabetic medication discontinuation among Tropical and Sub-Saharan African DM patients (32, 33). Hence, it would be matter-of-factly to devise strategies to ensure accessible standard DM care in the region and abate the dreadful consequences of noncompliance.

The median length of hospital stay in our study was 7 days. Even though this is shorter than the findings of studies from Nigeria and Colombia (5, 24, 25), it still is longer than the reports from Jimma and South Africa (22, 34). The inconsistency may be due to the difference among the settings in the effective and efficient management of DM patients presenting with HE. As DFU is associated with long hospital stay (24, 34), the relatively higher proportion of patients with DFU in our study may further justify the lengthier hospital stay duration.

The overall mortality rate recorded in the present study was 16.5%. Despite being lower than the mortality rates reported from Kenya (16) and Nigeria (14, 15), it stands higher than a series of mortality rates, 2.3%-9.8%, reported from Jimma (22), South Africa (34), Thailand (6), Australia (7), and Colombia (5). The relatively greater percentage of HHS cases in our study (52.3% vs. 13.2-27.3%) might have inflated the mortality among our study participants. The variations among the settings in terms of patient's admission feature, HE precipitating conditions, and the patient management approaches might have taken a substantial part in the observed disparity.

The independent predictors of mortality among DM patients hospitalized for HE were infection, comorbidity, and lower admission GCS ≤ 8. Being elderly and raised admission SCr. greater than 1.2 mg/dL were significantly associated with mortality in the bivariable binary logistic regression analysis. Nonetheless, the associations went statistically insignificant when fitted into the multivariable binary logistic regression model. It would be pragmatically sound to instigate operative interventions targeting these modifiable predictive factors of mortality among DM patients hospitalized for HE.

Limitations of the study

There is a substantial gap in the current management of HE patients in Ethiopia, which is momentously backed by the financially constrained health care service. The diagnostic criteria for DKA and HHS were based on BGL and urine ketones. These criteria lacked ample rigor, which would have been attained with arterial pH, serum bicarbonate, anion gap, and serum osmolality. There is no comprehensive patient assessment, and vigilant follow up for possible complications. Patients were not followed after hospital discharge, and their status was not identified. This study was a retrospective study and would not provide a blank space for authors to modify the existing practice in the study area.

Conclusion

With its dreadful treatment outcome, HE remains among the most awful lifetime experiences of DM patients in Ethiopia. HHS was the major diagnosis among DM patients hospitalized with HE. The majority of the participants were known DM patients on treatment. Comorbidities were common. Infection was the foremost precipitant of HE followed by noncompliance followed by newly diagnosed DM. Mortality and duration of hospital stay stand high. Infection, comorbidity, and lower admission GCS ≤ 8 are the independent predictors of mortality. Hence, operative strategies towards maintaining accessible standard DM care and modifying the predictors ought to be devised so as to reduce the HE morbidity and mortality.

Abbreviations

BGL: Blood Glucose Level; BUN: Blood Urea Nitrogen; DBP: Diastolic Blood Pressure; DFU: Diabetic Foot Ulcer; DKA: Diabetic Ketoacidosis; DM: Diabetes Mellitus; GCS: Glasgow Coma Scale; HE: Hyperglycemic Emergency; HHS: Hyperosmolar Hyperglycemic State; HFSUH: Hiwot Fana Specialized University Hospital; HTN: Hypertension; SBP: Systolic Blood Pressure; SCr.: Serum Creatinine; T1DM: Type 1 Diabetes Mellitus; T2DM: Type 2 Diabetes Mellitus

Declarations

Ethics approval and consent to participate

This study was approved by the Research and Ethics Review Committee of the College of Medicine and Health Sciences, University of Gondar. Owing to the study design employed, the consent to participate in this study was waived.

Consent for publication

Not applicable.

Availability of data and materials

All generated data are comprised.

Competing interests

No competing interests.

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Funding was received for this research work from the University of Gondar.

Authors' contributions

PA conceived and designed the study, developed the data collection tool, acquired the fund, supervised the data collection, analyzed the data and wrote the manuscript. GB, AA and BM contributed to the study design, development of the data collection tool, statistical analysis and manuscript drafting. We all the authors red and approved the final manuscript.

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