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.

Method:

Four-year medical records of DM patients admitted for HE at Hiwot Fana Specialized University Hospital (HFSUH) were reviewed retrospectively. The data abstraction tool was adapted from the preceding studies. Data were entered into and cleaned by Epi-InfoTM7 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 $AOR \neq 1$ within a 95% CI and $P\text{-value} < 0.05$. 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 for HE at HFSUH. Infection, comorbidity, and lower admission GCS ≤ 8 are the independent predictors of HE mortality. Operative strategies targeting the predictors ought to be devised to control the morbidity and mortality among DM patients hospitalized for HE.

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 collective DKA and HHS mortality rate of 20% 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 for 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 for HE at Hiwot Fana Specialized University Hospital (HFSUH) from 01 January, 2016 to 31 December, 2019 were reviewed retrospectively. Ethical clearance was attained from the Research and Ethics Review Committee of the College of Medicine and Health Sciences, University of Gondar. This study included all HE patients admitted at the age of 15 years and above. Patients whose medical records lacked adequate information were excluded from this study. The data abstraction tool was adapted from the preceding studies. Sociodemographic, clinical, biochemical, hospital stay duration, and mortality data were extracted exclusively from the patient's respective medical records.

Data were entered into and cleaned by Epi-InfoTM7 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 $\neq 1$ within a 95% CI and P-value < 0.05. The model was verified using the Hosmer-Lemeshow goodness of fit test (P = 0.392).

Operational definitions

DKA was denoted to an admission blood glucose level >250 mg/dL with significant ketonuria (urine dipstick ketone level $\geq +2$).

HHS was denoted to an admission blood glucose level >600 mg/dL without significant ketonuria (urine dipstick test result: no or +1 urine ketone).

The primary study outcome mortality was referred to in-hospital mortality of DM patients diagnosed with HE and started on the HE management protocol.

Results

Patients fulfilled the inclusion criteria and included in this study were 321 of the entire 613 DM patients admitted and treated for HE at HFSUH within the four years.

Sociodemographic characteristics

The study participants were comprised of 192 (59.8%) females and 129 (40.2%) males. The female to male sex ratio was 1.5:1. The mean admission age of the participants was 43.3 ± 18.4 years. Their age ranged from 15 to 85 years. Patients admitted from the urban areas were 163 (50.8%) and the remaining 158 (49.2%) patients were from the rural areas.

Morbidity features

The HE cases were 168 (52.3%) HHS and 153 (47.7%) DKA. Patients with T1DM and T2DM were 143 (44.5%) and 178 (55.5%). At admission, 117 (36.4%) patients had no DM history and the rest 204 (63.6%) were known DM patients on antidiabetic treatment for the median duration of 4 years. Hundred-four (32.4%) patients presented with comorbidities. The comorbidities comprised hypertension (HTN) (44.2%), congestive heart failure (11.5%), stroke (10.6%), ischemic heart disease (6.7%), chronic kidney disease (9.6%), chronic liver disease (9.6%), asthma (1.9%), chronic obstructive pulmonary disease (1.9%) and epilepsy (3.8%).

Clinical admission features

The clinical admission features of the study participants considered in this study were the vital signs measured at admission for HE. 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 1.

Table 1: Clinical admission features of hyperglycemic emergency patients; DKA vs. HHS

Variables	DKA (Mean $\pm$ SD)	HHS (Mean $\pm$ SD)	P-value
SBP (mmHg)	107.4 $\pm$ 12.0	110.0 $\pm$ 20.6	<0.001
DBP (mmHg)	69.7 $\pm$ 5.6	70.2 $\pm$ 10.1	<0.001
Pulse rate (bpm)	97.2 $\pm$ 12.4	93.4 $\pm$ 11.4	0.317
Respiratory rate (bpm)	25.9 $\pm$ 3.3	20.5 $\pm$ 3.7	0.615
Temperature ($^{\circ}$ C)	36.7 $\pm$ 0.9	36.6 $\pm$ 0.9	0.705
GCS score	12.4 $\pm$ 2.0	10.5 $\pm$ 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 $\pm$ 123.1 mg/dL. Admission BGL, serum creatinine (SCr.) and blood urea nitrogen (BUN) were significantly higher in patients admitted for HHS. The biochemical admission features of the study participants as DKA compared to HHS are displayed in Table 2.

Table 2: Biochemical admission features of patients with hyperglycemic emergencies

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

Of the precipitating conditions of HE, infection and noncompliance were documented in 154 (48.0%) and 124 (38.6%) of the study participants. Pneumonia was documented in 58 (37.7%) of the patients with infection. The type of noncompliance in 83 (66.9%) of the noncompliant patients was antidiabetic medication discontinuation.

Table 4: Hyperglycemic emergency precipitating conditions

Precipitating conditions	Frequency (%)
Infection	154 (48.0)
Pneumonia	58 (37.7)
UTI	39 (25.3)
Sepsis	29 (18.8)
DFU	11 (7.2)
Others	17 (11.0)
Non-compliance	124 (38.6)
Medication discontinuation	83 (66.9)
Missed insulin doses	41 (33.1)
Newly diagnosed DM	63 (19.6)
Cardiovascular events	18 (5.6)
Physical traumatic injury	3 (0.9)

DFU: Diabetic Foot Ulcer; DM: diabetes mellitus; UTI: Urinary Tract Infection

Treatment outcome of HE

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

Predictors of mortality among DM patients 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 ≤ 8 (AOR = 2.58, 95% CI: 1.17-5.71, $P = 0.019$) were the independent predictors of mortality among DM patients hospitalized for HE. Table 3 illustrates the predictors of mortality among DM patients hospitalized for HE.

Table 3: Predictors of mortality among DM patients hospitalized for hyperglycemic emergency

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 in our study. This finding goes in line with studies from Nigeria and Taiwan (15, 23–26) 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 majority of our study participants were T2DM patients and HHS often raids patients with uncontrolled T2DM (27). In addition, the higher percentage of known DM patients in our study might also have lifted the HHS prevalence as it was reported that HHS is common in patients with a prior history of DM (25). This implies that HHS is on the rise and demands great attention.

The rate of comorbidity in our study was 32.4%. This is higher than the 22.1% rate 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. This is because 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 (28). Therefore, works need to be done to standardize the DM care.

The 48% rate of infection documented in our study was higher than the rates, ranging from 22.5–32%, reported from South Africa, Saudi Arabia and Colombia (5, 29, 30). The reason for the upstretched infection rate documented among our study participants might be the incapacitating poverty restraining the healthcare systems in the Sub-Saharan Africa (31). 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 (31, 32). Hence, it would be matter-of-factly to devise strategies to ensure accessible standard DM care in the region and abate the imminent dreadful consequences of noncompliance like HE.

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, 23, 24), it still is longer than the reports from Jimma and South Africa (22, 33). 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 (23, 33), the relatively higher proportion of patients with DFU in our study may further justify the lengthier hospital stay duration.

The overall HE mortality 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 (33), 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 features, 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 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.

Conclusion

With its dreadful treatment outcome, HE remains among the most awful lifetime experiences of DM patients in Ethiopia. Put it in brief, HHS was the major diagnosis of DM patients hospitalized for HE at HFSUH. 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. Therefore, it would be pragmatically sound to devise operative strategies targeting these modifiable predictive factors of mortality in attempt to control the morbidity and mortality among DM patients hospitalized for HE.

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 read and approved the final manuscript.

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