Treatment Outcome and Predictors of Mortality among Adult Diabetic Patients Admitted with Hyperglycemic Crises at Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia

Pawlos Asfaw Tekeste[1]*, Gashaw Binega Mekonnen[2], Achenef Asmamaw Muche[3], and Bereket Molla Tigabu[4]

[1]School of Pharmacy, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia
[2]Department of Clinical Pharmacy, School of Pharmacy, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia
[3]Department of Epidemiology and Biostatistics, Institute of Public Health, University of Gondar, Gondar, Ethiopia
[4]Department of Pharmacy, Komar University of Science and Technology, Kurdistan, Iraq

Abstract

Background: Hyperglycemic crises are frequently experienced and yet perilous acute metabolic complications of diabetes mellitus. However, Treatment outcomes and predictors of mortality among adult diabetic patients admitted with hyperglycemic crises were not well studied in the study area. Therefore this study aimed to assess treatment outcomes and predictors of mortality among adult diabetic patients admitted with hyperglycemic crises at Hiwot Fana Comprehensive Specialized University Hospital.

Methods: A cross-sectional study was conducted on 213 adult diabetes patients admitted with hyperglycemic crises at the emergency department and medical wards of Hiwot Fana Comprehensive Specialized University Hospital from January 1, 2017, to December 31, 2019. Information on patient admission, treatment, and outcome attributes was extracted from medical records. The statistical analysis was performed using SPSS version 24. Logistic regression analysis was done to examine predictors of mortality.

Results: Diabetes ketoacidosis was the most common hyperglycemic crisis detected in 67.6% (95% CI: 61.05% - 73.54%) of the study participants. Recurrent hyperglycemia and hypoglycemia occurred in 124 (58.2%) and 51 (23.9%) of the patients, respectively. The mortality rate from hyperglycemic crises was 17.8% (95% CI: 12.9%-23.7%). Known diabetes (AOR = 3.6; 95% CI: 1.3 – 9.5), hypokalemia (AOR = 7.3; 95% CI: 1.2 – 23.7), serum creatinine >1.2 mg/dl (AOR = 3.1; 95% CI: 1.3 – 7.2), stroke (AOR = 5.3; 95% CI: 1.8 – 16.2), and sepsis (AOR = 4.4; 95% CI: 1.7–11.5) were independent predictors of mortality.

Conclusion: Mortality from hyperglycemic crises in the study setting was high. Metabolic treatment complications were common. A prior history of diabetes, hypokalemia, raised serum creatinine, stroke, and sepsis were independent predictors of mortality. Hence, clinicians ought to focus on these predictive factors and improve the treatment outcome of diabetes patients.

Keywords: Hyperglycemic crises, Mortality, Complications, Predictors, Adults, Eastern Ethiopia

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Introduction

Diabetes mellitus (DM) is a rapidly growing global health concern affecting almost every society. It was estimated in 2021 about 6.7 million adults have died from diabetes and its complications, accounting for 12.2% of global adult deaths. Diabetes is common in Sub-Saharan Africa where Ethiopia had the 4th highest number of adults with diabetes (Federation, 2021). Hyperglycemic crises are frequently experienced and yet perilous acute metabolic complications of DM.

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the two hyperglycemic crises with extreme metabolic derangements requiring immediate medical intervention (Kitabchi *et al*., 2009).

Hyperglycemic crises are common causes of morbidity and mortality worldwide. In the United States, adult emergency department visits and inpatient admissions for both DKA and HHS are continually rising (Benoit *et al*., 2020). The mortality in adults with

Corresponding Author; Email: pawlos.a.213@gmail.com
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DKA and HHS was reported to be ≤0.4% and 10%–20% respectively (Benoit *et al*., 2018; Pasquel & Umpierrez, 2014).

A hospital-based retrospective study in Thailand reported that the 5-year incidence of hyperglycemic crises was 7.5%. Treatment complications included recurrent hyperglycemia (69.9%), hypokalemia (48.2%), hypernatremia (21.7%), and hypoglycemia (15.7%). The overall mortality rate of hyperglycemic crises was 8.4%. Serum sodium level on admission was an independent predictor of mortality from hyperglycemic crises (Anthanont *et al*., 2012).

In Africa, hyperglycemic crises are associated with a mortality rate of 21.7% in Cameroon and 34% in Nigeria (Nkoke *et al*., 2021; Olugbemide *et al*., 2017) in adult diabetic patients. Various factors including sex, age, newly diagnosed diabetes, infection, and diabetic foot ulcer have been associated with the mortality of adult diabetic patients with hyperglycemic crises (Ezeani *et al*., 2013; Nkoke *et al*., 2021; Ogbera *et al*., 2009).

Hospitalization of diabetic patients in Ethiopia is mainly due to hyperglycemic crises (Abejew et al., 2015; Adem et al., 2011; Kefale *et al*., 2016; Negara *et al*., 2020). Few hospital-based studies have been conducted on adults with DKA (Kassaye *et al*., 2018; Mekonnen et al., 2022; Taye *et al*., 2021). As a result, the evidence is scant, particularly in eastern Ethiopia. Therefore, the current study aimed to assess treatment outcomes and predictors of mortality among adult diabetic patients admitted with hyperglycemic crises at Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH).

Materials and Methods

Study Setting, Design, and Period

This cross-sectional study was conducted at Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH), Harar, Ethiopia from July to August 2020. Harar is the capital city of Harari Regional State located 518 km to the east of Addis Ababa, Ethiopia. There are two public hospitals in the Harari Region. The HFCSH is a public hospital providing tertiary-level care in its various inpatient and outpatient units, including the emergency department, medical wards, and diabetes clinic, for about 5,800,000 catchment population from the entire of eastern Ethiopia.

Population, Inclusion/ Exclusion Criteria

The source population consisted of every chart of an adult patient (>18 years old) who had been hospitalized in the emergency department and medical wards of HFCSH with hyperglycemic crises and all patients charts with the complete record from January 1, 2017, to December 31, 2019, were included in this study.

Sample Size and Sampling Technique

The sample size was determined using single population proportion formula, considering a proportion of 9.8% mortality (Desse *et al*., 2015), a 95% confidence interval, and a 5% marginal error (d). The calculated sample size was 136, but throughout the three-year study period, a total of 352 patients were admitted to the emergency and medical wards of HFCSH with hyperglycemic crises, and a total of 213 patients had complete medical records. Despite this, even though our calculated sample was 136, we included all of the patients with complete data (213) because we could manage with the budget that was allotted.

Definition of Terms

Hyperglycemic crises: referred to as diabetic ketoacidosis and hyperosmolar hyperglycemic state, are the two most common acute metabolic complications of diabetes (Kitabchi *et al*., 2009).

Diabetic ketoacidosis: referred to random blood glucose level ≥250 mg/dl and the presence of ketonuria, urine dipstick ketone level ≥ +2 (Desse *et al*., 2015).

Hyperosmolar hyperglycemic state: referred to random blood glucose level ≥600 mg/dl, altered mental status, and absent ketonuria or urine dipstick ketone level < +2 (Desse *et al*., 2015).

Treatment outcomes of hyperglycemic crises: referred to in-hospital mortality, discharge with improvement, left against medical advice, and treatment complications (hyperglycemia and hypoglycemia) due to hyperglycemic crises.

Hyperglycemia: referred to random blood glucose levels >200 mg/dl (Desse *et al*., 2015).

Hypoglycemia: referred to blood glucose levels <70 mg/dl (Desse *et al*., 2015).

Data Collection Tool and Techniques

Medical records of patients admitted with the diagnosis of hyperglycemic crises were traced back from patient logbooks and drawn from card rooms using card numbers. Data were extracted using a data abstraction tool developed as per the study objectives and literature searches. The tool contains socio-demographic characteristics (sex, age, and residence); admission clinical features (hyperglycemic crises type, diabetes type, diabetes history, diabetes-related comorbidity, hyperglycemic crises precipitating factors, and vital signs); biochemical features (serum glucose, electrolytes, creatinine, urea nitrogen, and urine ketone); hyperglycemic crises treatment and outcome. The data collection was done by three trained clinical pharmacists.

Data Quality Control

Before the commencement of the actual data collection, the data abstraction tool was pretested on 5% of the total study population at Jugal Hospital, and necessary refinements were made in the final version. The data collectors were trained for two days on the study objectives, data abstraction tool, and method. The data collection was strictly supervised by a well-trained supervisor. All collected data were checked for correctness, completeness, and consistency throughout the data management, storage, and analysis processes.

Data Processing and Analysis

The data were entered, cleaned, and analyzed using Statistical Packages for Social Sciences (SPSS) version 24. The mean ± standard deviation (SD) or frequency with percentage was done to describe variables. To examine predictors of mortality, variables with p-values ≤0.25 on a bivariable analysis were exported into a multivariable model. Statistical significance was declared at p-value < 0.05. The model was verified using the Hosmer-Lemeshow goodness of fit test (P = 0.392). Multicollinearity among selected independent variables was checked using the variance inflation factor (VIF) and none was found.

Ethical Consideration

Ethical clearance of the study was obtained from the School of Pharmacy on behalf of the ethics review committee of the College of Medicine and Health Sciences, University of Gondar (Reference number: SOPS 015/2019). The hospital was requested with a formal letter of cooperation to access medical records for data abstraction. Confidentiality of information was maintained throughout the study period, and extracted data were used only for research purposes.

Results

Socio-demographic Characteristics and Clinical Presentation of the Study Participants

A total of 213 patients were included in this study. The mean age of the patients was 44.2 ± 16.3 years (range 18–82 years). The majority of patients were male (57.3%), urban residents (59.6%), with type 1 diabetes (53.5%), with known diabetes (64.3%), with DKA (67.8%), and had an infection (62.4%). Diabetes-related comorbidities were recorded in 76 (35.7%) patients. The mean blood glucose level of patients was 508.4 ± 114 mg/dl. Hypotension (blood pressure <90/60 mmHg) was recorded in 26 (12.2%) patients. Hypokalemia (serum potassium <3.5 mEq/l) occurred in 37 (17.4%) of the patients. Fifty-nine (27.7%) patients had serum creatinine >1.2 mg/dl (Table 1)

Treatment of Hyperglycemic Crises

Fluid therapy was initiated in every patient using isotonic saline intravenous (IV) infusion with the rate of 2–3 liters per 1–3 hours. Subsequent fluid therapy using IV isotonic saline was administered to 65 (94.2%) HHS patients with BGL >300 mg/dl and 129 (89.6%) DKA patients with BGL >250 mg/dl. Similarly, IV isotonic saline with 5% dextrose was administered to the remaining 15 (11.4%) DKA and 4 (6.8%) HHS patients with BGLs of 250 mg/dl and 300 mg/dl, respectively. Insulin therapy was initiated in every patient with regular insulin 10 units IV and 10 units intramuscular (IM) stat. This was followed by regular insulin 5 units IM in 101 (47.4%) and 5 units subcutaneously (SC) in 112 (52.6%) patients every hour until crisis resolution. Sliding scale regular insulin 4 to 16 units IV every 5 hours was used in 116 (54.5%) patients. Potassium replacement was administered to 29 (13.6%) patients.

Treatment Outcome of Hyperglycemic Crises

The overall mortality from hyperglycemic crises was 38 (17.8%). Episodes of hyperglycemia and hypoglycemia occurred during treatment in 124 (58.2%) and 51 (23.9%) of the patients, respectively. Patients discharged with improvement were 169 (79.3%) (Table 2).

Table 1: Socio-demographic characteristics and clinical presentation of patients admitted with hyperglycemic crises at HFCSUH, Harar, eastern Ethiopia, January 1, 2017, to December 31, 2019. (n=213).

Socio-demographic characteristics and clinical presentation	Frequency (%)
Sex	
Male	122 (57.3%)
Female	91 (42.7%)
Residence	
Urban	127 (59.6%)
Rural	86 (40.4%)
Type of diabetes	
Type 1	114 (53.5%)
Type 2	99 (46.5%)
History of diabetes	
Newly diagnosed diabetes	76 (35.7%)
Known diabetes	137 (64.3%)
Diabetes-related comorbidities	
Cardiovascular disease	51 (23.9%)
Chronic kidney disease	14 (6.6%)
Others*	11 (5.2%)
Precipitating events	
Infection	133 (62.4%)
Noncompliance	73 (34.3%)
New onset diabetes	76 (35.7%)
Trauma	18 (8.5%)
Hyperglycemic crises	
Diabetes ketoacidosis	144 (67.6%)
Hyperosmolar hyperglycemic state	69 (32.4%)
The vital signs (Mean ± SD)	**Mean ± SD**
Systolic blood pressure (mmHg)	108.3 ± 16.3
Diastolic blood pressure (mmHg)	71.2 ± 10.1
Pulse rate	95.3 ± 12.2
Respiratory rate	23.1 ± 4.4
Temperature (^{O}C)	36.7 ± 0.9
Glasgow Coma Scale	12.6 ± 2.6
Laboratory data (Mean ± SD)	**Mean ± SD**
Blood glucose level (mg/dl)	508.4 ± 114
Serum sodium (mEq/l)	136.8 ± 5.4
Serum chloride (mEq/l)	108.6 ± 6.3
Serum potassium (mEq/l)	3.9 ± 0.6
Serum creatinine (mg/dl)	1.3 ± 0.7
Blood urea nitrogen (mg/dl)	30.4 ± 24.8

*SD; standard deviation, * diabetes foot syndrome, retinopathy, and neuropathy, mmHg; millimeters of mercury, mEq/l; mill equivalents per liter, mg/dl= milligrams per deciliter*

Table 2: Treatment outcome among patients with hyperglycemic crises at HFCSUH, Harar, eastern Ethiopia from January 1, 2017, to December 31, 2019

Treatment outcome	**Frequency (%)**	**95%CI**
Died	38 (17.8)	12.9%-23.7%
Episodes of hyperglycemia	124 (58.2)	51.3%-64.9%
Episodes of hypoglycemia	51 (23.9)	18..4%-30.3%
Discharged with improvement	169 (79.3)	73.3%-84.6%
Left against medical advice	6 (2.8)	1.0%-6.0%

Table 3: Predictors of mortality among patients admitted with hyperglycemic crises at HFCSUH, Harar, eastern Ethiopia from January 1, 2017, to December 31, 2019.

Predictors	Died		COR (95% CI)	P-value	AOR (95% CI)
	Yes n (%)	No n (%)			
History of diabetes					
Known diabetes	31 (22.6)	106 (77.4)	2.9 (1.2, 6.9)	0.02	3.6 (1.3, 9.5)
Newly diagnosed diabetes	7 (9.2)	69 (90.8)	1		1
Hypoglycemia					
Yes	15 (29.4)	36 (70.6)	2.5 (1.2, 5.3)	0.02	1.5 (0.3, 7.9)
No	23 (14.2)	139 (85.8)	1		1
Hypokalemia					
Yes	15 (40.5)	22 (59.5)	4.5 (2.1, 9.8)	0.001	7.3 (1.2, 23.7)
No	23 (13.1)	153 (86.9)	1		1
Serum Creatinine					
≤ 1.2 mg/dl	21 (13.6)	133 (86.4)	1	0.01	1
> 1.2 mg/dl	17 (28.8)	42 (71.2)	2.6 (1.2, 5.3)		3.1 (1.3, 7.2)
Stroke					
Yes	9 (39.1)	14 (60.9)	3.7 (1.4, 9.0)	0.007	5.3 (1.8, 16.2)
No	29 (15.3)	161 (84.7)	1		1
Sepsis					
Yes	13 (40.6)	19 (59.4)	4.3 (1.9, 9.7)	0.001	4.4 (1.7, 11.5)
No	25 (13.8)	156 (86.2)	1		

**;Statistically significant, AOR; adjusted odds ratio,COR; crude odds ratio, mg/dl; milligrams per deciliter, mEq/l; milliequivalents per liter*

Predictors of Mortality of Hyperglycemic Crises

In bivariable logistic regression analysis, known diabetes, hypokalemia, serum creatinine during admission >1.2 mg/dl, stroke, sepsis, and treatment-induced hypoglycemia were candidates for the multivariable model.

In a multivariable model, known diabetes, hypokalemia, serum creatinine >1.2 mg/dl, stroke, and sepsis were found to be independent predictors of mortality. The likelihood of death from hyperglycemic crises was 3.6 times higher in patients with known diabetes compared to those with newly diagnosed diabetes (AOR = 3.6; 95% CI: 1.3–9.5).

Patients with hypokalemia had a 7.3 times higher likelihood of death from hyperglycemic crises compared to those without hypokalemia (AOR = 7.3; 95% CI: 1.2–23.7). The odds of death from hyperglycemic crises were 3.1 times higher in patients with serum creatinine >1.2 mg/dl compared to those with serum creatinine ≤1.2 mg/dl (AOR = 3.1; 95% CI: 1.3–7.2). Patients with stroke had a 5.3 times higher likelihood of death from hyperglycemic crises compared to those without stroke (AOR = 5.3; 95% CI: 1.8–16.2). The likelihood of death from hyperglycemic crises was 4.4 times higher in patients with sepsis compared to those without sepsis (AOR = 4.4; 95% CI: 1.7–11.5) (Table 3).

Discussion

In this study, DKA was the common clinical presentation of patients with hyperglycemic crises (67.6%). This is lower than the study findings from Jimma(93%) (Desse *et al*., 2015), but higher than the finding of a study from Nigeria (31%) (Ezeani *et al*., 2013) where HHS was the index case. The higher rate of DKA may be attributable to the relatively higher proportion of type 1 DM patients in this study than in the study from Nigeria (53.5% vs. 13.3%). DKA occurs more frequently in patients with type 1 than those with type 2 DM (Association, 2017).

Episodes of hyperglycemia and hypoglycemia occurred in 58.2% and 23.9% of the patients, respectively. These were similar to the Jimma study's findings, which show that 20.9% of participants had hypoglycemia and 54% had hyperglycemia. (Desse *et al*., 2015). A higher rate of hyperglycemia (69.9%) and a lower rate of hypoglycemia (15.7%) were reported in Thailand (Anthanont *et al*., 2012). The observed disparities in the rates of treatment complications may be due to variations in patient admission features or amounts of insulin used. Hence, clinicians need to remain vigilant for the prospect of complications during hyperglycemic crisis treatment.

The mortality rate from hyperglycemic crises was 17.8%. This was similar to 13.2% and 21.7% mortality reported from northern Ethiopia and Cameroon (Gebremedhin *et al*., 2021, Nkoke *et al.*, 2021), but higher than from southwest Ethiopia (9.8%) (Desse *et al.,* 2015), Thailand (8.4%) (Anthanont *et al*., 2012), and in Colombia (2.3%) (Builes-Montaño et al., 2018). It is lower than 21% and 34% mortality in Cameroon and Nigeria (Nkoke *et al*., 2021; Olugbemide *et al*., 2017). The discrepancies may be due to setting variations in the clinical presentation of patients and efficient detection and management of hyperglycemic crises, precipitating factors, and complications. Nonetheless, such an inflated mortality rate is inadmissible.

The likelihood of death from hyperglycemic crises was higher in patients with known diabetes compared to those diagnosed with diabetes on admission. This finding was in line with a study in Tigray (Gebremedhin *et al*., 2021), but contrary to a study in Nigeria (Ogbera *et al.,* 2009). Increased mortality in known diabetes patients might be due to continually existing uncontrolled diabetes and related complications. A great emphasis ought to be placed on strengthening diabetes care and the prevention of complications.

Patients with hypokalemia had a higher likelihood of dying from hyperglycemic crises compared to those without hypokalemia. This finding is consistent with a study in Nigeria (Ogbera *et al*., 2009). Patients with hyperglycemic crises have depleted total body potassium due to hypoinsulinemia, metabolic acidosis, and hyperosmolarity. This can swift to severe hypokalemia causing cardiac arrhythmia and death upon initiation of insulin therapy, correction of acidosis, and volume expansion (Kitabchi *et al*., 2009). Hence, prompt correction and meticulous monitoring of electrolyte levels, potassium levels particularly, is critical.

The odds of death from hyperglycemic crises were higher in patients with raised serum creatinine >1.2 mg/dl compared to those with serum creatinine ≤1.2 mg/dl. This finding is consistent with a study from Jimma (Desse *et al*., 2015). Prompt detection and adequate management of complications should be emphasized.

Patients with stroke had a higher likelihood of death from hyperglycemic crises compared to those without stroke. This finding is consistent with a study in Tigray (Gebremedhin *et al.,* 2021). Emphasis should be placed on strengthening diabetes control and prevention of diabetes-related comorbidities.

The likelihood of dying from hyperglycemic crises was higher in patients admitted with sepsis compared to those without sepsis. This finding is consistent with a study in Jimma and Nigeria (Desse *et al*., 2015; Ogbera *et al*., 2009). Patient education on diabetes self-care and infection prevention as well as prompt detection and management of infection and sepsis should be promoted.

In general, this study provided a comprehensive opportunity to overview the treatment outcome and pre

dictors of mortality in adults with hyperglycemic crises at HFCSH. Yet, it has the limitation of generalizability mainly due to the dearth of laboratory investigations such as arterial pH, serum bicarbonate, serum osmolality, and electrolytes in the setting to rigorously diagnose and manage cases. Besides, poor documentation practice in the setting resulted in the exclusion of a large number of incomplete medical records.

Conclusion

This study revealed high mortality and recurrent episodes of hyperglycemia and hypoglycemia among adults admitted with hyperglycemic crises at HFCSH. Known diabetes, hypokalemia, raised serum creatinine, stroke, and sepsis were independent predictors of mortality from hyperglycemic crises. Hence, clinicians ought to focus on the predictors to reduce in-hospital mortality from hyperglycemic crises and work to effectively deter treatment complications. Furthermore, multicenter longitudinal studies assuming rigorous diagnostic criteria and treatment protocol are sought to precisely determine the extent of the problem at the national level.

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Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

PA was involved in the conception and designing of the study, developed the data abstraction tools, supervised the data collection, analyzed the data, and wrote the manuscript. GB, AA, and BM participated in the study designing, development of the data abstraction tools, data analysis, and manuscript editing. All authors read and approved the final manuscript.

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