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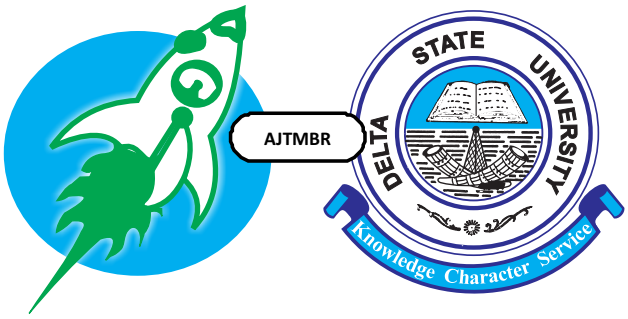

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Focus and Scope

The African Journal of Tropical Medicine and Biomedical Research is a multidisciplinary and international journal published by the College of Health Sciences, Delta State University of Abraka, Nigeria. It provides a forum for Authors working in Africa to share their research findings on all aspects of Tropical Medicine and Biomedical Sciences and to disseminate innovative, relevant and useful information on tropical medicine and biomedical sciences throughout the continent. The journal will publish original research articles, reviews, editorials, commentaries, short reports, case reports and letters to the editor. Articles are welcome in all branches of medicine and dentistry including basic sciences (Anatomy, Biochemistry, Physiology, Pharmacology, Psychology, Nursing etc) and clinical sciences (Internal Medicine, Surgery, Obstetrics and Gynaecology, Dental surgery, Child Health, Laboratory Sciences, Radiology, Community Medicine, etc). Articles are also welcome from social science researchers that document the intermediating and background social factors influencing health in countries of Africa. Priority will be given to publication of articles that describe the application of the principles of primary health care in the prevention and treatment of diseases.

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Table of Contents

Hyperglycemic emergencies in a tertiary health facility: clinical presentation and predictors of mortality

Beatrice Ohunene Bello-Ovosi[1], Joseph Ogirima Ovosi[2], Isa Kweumpo Bansi[3],

Abstract

Aim: To assess the clinical presentations and predictors of mortality of hyperglycemic emergencies (HE) in persons with diabetes mellitus (DM) presenting in a tertiary health facility in Nigeria.

Methods: This was a two-year retrospective review of hospital records of persons with DM in a tertiary hospital in Nigeria. We retrieved data on person's demographics, clinical and laboratory characteristics into Microsoft Excel and analyzed with STATA version 14.

Results: A total of 195 (42.4%) out of 460 persons admitted with DM fulfilled the eligibility criteria. Diabetic ketoacidosis (DKA) was present in 42.6%, mixed hyperglycemic emergency (MHE) in 34.9% and hyperglycemic hyperosmolar state (HHS) in 22.5%. Mortality in HE was 8.7%. The common clinical presentation were: osmotic symptoms (71.3%), tachypnoea (46.7%), tachycardia (42.6%). Elevated anion gap (89.2%) and anemia (80.5%) were the common laboratory findings. Infections (86.7%), non-compliance (79.5%) and newly diagnosed DM were the common precipitants of HE. Significant predictors of mortality were: duration of DM between 5-9 years, Glasgow Coma Scale (GCS) < 8, hypotension, and hypokalemia.

Conclusion: HE is still a common cause of hospitalization and mortality in persons with DM; and features such osmotic symptoms, tachypnea and high anion gap metabolic acidosis should alert the clinician.

Keywords: Hyperglycemic emergencies, diabetes ketoacidosis, hyperglycemic hyperosmolar state, mortality

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1. Introduction

In 2019, the global estimate of persons with diabetes mellitus (DM) was 463 million, out of which 19 million were living in Africa; and DM was responsible for 366,200 deaths (6.8% of all-cause mortality) in the sub-region.[1] Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are two of the extreme life-threatening and overlapping spectrum of acute metabolic complications, termed hyperglycemic emergencies (HE), which are largely seen in people with uncontrolled DM; and contribute significantly to the morbidity and mortality attributed to the disease.[2,3]

In DKA, absolute or relative insulin deficiency is accompanied by increase in counter-regulatory hormones resulting in hyperglycemia, ketonemia and acidosis.[4] HHS, however, results from relative insulin deficiency and/or insulin resistance which

leads to marked hyperglycemia, severe extracellular volume contraction, hyperosmolality usually > 320 mOsmol/kg and minimal ketonemia.[2,5,6] While in DKA, the insulin deficiency is marked enough to stimulate lipolysis and ketogenesis which are its hallmark; in HHS, the insulin deficiency is not marked enough, hence, the minimal ketonemia seen.[7]

The majority of the people with DM are undiagnosed and could present for the first time with HE,[8-11] and this may be worse in Africa, where about 59.4% of people living with DM are undiagnosed.[1] In the UK, about one-quarter of the diagnosis of type 1 DM are made for the first time in the presence of DKA, resulting in an expenditure of 1,387GBP per hospitalization; and up to 20% of HHS do not have previous diagnosis of DM.[1,12] In the US, hyperglycemic emergencies accounted for 207,000 hospitalizations in 2014, and 168,000 of these were due to DKA, accounting for 7,470-20,864 USD per hospitalization.[13,14] In Nigeria, the exact burden of HE is not known. However, hospital-based studies have reported incidences in the range 11 – 40%,[15-17] and mortality in the range 18-22% for DKA and 25-35% for HHS.[18,19] Despite the high morbidity and mortality attributed to HE in Nigeria, few studies have assessed the clinical presentations and the factors that predict mortality among them. This study, therefore, assessed the clinical presentations and predictors of mortality in persons with HE in Ahmadu Bello University Teaching Hospital (ABUTH), Zaria – a tertiary health facility in Nigeria.

2. Methods

2.1 Study Area

ABUTH is a 500-bed public tertiary health facility located in Zaria, northwestern Nigeria. It serves clients from most northern Nigerian states and neighboring countries of Niger and Chad Republics.

2.2 Study design

We conducted a retrospective review of hospital records of all adult patients admitted for HE at ABUTH, Zaria over two years, from 1 January 2015 – 31 December 2016.

2.3 Study population

Subjects were considered eligible if they were adults aged 18 years and above, and were confirmed to be persons with DM by the admitting physician and presenting with hyperglycemic emergency during the period. Pregnant women and patients with incomplete information were excluded from the study.

2.4 Data collection

Data was extracted using a structured-questionnaire that included sections on socio-demographics, clinical and laboratory information. Clinical and laboratory data retrieved were: type of DM, duration of DM, number and types of anti-diabetic medications, compliance, past history of HEs, co-morbidities, presenting symptoms, physical examination findings, serum urea and electrolyte and complete blood count. The primary outcome measure was in-hospital mortality due to HE.

2.5 Measurement of variables

DKA was defined as blood glucose between 16.6 – 33.3 mmol/L, serum bicarbonate (HCO_3^-) ≤ 18 mmol/L and urine dipsticks ketones of at least +2.[20] HHS was blood glucose > 33.3 mmol/L, serum HCO_3^- > 18 mmol/L, serum osmolality > 320 mmOsm/kg and absence of urine dipsticks ketones or urine dipsticks ketones of not more than +1.[2,3] Mixed hyperglycemic emergency (MHE) was admitting blood glucose > 16.6 mmol/L, serum HCO_3^- < 18 mmol/L, serum osmolality < 320 mmOsmol/kg and absent or

urine dipsticks of +1.[4,21] Type 1 DM referred to patients with DM who had been on insulin since diagnosis and required insulin for survival and type 2 DM were patients with DM who were previously managed on lifestyle modification, or on oral hypoglycemic agents; or insulin-requiring patients who initially were not insulin-dependent.[19] Osmotic symptom was documented history of polyuria, polydipsia and/or weight loss. Fever was admitting oral temperature > 37.2^{0}C and hypothermia, oral temperature < 36.4^{0}C.[22,23] Tachycardia was admitting pulse rate > 100 beats/minute,[24,25] and tachypnea admitting respiratory rate > 20 cycles/minute.[26] Alteration in sensorium was mild, if Glasgow Coma Scale (GCS) was 13-15; moderate if 9-12 and severe if £ 8.[27] Hypertension was defined as systolic blood pressure of ≥140 mmHg or diastolic blood pressure ≥90 mmHg or a documentation of treatment with anti-hypertensive medications[28]; hypotension was blood pressure recording of ≤ 90/60 mmHg.[29]

Electrolyte parameters were defined as follows: Hypernatremia, serum sodium (Na^+) > 142 mmol/L; hyponatremia, serum sodium < 135 mmol/L.[30] Hyperkalemia, serum potassium (K^+) > 5.0 mmol/L; and hypokalemia, serum potassium < 3.5 mmol/L.[31] Acidosis was serum HCO_3^- ≤ 18 mmol/L and further classified as mild when bicarbonate was 15 – 18 mmol/L, moderate when 10 – 14 mmol/L and severe when < 10 mmol/L.[20] Serum anion gap was calculated from the formula: $(Na^+ + K^+) – (Cl + HCO_3)$ and classified as high, if > 18 mEq/L.[32] Serum osmolality was calculated from the formula: 2 (Na^+) + glucose (mmol/L) + Urea (mmol/L), and classified as high if > 320 mmOsm/kg.[33] Leucocytosis was white blood cell count (WBC) > 12.0×10^9 /L and leucopenia as counts < 4.0×10^9 /L.[34] Anemia was defined as hemoglobin (Hb) < 12g/dL and elevated urea, serum urea > 8.6 mmol/L.[35] Compliance – referred to admittance to taking anti-diabetic medications for more than 75% of the drug schedule time as at the time of admission or adhering to the dietary regimen prescribed for most of the days of the month in the preceding three months.

2.6 Statistical analysis

Data were coded and entered into STATA version 14 (Stata Corp, College Station, Texas) for analysis. Continuous variables were expressed as means ± standard; and categorical variables, as frequencies and percents. Student's t test and one-way analysis of variance (ANOVA) were used to test association with continuous outcome variables; and Chi square test and Fisher's exact test were for categorical outcome variables. Multivariate logistic regression was used to identify independent predictors of mortality by entering variables with $p < 0.25$ on bivariate analysis into the model, and variables with $p < 0.05$ were considered statistically significant.

2.7 Ethical Approval

We sought and obtained ethics approval for the conduct of the research and the use of data from ABUTH Research Ethics Committee (ABUTH-REC), and permission for use of the data from the medical records. We did not obtain a written informed consent from the subjects due to the retrospective nature of the study, but we maintained privacy and confidentiality by ensuring that each case file was assigned a unique numerical identifier for tracking purposes only; and data was retrieved anonymously.

3. Results

3.1 Summary of study enrolment

A total of the 460 persons with DM were admitted during the study period, out of which

195 (42.4%) fulfilled the eligibility criteria and had complete data for analysis. Eighty-three (42.6%) of this had DKA, 68 (34.9%) had MHE and 44 (22.5%) had HHS. The overall mortality of HE was 17 (8.7%); 7 (8.4%) in DKA; 6 (13.6%) in HHS and 4 (5.9%) in MHE (Figure 1).

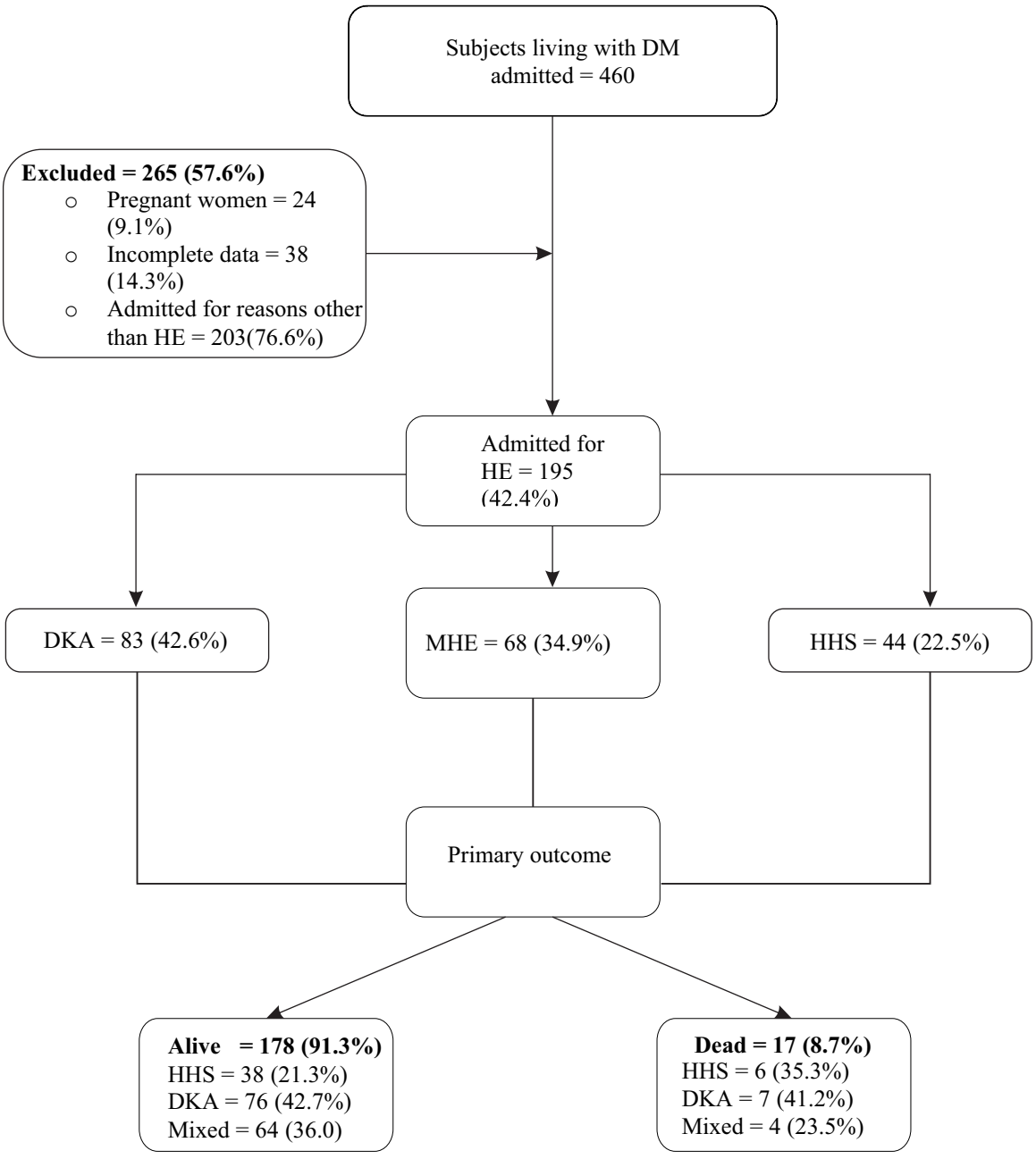

Figure 1: Summary of flow chat of participants

3.2 Background characteristics of patients with hyperglycemic emergencies

The mean age of the subjects was 53.6 ± 14.5 years. Majority (56.9%) of subjects were aged 41 – 64 years while only 46 (23.6%) were aged ³ 65 years. One hundred and forty-six (74.9%) were males and 145 (74.4%) belong to the Hausa/Fulani ethnic group. A significant proportion (94.4%) had type 2 DM, and 108 (55.4%) were on some treatment for DM with only 41 (21.0%) having good compliance. Eighty (41.0%) had previous episodes of HE and 107 (54.9%) patients had at least one co-morbidity (Table 1).

3.3 Clinical and laboratory characteristics of hyperglycemic emergencies

One hundred and thirty-nine (71.3%) of persons with HE had osmotic symptom; 47 (24.1%) had lassitude, 23 (11.8%) had dysuria, 17 (8.7%) had nausea/vomiting, 15 (7.7%) had muscle aches and 7 (3.6%) had headache.

Tachypnoea was the commonest sign and was present in 91 (46.7%) of persons with HE and this was followed by tachycardia, 83 (42.6%); fever, 82 (42.0%); foot ulcer/sepsis, 78 (40.0%); and hypertension, 61 (31.3%). All persons with HE had some degree of alteration in sensorium, but overall, 22 (11.3%) had moderate-severe impairment (14.4% in DKA vs. 18.2% in HHS vs. 2.9% in MHE, p = 0.012). Twenty (10.3%) had hypothermia and 14 (7.2%) had hypotension (Tables 2 and 3).

High anion gap was the commonest laboratory finding, occurring in 174 (89.2%) of persons with HE (98.8% in DKA vs. 81.8% in HHS and 82.3% in MHE, p = 0.001). Others were: anaemia, 157 (80.5%); hyponatremia, 67 (34.4%); elevated urea, 62 (31.8%); leukocytosis, 57 (29.2%); acidosis, 54 (27.7%); hyperkalemia, 32 (16.4%); hyperosmolarity, 31 (15.9%); leucopenia, 27 (13.9%); hypernatremia, 20 (10.2%) and hypokalemia, 18 (9.2%).

Table 1: Background characteristics of subjects with hyperglycemic emergencies studied

Characteristics	**Frequency (N =195)**	**Percentage**
Age group, (years)		
≤ 40	38	19.5
41 – 64	111	56.9
≥ 65	46	23.6
Sex		
Female	49	25.1
Male	146	74.9
Ethnicity		
Hausa/Fulani	145	74.4
Others	50	25.6

Employment status		
Unemployed	66	33.9
Employed	129	66.1
Marital status		
Single	47	24.1
Married/Divorced/Separated/Widowed	148	75.9
Type of DM		
Type 1	11	5.6
Type 2	184	94.4
Duration of diagnosis, (years)		
< 5	97	49.7
5 – 9	40	20.5
≥ 10	58	29.7
On treatment for DM		
No	87	44.6
Yes	108	55.4
Compliance with diet/medications		
No	154	79.0
Yes	41	21.0
Past history of HE		
No	115	59.0
Yes	80	41.0
Co-morbidities		
Absent	88	45.1
Present	107	54.9
No of co-morbidities, n = 107		
1	71	66.4
> 1	36	33.6
Type of co-morbidity*		
Hypertensive heart disease	93	47.7
Cerebrovascular accident	19	9.7
Chronic renal failure	21	10.8
Chronic liver disease	7	3.6
Malignancy	5	2.6

DM = Diabetes Mellitus, HE = Hyperglycemic Emergencies, *Note: categories are not mutually exclusive

Table 2: Clinical and biochemical characteristics of subjects with hyperglycemic emergencies studied

Characteristics	**Frequency (N =195)**	**Percentage**
Symptoms		
Osmotic symptoms	139	71.3
Weakness/lassitude	47	24.1
Dysuria	23	11.8
Vomiting	17	8.7
Muscle aches	15	7.7
Headache	7	3.6
Signs		
Tachypnoea	91	46.7
Tachycardia	83	42.6
Fever	82	42.1
Foot sepsis	78	40.0
Hypertension	61	31.3
Moderate-severe altered sensorium	22	11.3
Hypothermia	20	10.3
Hypotension	14	7.2
Laboratory para meters		
Elevated anion gap	174	89.2
Anemia	157	80.5
Hyponatremia	67	34.4
Elevated urea	62	31.8
Leukocytosis	57	29.3

Acidosis	54	27.7
Hyperkalemia	32	16.4
Hyperosmolarity	31	15.9
Leucopenia	27	13.9
Hypernatremia	20	10.3
Hypokalemia	18	9.2

DM = Diabetes Mellitus, HE = Hyperglycemic Emergencies; Note: categories are not mutually exclusive

Table 3: Presentation according to type of hyperglycemic emergencies

Characteristics	**DKA (n = 83)**	**HHS (n = 44)**	**Mixed (n = 68)**	**P value**
Osmotic symptom, n (%)	56 (67.5)	35 (79.5)	48 (70.6)	0.355
Headache, n (%)	1 (1.2)	4 (9.1)	2 (2.9)	0.086
Vomiting, n (%)	9 (10.8)	4 (9.1)	4 (5.9)	0.613
Weakness/lassitude, n (%)	24 (28.9)	11 (25.0)	12 (17.7)	0.270
Muscle aches, n (%)	3 (3.6)	4 (9.1)	8 (11.8)	0.142
Dysuria, n (%)	10 (12.0)	9 (20.5)	4 (5.9)	0.065
Diabetic foot sepsis, n (%)	26 (31.3)	11 (25.0)	33 (48.5)	0.021
GCS, n (%)				0.012
Mild	71 (85.6)	36 (81.8)	66 (97.1)	
Moderate	6 (7.2)	7 (15.9)	2 (2.9)	
Severe	6 (7.2)	1 (2.3)	0 (0)	
Body temperature, n (%)				0.338
Hypothermia	8 (9.6)	3 (6.8)	9 (13.2)	
Normothermia	44 (53.0)	17 (38.6)	32 (47.1)	
Fever	31 (37.4)	24 (54.6)	27 (39.7)	
Anemia, n (%)	65 (78.3)	38 (86.4)	54 (79.4)	0.530

WBC counts, n (%)				0.073
Leucopenia	17 (20.5)	7 (15.9)	3 (4.4)	
Normal	42 (50.6)	25 (56.8)	44 (64.7)	
Leucocytosis	24 (28.9)	12 (27.3)	21 (30.9)	
Tachypnoea, n (%)	47 (56.6)	21 (47.7)	23 (33.8)	0.027
Tachycardia, n (%)	40 (48.2)	22 (50.0)	21 (30.9)	0.053
Blood pressure, n (%)				0.979
Hypotension	7 (8.4)	3 (6.8)	4 (5.9)	
Normotension	49 (59.1)	28 (63.6)	43 (63.2)	
Hypertension	27 (32.5)	13 (29.6)	21 (30.9)	
Elevated Urea, n (%)	34 (41.0)	12 (27.3)	16 (23.5)	0.056
Random blood sugar, mmol/L				0.000
< 16.6	15 (18.0)	1 (2.2)	23 (33.8)	
16.7 – 33.2	36 (43.4)	20 (45.5)	45 (66.2)	
> 32.2	32 (38.6)	23 (52.3)	0 (0)	
Serum Sodium, n (%)				0.001
Hyponatremia	31 (37.4)	6 (13.6)	30 (44.1)	
Normonatremia	48 (57.8)	28 (63.6)	32 (47.1)	
Hypernatremia	4 (4.8)	10 (22.8)	6 (8.8)	
Acidosis, n (%)	39 (47.0)	10 (22.7)	5 (7.4)	0.00
Elevated Anion gap, n (%)	82 (98.8)	36 (81.8)	56 (82.3)	0.001
High Osmolality, n (%)	4 (4.8)	17 (38.6)	10 (14.7)	0.000

(HE = Hypertensive emergencies; DKA = Diabetic Keto Acidosis; MHE = Mixed Hyperglycemic Emergencies)

3.4 Precipitant of hyperglycemic emergencies

The commonest precipitant of HE was infection 169 (86.7%). Others were: non-compliance to dietary advice/medication, 155 (79.5%); newly diagnosed, 47 (24.1%); trauma, 6 (3.1%), and 2 (1.0%) had unknown precipitants. Diabetes foot/hand sepsis 83 (49.1%), urinary tract infection 50 (29.6%), sepsis 12 (7.1%), pneumonia 10 (5.9%), malaria 7 (4.1%), cellulitis 5 (3.0%) and acute diarrhoeal disease 2 (1.2%) were the infections precipitating HE.

3.5 Predictors of mortality in hyperglycemic emergencies

In a univariate analysis, two factors were associated with mortality: Glasgow Coma Scale (p = 0.006) and duration of hospital stay (p = 0.032). The two statistically significant factors, as well as variables with a p-value < 0.25 (Table 4) were selected for the multivariate logistic model. Factors that remained significant were: duration of diabetes between 5 – 9 years (OR = 6.8; 95% CI = 1.1 – 42.1, p = 0.040), GCS < 8 (OR = 10.2, 95% CI = 1.03 – 101.6, p = 0.047), normotension (OR = 0.045, 95% CI = 0.005 – 0.4, p = 0.005), hypertension (OR = 0.067, 95% CI = 0.007 – 0.644, p = 0.019), normokalemia (OR = 0.1, 95% CI = 0.015 – 0.66, p = 0.017), hyperkalemia (OR = 0.04, 95% CI = 0.002 – 0.83, p = 0.038).

Table 4: Outcome of hyperglycemic emergencies by subjects' characteristics

	Outcome		
Characteristics	**Alive (n = 178)**	**Dead (n = 17)**	**P – value**
Age group, n (%)			0.119
≤ 40	37 (20.8)	1 (5.9)	
41 – 64	102 (57.3)	9 (52.9)	
≥ 65	39 (21.9)	7 (41.2)	
Sex (male), n (%)	132 (74.2)	14 (82.3)	0.457
Tribe, n (%)			0.340
Hausa/Fulani	134 (75.3)	11 (64.7)	
Others	44 (24.7)	6 (35.3)	
Employment status, n (%)			0.059
Unemployed	64 (36.0)	2 (11.8)	
Employed	114 (64.0)	15 (88.2)	
Marital status			0.259
Single	41 (23.0)	6 (35.3)	
Married/Divorced/Separated/Widowed	137 (77.0)	11 (64.7)	
Type of DM			0.603
Type 1	11 (6.2)	0 (0)	
Type 2	167 (93.8)	17 (100)	
Duration of Diabetes, years, n (%)			0.173
< 5	92 (51.7)	5 (29.4)	
5 – 9	36 (20.2)	4 (23.5)	
≥ 10	50 (28.1)	8 (47.1)	
Treatment for DM, n (%)	98 (55.1)	10 (58.8)	0.765
Compliance to treatment, n (%)	38 (21.3)	3 (17.6)	1.00

Past history of hyperglycemic emergencies, n (%)	72 (40.4)	8 (47.1)	0.595
Co-morbidities, n (%)	96 (53.9)	11 (64.7)	0.394
Type of co-morbidity, n (%)			
Hypertensive heart disease	84 (47.2)	9 (52.9)	0.650
Cerebrovascular accident	16 (9.0)	3 (17.7)	0.221
Chronic renal failure	20 (11.2)	1 (5.9)	0.700
Chronic liver disease	5 (2.8)	2 (11.8)	0.116
Malignancy	3 (1.7)	2 (11.8)	0.061
No of co-morbidities, n = 107 (%)			1.00
≤ 1	64 (66.7)	7 (63.6)	
> 1	32 (33.3)	4 (36.4)	
Type of HE			0.362
DKA	76 (42.7)	7 (41.2)	
HHS	38 (21.3)	6 (35.3)	
Mixed	64 (36.0)	4 (23.5)	
Random blood sugar, mmol/L			0.402
< 16.6	37 (20.8)	2 (11.8)	
16.7 – 33.2	93 (52.2)	8 (47.1)	
> 32.2	48 (27.0)	7 (41.1)	
Temperature, n (%)			0.274
Hypothermia (≤ 36.1^{0}C)	18 (10.1)	2 (11.8)	
Normothermia (36.2^{0}C – 37.2^{0}C)	88 (49.4)	5 (29.4)	
Fever (> 37.2^{0}C)	72 (40.5)	10 (58.8)	
GCS, n (%)			0.006
Mild	162 (91.0)	11 (64.7)	
Moderate	11 (6.2)	4 (23.5)	
Severe	5 (2.8)	2 (11.8)	
Blood pressure, n (%)			0.096
Hypotension	11 (6.2)	3 (17.6)	
Normotension	113 (63.5)	7 (41.2)	
Hypertension	54 (30.3)	7 (41.2)	
Tachycardia, n (%)	77 (43.3)	6 (35.3)	0.526
Tachypnoea, n (%)	82 (46.1)	9 (52.9)	0.587
Anemia, n (%)	143 (80.3)	14 (82.3)	1.00
Elevated urea, n (%)	54 (30.3)	8 (47.1)	0.157

WBC counts, n (%)			0.688
Leucopenia	24 (13.5)	3 (17.7)	
Normal	103 (57.9)	8 (47.1)	
Leucocytosis	51 (28.6)	6 (35.2)	
Serum sodium, n (%)			0.144
Hyponatremia	61 (34.3)	6 (35.3)	
Normonatremia	101 (56.7)	7 (41.2)	
Hypernatremia	16 (9.0)	4 (23.5)	
Serum potassium, n (%)			0.081
Hypokalemia	14 (7.9)	4 (23.5)	
Normokalemia	133 (74.7)	12 (70.6)	
Hyperkalemia	31 (17.4)	1 (5.9)	
Acidosis, n (%)	48 (27.0)	6 (35.3)	0.463
Elevated anion gap, n (%)	161 (90.4)	13 (76.5)	0.093
Hyperosmolarity, n (%)	26 (14.6)	5 (29.4)	0.111
Duration of hospital stay, n (%)			0.032
≤ 7 days	20 (11.2)	5 (29.4)	
> 7 days	158 (88.8)	12 (70.6)	

(HE = Hypertensive emergencies; DKA = Diabetic Keto Acidosis; MHE = Mixed Hyperglycemic Emergencies)

Table 5: Multivariate logistic regression of predictors of mortality in hyperglycemic emergencies

Characteristics	**Odds ratio**	**95% CI of Odds Ratio**	**P – value**
Age group, n (%)			
≤ 40	Reference		
41 – 64	9.1	0.56 – 146.9	0.120
≥ 65	18.9	0.93 – 383.4	0.056
Employment status, n (%)			
Unemployed	Reference		
Employed	6.1	0.77 – 48.2	0.087
Duration of Diabetes, years, n (%)			
< 5	Reference		
5 – 9	6.8	1. – 42.1	0.040
≥ 10	3.8	0.79 – 17.8	0.097

Co-morbidity, n (%)			
No	Reference		
Yes	0.82	0.18 – 3.6	0.790
GCS, n (%)			
Mild	Reference		
Moderate	4.6	0.73 – 29.2	0.103
Severe	10.2	1.03 – 101.6	0.047
Blood pressure, n (%)			
Hypotension	Reference		
Normotension	0.045	0.005 – 0.400	0.005
Hypertension	0.067	0.0070 – 0.644	0.019
Elevated urea, n (%)			
No	Reference		
Yes	0.80	0.20 – 3.4	0.768
Serum sodium, n (%)			
Hyponatremia	Reference	0.2 – 3.5	0.698
Normonatremia	0.73	0.07 – 27.7	0.803
Hypernatremia	1.4		
Serum potassium, n (%)			
Hypokalemia	Reference	0.015 – 0.66	
Normokalemia	0.1	0.002 – 0.83	0.017
Hyperkalemia	0.04		0.038
Hyperosmolarity, n (%)			
No	Reference		
Yes	1.05	0.07 – 16.1	0.970
Duration of hospital stay, n (%)			
≤ 7 days	Reference		
> 7 days	0.23	0.04 – 1.4	0.113

CI = Confidence Interval

4. Discussion

Hyperglycemic emergencies are increasingly common indications for hospital admissions in those living with DM. [2,4] In this study, 42.4% of the hospitalization in people living with DM was a result of HE. This is similar to the 40% reported by Ogbera *et al*,[37] and 46% reported by Oguejiofor *et al*[38] in tertiary health facilities in Nigeria; and 43.5% by Ekpebegh *et al*[39] in South Africa but higher than the 29.8% reported by Chijioke *et al*[40] and 11.8% by Ajayi *et al*.,[15] in other tertiary health facilities in Nigeria. Other studies in Nigeria reported higher prevalence in the range 76.9 – 83.0%.[41-43] These differences may have arisen due to the variations in operational definitions of HE in these studies. Diabetic Ketoacidosis was the commonest HE occurring in 42.6% of the admissions while MHE and HHS

accounted for 34.9% and 22.5% of HE respectively. This is in contrast with reports from other studies in Nigeria where HHS tend to predominate,[44-47] but similar to the reports of Desse *et al*,[48] and Ogbera *et al*.[19]

The overall mortality due to HE in this study was 8.7%. This is similar to the mortality range of 6.8% - 20.2% reported in similar studies across Africa [19, 39]. This underscores the need for more efforts towards diabetic education and management in this region.

The mean age of our study subjects was 53.6 ± 14.5 years, with majority between 41 – 64 years and 94.4% of all subjects having type 2 DM. This is in agreement with similar studies in Nigeria and the global trend where most type 2 DM occur in the fifth and sixth decades of life.[1,16] Furthermore, 54.9% of the subjects had at least one co-morbidity and hypertensive heart disease was the commonest. This is unsurprising given the fact that previous studies had documented higher cardiovascular risk among subjects living with DM compared to the general population.[49] In addition, diabetes is associated with cluster of metabolic risk factors including hypertension, dyslipidemia and central obesity.[50] This observation underscores the need for continuous surveillance and management of cardiovascular risk in this population.

Accurate and prompt diagnosis of HE is premised on the understanding of the signs and symptoms that constitute the syndrome. In our study, HE presented with diverse clinical and laboratory features. However, osmotic symptom was the commonest seen in 71.3%, and this was slightly higher in HHS compared to DKA and MHE. This could be the result of osmotic diuresis and the greater degree of dehydration that characterize HHS. Tachypnea was the commonest sign, present in 46.7%, and more in DKA (56.6%) compared to HHS (47.7%) and MHE (33.85%). This is expected in view of the profound ketosis that is usually associated with DKA which triggers hyperventilatory response to metabolic acidosis. There were varying degree of mental alteration in the subjects with HE, but the highest proportion of moderate-severe impairment was seen in the those with HHS. Reports from other studies have demonstrated similar alteration in mental status as characteristic of HHS, and this is believed to be the result of hyperosmolality.[2,20] Nonetheless, alteration in mental status in HHS usually resolves once osmolality returns to normal.

High anion metabolic acidosis was the commonest biochemical abnormality and this was profoundly more in DKA (98.8% vs. 81.8% vs. 82.3%, p = 0.001). This underscores the effect of insulin deficiency and the increase counterregulatory hormones in DKA with resultant lipolysis and unrestrained hepatic fatty acid oxidation to ketone bodies.[2]

Other clinical and biochemical presentations seen in this study were as described in previous studies.[2,4,17,19]

Infection, non-compliance to medication and dietary regimen; newly diagnosed DM, trauma, and CVA were the precipitating factors of HE in this study and this is similar to what has been previously documented.[19,48] The observation that diabetic hand and foot sepsis; UTI, other sepsis, pneumonia, malaria and cellulitis rank high among the people living with DM is of clinical importance, and efforts should be made by the managing physicians to routinely look out for these conditions as soon as individuals with HE present to the hospital.

In this study, duration of diabetes between 5-9 years, severe coma, hypotension and hypokalemia

were identified as the significant predictors of mortality among people living with DM and presenting with HE.

The authors recognize that the study has limitations. The classification of DM into type 1 or type 2 was purely based on epidemiology and clinical response to insulin or oral antidiabetic medications, as assessment of C-peptides or auto-antibodies were not routinely done in the study center, and so largely missing in almost all patients records. Nevertheless, the study proves that hyperglycemic emergencies are still common causes of hospital admission and mortality among people living with DM and it manifests with myriads of clinical and biochemical presentations. The study also identified some features that should alert managing physicians to suspect the possibility of HE. These features are osmotic symptom, tachypnoea and high anion metabolic acidosis. The study also identified the commonest precipitating factors. Further studies should include lower level health facilities where most patients access care and where expertise could be limited. This could give a better estimate of overall mortality from HE among persons living with DM.

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