Clinical profile and outcomes of adult patients with hyperglycemic emergencies managed at a tertiary care hospital in Nigeria

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INTRODUCTION

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are acute complications of diabetes mellitus (DM) that are potentially life threatening if left untreated.\(^1\) DKA is common in type 1 diabetes mellitus (T1DM) while HHS is common in type 2 diabetes mellitus (T2DM). However, there are also reports of ketosis-prone type T2DM where patients are able to discontinue insulin therapy and remain insulin-independent.\(^2,3\) An epidemiologic study of hyperglycemic states has shown that occurrence of DKA varied among different ethnic groups in Texas, USA.\(^4\) Eighty percent of whites admitted with DKA were classified as having T1DM while only 53% of African Americans and 34% of Hispanic patients who were admitted with DKA had T1DM. Hyperglycemic emergencies (HE) are one of the main reasons for diabetic admissions in Nigeria.\(^5\) The prevalence of HE in Nigeria is unknown. Hyperglycemic emergencies accounted for 40% of DM admissions in an urban hospital in Lagos, South-western Nigeria.\(^6\) HE mortality in that report was 46%.\(^6\) HE often requires in-patient management with the resultant high hospital bills. There is scarcely any data on HE from other parts of Nigeria. It is important that the clinical profile, precipitating factors, and outcomes of DKA and HHS are documented in order to provide measures to prevent HE and its associated morbidity and mortality. This study was designed to document the precipitating factors, clinical profile, and treatment outcomes of DKA and HHS managed in a tertiary care hospital.

ABSTRACT

Background: To document the clinical profile and treatment outcomes of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) managed in a tertiary care hospital. Materials and Methods: This was a retrospective review of hospital records of patients with DKA and HHS admitted to a tertiary care hospital over a 24-month period. Data on demographics, precipitating factors, clinical features, serum electrolytes, duration of hospital admission, and mortality were extracted. Results: Eighty-four patients were included in the study. Fifty (59.5%) were females. Ten (11.9%) persons had type 1 diabetes mellitus (T1DM) and 74 (88.1%) had type 2 diabetes mellitus (T2DM). There were 35 cases of DKA and 49 cases of HHS. Nine patients with T1DM presented in DKA and one in HHS. Forty-eight (55.2%) subjects were previously not diagnosed of diabetes mellitus (DM). The mean±SEM age, casual blood glucose, calculated serum osmolality, and duration of hospital stay of the study subjects were 50.59±1.63 years, 517.98±11.69 mg/dL, 313.59±1.62 mOsmol/L, and 18.85±1.78 days, respectively. Patients with T2DM were significantly older than those with T1DM (54.32±1.34 vs. 23.40±1.38 years, \(P<0.001\)). The precipitating factors were poor drug compliance 23 (27.4%), malaria 12 (14.3), urinary tract infection 10 (11.9%), lobar pneumonia 4 (4.8%), and unidentifiable in 29 (34.5%). Common electrolyte derangements were hyponatremia, 31 (36.9%) and hypokalemia 21 (25%). Mortality rate was 3.6%. Conclusion: DKA is common in patients with T2DM. Over 50% of the patients presenting with DKA or HHS have no previous diagnosis of DM. Non-compliance, malaria, and infections are important precipitants. Mortality rate is low. Key words: Diabetic ketoacidosis, hyperosmolar hyperglycemic state, precipitating factors
MATERIALS AND METHODS

This was a retrospective review of hospital records of all adult patients admitted and treated for DKA and HHS over a 24-month period. Data extracted included age and gender of patient, clinical features, type of DM, duration of DM, systolic blood pressure, diastolic blood pressure, preceding events, results of laboratory investigations (casual blood glucose, serum electrolytes, urea, and creatinine at presentation), and duration of hospital stay. Patients with grossly incomplete data such as demographics, results of laboratory investigations, and treatment outcome were excluded.

The management protocol used for patients with DKA and HHS was as follows: Rehydration with intravenous infusion of 0.9% normal saline (or 0.45%) if there was hypotension. One liter of 0.9% normal saline was given fast, 1 L of 0.9% normal saline was given over the next 30 min, 1 L of 0.9% normal saline was given over the next 1 h, 1 L of 0.9% normal saline was given over the next 2 h, and 500 mL of infusion was given every 4 h. The infusion was changed to 5% dextrose in saline when casual blood glucose was <250 mg/dL. Hyperglycemia was controlled by giving bolus intravenous soluble insulin 10 units stat and intramuscular soluble insulin 10 units stat, then 6-8 units of soluble insulin every hour until casual blood glucose <250 mg/dL. Soluble insulin was then added to 5% dextrose infusion. When the patient was much improved clinically and was able to eat adequately, pre-meal subcutaneous soluble insulin was then introduced while the dextrose-insulin infusion was maintained for a further 2 h before the dextrose-insulin infusion was discontinued. Hypokalemia was corrected with potassium chloride given in intravenous fluid infusion slowly after ensuring that the patient was passing urine. Precipitating factors were sought and treated.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 16. The mean ± SEM values were calculated for all the variables. Comparison of means was done using t-test for continuous data and Chi-square test for categorical data. Logistic regression analysis was performed to examine the association of some risk factors for outcomes (precipitants of HE, metabolic abnormalities, and hypertension). Level of statistical significance was set at P<0.05.

Definition of terms

DKA was defined as the presence of hyperglycemia (glucose >250 mg/dL), serum ketonemia and/or ketonuria, and acidaemia (serum bicarbonate <18 mmol/L).1

HHS was defined by the presence of severe hyperglycemia (glucose >600 mg/dL) and hyperosmolality >320 mOsmol/L with little or no ketonemia/ketonuria.1,7

Anion gap is (sodium + potassium) – (bicarbonate + chloride).

RESULTS

Eighty-four patients seen during the study period comprised 34 (40.5%) males and 50 (59.5%) females. There were 10 (11.9%) patients with T1 DM and 74 (88.1%) with T2DM. Twenty-three (27.38%) were hypertensive. There were 35 (41.7%) cases of DKA and 49 (58.3%) cases of HHS. Forty-eight (55.2%) of all the study subjects who presented in DKA or HHS were not known to be diabetic prior to presentation. Nine of all the T1DM patients presented in DKA while one presented in HHS. The characteristics of the study subjects are summarized in Table 1. The median age of all the study subjects was 52 years with a range of 17-80.

The precipitating factors of hyperglycemic emergencies by type of HE are represented in Figure 1. The major precipitants were infections and non-compliance with glucose-lowering drugs. “Others” in Figure 1 comprised one (1.2%) case each of emotional stress and physical assault with trauma.

The frequency of the presenting symptoms and that of electrolyte derangement in patients with DKA and HHS are documented in Tables 2 and 3 respectively. The frequency of electrolyte derangement was as follows:

| Parameter            | Median   | Range   |
|----------------------|----------|---------|
| Age (years)          | 52       | 17-80   |
| DMDU (years)         | 0.1      | 0-20    |
| SBP (mmHg)           | 130      | 80-220  |
| DBP (mmHg)           | 80       | 40-150  |
| CBG (mg/dL)          | 578      | 283-620 |
| Urea (mg/dL)         | 45       | 11-163  |
| Sodium (mmol/L)      | 135      | 120-148 |
| Potassium (mmol/L)   | 3.8      | 3-6     |
| Bicarbonate(mmol/L)  | 20       | 5-31    |
| Chloride (mmol/L)    | 100      | 84-122  |
| Creatinine (mmol/L)  | 1.2      | 0.3-4.8 |
| Osmolal (mOsmol/kg)  | 311.03   | 280.29-346.17 |
| DuAdm (days)         | 15.5     | 3-84    |

DMDU = Duration of diabetes mellitus; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; CBG = Casual blood glucose; DuAdm = Duration of admission
hyponatremia, 31 (36.90%); low bicarbonate, 27 (32.14%); hypokalemia, 21 (25%); hyperkalemia, 3 (3.57%); and hypernatremia, 1 (1.20%). The characteristics of Nigerians with hyperglycemic crisis by type of DM are documented in Table 4. Patients with T2DM were significantly older than those with T1DM (54.32±1.34 vs. 23.40±1.38 years, P<0.001). Patients with T1DM had higher serum potassium and lower bicarbonate levels than patients with T2DM (4.5±0.5 vs. 3.82±0.08, P<0.020 and 12.78±1.86 vs. 19.68±0.74, P<0.002). Among the T2DM patients, those who had ketonuria were younger than those without ketonuria (53.71±7.47 vs. 59.50±10.60 years, P<0.014).

The characteristics of study subjects with hyperglycemic crisis by type of HE are shown in Table 5. Patients with HHS were significantly older than those with DKA (56.98±1.78 vs. 41.97±2.37 years, P<0.001). They also had significantly higher mean systolic and diastolic blood pressures. Patients with DKA had higher anion gap and lower bicarbonate levels than patients with HHS (22.02±1.54 vs. 18.33±1.05, P<0.046 and 15.77±1.24 vs. 20.83±0.70, P<0.001).

Table 4: Characteristics of Nigerians with Hyperglycemic crisis by type of DM

| Parameter          | Type 1 DM | Type 2 DM | P value |
|--------------------|-----------|-----------|---------|
| Age (years)        | 23.40±1.34| 54.32±1.34| 0.001   |
| DMDU (years)       | 2.33±1.21 | 3.62±0.60 | 0.541   |
| SBP (mmHg)         | 113.33±6.01| 136.30±14.72| 0.37    |
| DBP (mmHg)         | 72.22±5.21 | 84.47±12.30| 0.076   |
| CBG (mg/dL)        | 476.22±50.13| 522.06±11.73| 0.224   |
| Urea (mg/dL)       | 521±14.0  | 46.97±13.4 | 0.634   |
| Sodium (mmol/L)    | 132.71±7.5 | 137.40±6.0 | 0.344   |
| Potassium (mmol/L) | 4.50±0.5  | 3.82±0.08 | 0.020   |
| Bicarbonate (mmol/L)| 12.78±1.86| 19.68±0.74 | 0.002   |
| Chloride (mmol/L)  | 100.5±2.77| 99.12±0.91 | 0.629   |
| Creatinine (mmol/L)| 1.10±0.3 | 1.48±0.19 | 0.510   |
| AGAP               | 22.69±2.01| 19.55±0.97 | 0.374   |
| Osmol (mOsmol/kg)  | 309.09±5.52| 314.07±12.72| 0.349   |
| DuAdm (days)       | 16.33±1.71| 19.47±2.02 | 0.591   |

Table 5: Characteristics of Nigerians with hyperglycemic crisis by type of HE mean ± Sem

| Parameter        | DKA          | HHS          | P value |
|------------------|--------------|--------------|---------|
| Age (years)      | 41.97±2.37   | 56.98±1.78   | 0.001   |
| DMDU (years)     | 2.67±0.82    | 3.51±0.79    | 0.463   |
| SBP (mmHg)       | 120±33.48    | 142±35.14    | 0.001   |
| DBP (mmHg)       | 76.47±2.60   | 84.27±12.95  | 0.018   |
| CBG (mg/dL)      | 499.56±20.20| 541.94±12.72| 0.07   |
| Urea (mg/dL)     | 48.71±15.14 | 47.88±4.59   | 0.91    |
| Sodium (mmol/L)  | 134.22±10.88| 134.48±8.10 | 0.831   |
| Potassium (mmol/L)| 4.02±0.17    | 3.82±0.12    | 0.321   |
| Bicarbonate (mmol/L)| 15.77±1.24 | 20.83±10.70 | 0.001   |
| Chloride (mmol/L)| 99.51±2.62   | 99.43±0.95   | 0.960   |
| Creatinine (mmol/L)| 1.19±0.13 | 1.72±0.33   | 0.333   |
| AGAP             | 22.02±1.54   | 18.33±1.05   | 0.046   |
| Osmol (mOsmol/kg)| 312.61±2.37  | 315.04±2.37  | 0.477   |
| DuAdm (days)     | 18.54±3.08   | 19.47±2.02   | 0.076   |

Figure 1: Frequency of precipitating factors of diabetic ketoacidosis and hyperosmolar hyperglycemic state in Nigerians

![Figure 1](url)
There was no significant difference in terms of age, duration of DM, blood pressure, casual blood glucose, serum electrolytes, duration of admission, anion gap, and plasma osmolality by gender.

Treatment outcomes are stratified by type of HE in Table 3. Seventy-eight (92.86%) were discharged home after achieving good glycemic control, 3 (3.57%) died, and 3 (3.57%) discharged against medical advice. The causes of mortality in both patients with T1DM who had DKA were presumed septicemia while the patient with HHS was presumed to have died of uremic syndrome. There was no association between the type of HE and the length of hospital stay \( (P = 0.123) \). The precipitants, metabolic abnormalities, and hypertension status did not significantly affect the treatment outcomes.

**DISCUSSION**

Hyperglycemic crisis (DKA or HHS) was the index diagnosis in 55.2% of Nigerians who were not previously known to have DM. This finding suggests that many adult Nigerians remain undiagnosed of DM and only present for medical attention after development of complications of DM with significant morbidity and mortality. There is need for more public awareness campaigns on DM and screening for DM, especially for those who are above the age of 30 years and those with known risk factors for DM. The percentage of newly diagnosed diabetes mellitus in this index study is higher than that reported by Ogbera et al. in Lagos who documented that 14% of those presenting in HE had previously undiagnosed DM. It is not known with certainty the reason for this large difference. It may be that DM awareness and detection is greater in the more cosmopolitan city of Lagos. The finding of many cases of DKA (ketosis-prone T2DM) among patients with T2DM has also been reported by other researchers. Many of these patients are able to remain insulin independent and maintain good glycemic control on oral glucose-lowering drugs after the resolution of the DKA.

Previously undiagnosed diabetes, poor drug compliance, urinary tract infections, respiratory infections, and unidentifiable causes were the main precipitating factors of HE as previously documented in other studies. However, malaria was a common precipitant that was not previously emphasized. Yusuff et al. reported that 59% of Nigerians with T2DM were non-adherent with prescribed anti-diabetic drugs due to lack of finance to purchase the drugs. Two of the patients that died during the period of this study had T1DM. They had serious financial constraints and were unable to procure insulin and other medications required for their treatments.

The classical symptoms of DM, weakness, and fever were the common presenting symptoms. Coma was the presentation in about 10% of the patients. Casual blood glucose should thus be included in the initial evaluation of unconscious adult patients even when there is no prior history of DM in order not to miss a potentially treatable condition such as DKA or HHS. The rarity ofcoma as the mode of presentation of HE in contrast to the classical symptoms of DM has also been documented by Elmehdawi and Elmagerhei.

Casual blood glucose and calculated serum osmolality levels in DKA were similar to those in HHS. This is in contrast to the finding of higher values of these variables in HHS by Anumah and Ohwovoriole. A possible explanation for this difference may be due to the fact that some patients may have received some form of treatment in a peripheral health facility before presenting to the tertiary care hospital. Such prior therapy may alter the laboratory profile at presentation. Hyponatremia, hypokalemia, and metabolic acidosis were frequently documented in this index study as in previous reports. Isotonic sodium chloride is the fluid used as the initial fluid replacement in the management of the patients. This corrects the hyponatremia while hypokalemia is corrected with potassium chloride in normal saline infusion in patients who are passing urine. Metabolic acidosis is not routinely corrected.

Majority of the patients were successfully treated and achieved good glycemic control generally within 2-3 weeks of in-patient hospital management. The mortality rate was 3.57%. This is lower than mortality rates of 32-40% reported in previous studies in Nigeria. However, it is higher than the mortality rates of 0-2.4% documented in Peru and some Western countries. The success of the treatment of HE depends largely on the commitment of the house officers, resident doctors, and nurses in administrating the intravenous fluids and insulin therapy to the patients in a timely fashion with close monitoring of the patients. Resident doctors and house officers in the department are routinely updated on management of HE. This may have contributed to low mortality rate in the hospital.

In conclusion, the study showed that hyperglycemic emergencies commonly present as previously undiagnosed diabetes and that DKA is common in Nigerians with T2DM. Non-compliance, malaria, urinary tract infection, and respiratory infections are common precipitants. Mortality among the patients was low. There is need to put DM screening programs in place for persons above the age of 30 years and for those with risk factors for DM for early detection and treatment of DM.

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