Journal of Diabetes & Metabolic Disorders (2018) 17:143–148
https://doi.org/10.1007/s40200-018-0353-7

RESEARCH ARTICLE

Characteristics of hyperglycemic crises in an adult population in a teaching hospital in Colombia

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Received: 24 May 2018 / Accepted: 25 August 2018 / Published online: 19 September 2018

Abstract

Background Hyperglycemic crisis are the most serious forms of acute decompensation of diabetes mellitus and require urgent medical attention. The epidemiological data of these conditions in Latin America are scarce and in Colombia unknown, that is why we decided to describe the clinical characteristics and factors associated with the mortality of adults who presented with hyperglycemic crises in a teaching hospital in Colombia.

Materials and methods Retrospective cohort study of all episodes of hyperglycemic crisis treated in Pablo Tobón Uribe Hospital in a three-year period.

Results The records of 2233 hospitalization episodes related to diabetes mellitus were review, the prevalence of hyperglycemic crises was 2%, half of the events were diabetic ketoacidosis and 57% of the events occurred in people with type 2 diabetes mellitus, 32% of the events were precipitated by an infection and 27% by and inadequate therapy. The average hospital length of stay was 14 ± 3 days and the mortality rate 2.27%.

Conclusions In a teaching hospital in Latin America hyperglycemic crises are common, with diabetic ketoacidosis being the most frequent, and in a significant number of cases may be preventable. The hospital length of stay in our population is longer than reported in the literature.

Keywords Diabetic ketoacidosis · Hyperglycemic hyperosmolar Nonketotic coma · Latin America · Diabetes mellitus

Introduction

Diabetes mellitus (DM) is one of the most frequent metabolic disorders worldwide; with a prevalence of 8.8% in the general population which by 2015 translated into about 450 million people globally living with DM [1].

The epidemic behavior of type 2 DM is explained by multiple factors, race, changes in living habits and aging of the population are important in our region. In Latin America except for Argentina and Uruguay, most of the population is non-white of mixed European and Native American descent. In countries like Bolivia, Peru, Ecuador and Guatemala, more than 40% are Native American and there is an accelerated migration from rural to urban areas and this has been directly related to the rise in the prevalence of diabetes. The estimated prevalence of type 2 DM in rural areas is between 1 and 2% while in urban areas increase to 7 to 10% [2]. Colombia is an ethnic diverse country result of the crossbreeding of indigenous Amerindians, Spanish settlers and African slaves, the prevalence of T2DM in the urban area is around 7.5% and increases to more than 20% in those over 60 years that accounts for 3 to 4% of its population [3, 4]. Colombia is only second to Brazil in South America region for the highest number of people with diabetes and several factors have contributed to this; demographic and nutritional transition, internal migration related with urban development and violence and a high prevalence of sedentarism [5].

Acute complications associated with DM are Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS) although an overlap of both can occur in up to 30% of the cases [6]. These are the most severe states of an

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acute decompensation and require urgent medical attention [6, 7]. HHS is reported almost exclusively in people with type 2 DM [8], However, DKA is more often reported in younger individuals with type 1 DM [9–11]. DKA appears to be the most common form of crisis, followed in some reports by the mixed state and in others by HHS [8–10, 12–14]. The precipitating factors of both DKA and HHS are infections, followed by problems with the treatment such as abandonment or nonadherence [9, 10, 13, 15, 16]. DKA mortality does not exceed 1%, however, this may be higher in elderly with other comorbidities, where it can increase up to 5% being related to the precipitating factor rather than to DKA itself. In HHS, mortality is considerably higher between 5 and 20%, and this is probably because it tends to occur in older people with more comorbidities [6]. Some models have try to estimate the risk of death associated with DKA and HHS, however, they lack prospective validation and can be difficult to use since one requires a 24-h observation period [17, 18].

There is very little data in Latin America and Colombia on the epidemiology of DKA and HSS. Our objective with this study was to describe the clinical characteristics and factors associated with the mortality of adults who presented with hyperglycemic crises to a teaching hospital in Colombia and in an exploratory way describe in the patient cohort the performance of the mortality prediction models.

Material and methods

Study Retrospective observational cohort study over a 3-year period (2012 to 2014) using medical records.

Settings Pablo Tobón Uribe Hospital is a 454-bed stand-alone teaching hospital with an inpatient population of 18,000 patients, 80,000 emergency department visits and 95,000 outpatient visits per year. The hospital is part of the hospital network that provides highly specialized care to 5 million people from the city of Medellín-Colombia and its surrounding municipalities and it serves mainly low and middle-income population.

Inclusion criteria Medical records from patients older than 18 years to whom during the hospitalization one of the following international classification of diseases codes was assigned, ICD-10 code E10, E11, E13 or E14, with at least one measurement of blood or urine ketones and who met the criteria proposed for the diagnosis of a DKA and HHS [7]. In general, DKA was confirmed by the presence the following laboratory findings: arterial pH, less than 7.30; serum bicarbonate, less than 18 mEq/L; positive urine or blood ketones; and serum glucose, greater than 250 mg/dL. HHS was considered in patients with an arterial pH, greater than 7.30; serum bicarbonate, greater than 18 mEq/L; negative urine or blood ketones; and serum glucose, greater than 600 mg/dL.

Exclusion criteria Record with insufficient data.

Information The clinical records were reviewed by 4 of the authors and demographic and clinical variables and the treatment characteristics were recorded in a matrix in Excel2013®.

Statistical analysis Continuous variables are presented as medians with interquartile ranges or as means with standard deviations. Nominal variables are presented as absolute frequencies and proportions. To test the association between hospital length of stay with the clinical variables first a Shapiro Wilk or Fisher exact test (when the frequencies were low) were done to assess normality and then a bivariate analysis using the Chi square test for the dichotomous variables and the Wald test for the polytomous ones. For the entire statistical analysis, we used Epidat® version 4.1.

The protocol was approved by hospital ethics committee. Informed consent was not obtained because of the documentary nature of the study.

Results

After an exhaustive search we identified 2233 clinical records, Fig. 1 shows the selection of those that were considered for analysis. Multiple admissions for the same patient were included as individual events, Table 1 shows the general characteristics of the population.

A total of 44 events in 39 patients met the proposed criteria for DKA or HHS (Table 2), representing 1.97% (95%CI 1.43–2.63%) of the total hospitalizations related to DM, the average age of our population was 44 ± 17 years, most of them had a history of type 2 DM and the most frequent type of crisis was DKA. comorbidities were found: chronic renal disease (36.3%), immunosuppression (9%), congestive heart failure (4.5%) and cancer (2.3%). During hospitalization mortality was 2.56%, (95% CI 0.065–13.47%) and the main precipitating factor for either form of crisis was infection followed by and inadequate therapy, whether omitted or inadequately prescribed. Only 2 patients presented with DKA or HHS due to medication, both on therapy with steroids, and we didn't find any register data on the use of psychoactive drugs. The average hospital length of stay was 14 ± 3 days (Table 3).

Diabetic ketoacidosis half of the cases corresponded to diabetic ketoacidosis and 41% occurred in patients with type 2 DM. The mean age at the time of DKA was 38 ± 16 years with a mean osmolality of 298 ± 19 mOsm / L, pH 7.16 ± 0.23, serum glucose 445 ± 154 mg / dL, ketones 3.16 ± 0.19 mmol / L and an estimated water deficit of 0.63 ± 2.22 l, (Table 1). The main precipitating factor was infection, followed by inadequate therapy.

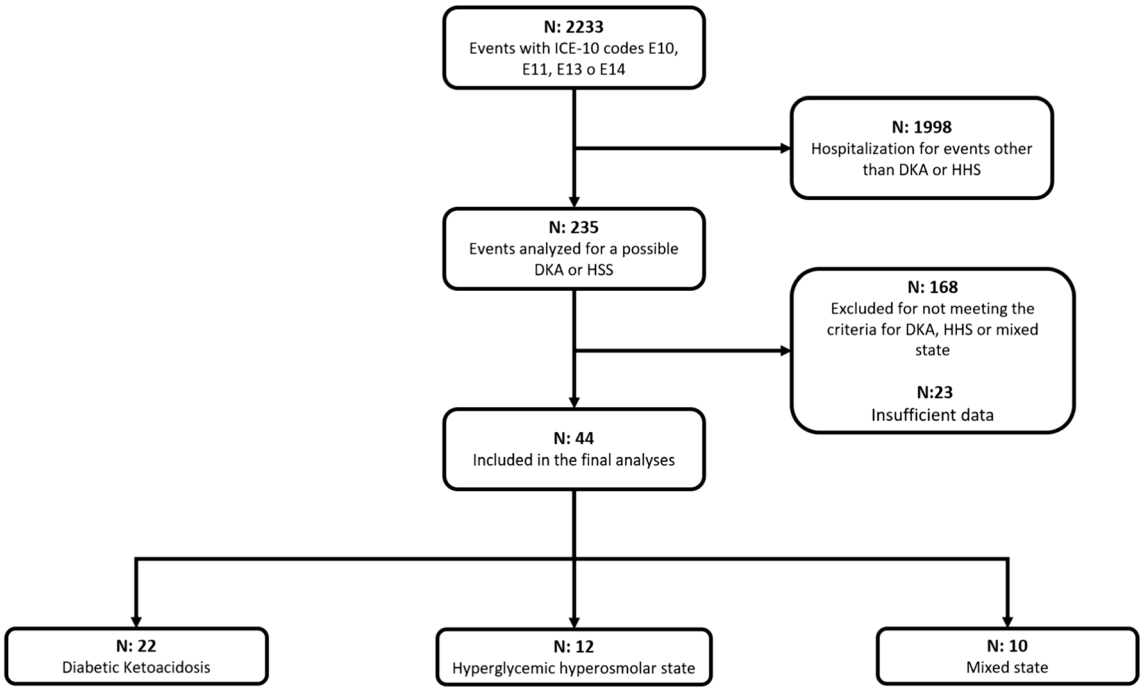

Fig. 1 Flow diagram of analyzed events

Hyperglycemic hyperosmolar state HHS was the second most common form of hyperglycaemic crisis**.** The mean age was 55 ± 14 years with an average osmolality of 338 ± 9 mOsm / L, pH 7.37 ± 0.14, serum glucose 883 ± 354 mg / dL and an estimated water deficit of - 2.74 ± 2.26 l. The main precipitating factor was also infection and treatment abandonment.

Mixed state A mixed state was the least frequent form of presentation. The mean age of the patients was 43 ± 18 years with an average osmolality of 301 ± 17 mOsm / L, pH 7.23 ± 0.24, serum glucose 948 ± 467 mg / dL and an estimated water deficit of - 2.07 ± 3.11 l. The main precipitating factor was an inadequate therapy and in 40% of the cases this was the first manifestation of the DM.

Hospital length of stay The hospital length of stay (HLS) in DKA was on average 18 ± 16 days, the longest of all groups, it exceeds that from HHS in 8 days 95% CI (−1.9 to 17.9) and the one of the mixed status in 8 days 95% CI (−2.8 to 18.8). A prolonged stay was defined as that which exceeded the weighted average for patients hospitalized for diabetes mellitus in the same period and classified at the most severe level according to the clinical risk group [19] that for the period of the analysis was 8 days. Overall, 59% of the patients had an extended stay, however, no association was found with any of the collected variables in the logistic regression.

Mortality The overall mortality was 2.27%, which was presented exclusively in DKA and explained in all cases by the precipitating factor. The low number of events did not allow any type of comparison or exploration of the mortality prediction models [17, 18].

Discussion

DKA and HSS are life-threatening events and knowing their possible precipitating factors is important for their initial treatment and prevention. This study aimed to characterize an adult population with hyperglycemic crisis in the city of Medellín. These events are a relatively frequent cause of hospitalization among patients with DM. Even though DKA was the most common form of hyperglycemic crisis, the proportion of patients with type 2 diabetes was high.

The precipitating factors of hyperglycemic crisis have been widely discussed, especially for DKA, but the frequency with which each one of these provoking factors present seems to be different around the world [6, 20–23]. This could be related to the fact that aspects such as education, adherence to treatment, medication supply among others depend to a greater or lesser extent on the health system which in turn depends on the economic conditions and policies of each community. In our cohort factors related to an inadequate therapy, like omitting medications, a potentially preventable factor, is the second cause of hyperglycemic crisis, this in part could be related to the financial and administrative barriers of the Colombian health care system, especially for the poorest that tend to putting of treatment or self-medicate [24]. Additionally, the value

Table 1 Population characteristics

	Population ($n = 44$)	DKA ($n = 22$)	HHS $n = 12$	Mixed state $n = 10$
Age, in years, mean ± SD	44 ± 17	38.8 ± 16	55.8 ± 14.1	43 ± 18.5
Men (%)	21 (48%)	11 (50%)	4 (33.3%)	6 (60%)
Type 2 diabetes (%)	25 (57%)	9 (41%)	11 (92%)	4 (44%)
Serum glucose mg/dL, mean ± SD	651 ± 378	445 ± 153	883 ± 354	948 ± 467
Sodium mmol/L, mean ± SD	133.5 ± 8.45	141 ± 7.55	128.9 ± 5.46	131 ± 10.3
Potassium mmol/L, mean ± SD	4.8 ± 1.01	4.73 ± 1.01	4.74 ± 0.98	5.3 ± 1.0
Chloride mmol/L, mean ± SD	102.33 ± 11.6	108.7 ± 9.33	94.5 ± 5.15	97.7 ± 14.1
Creatinine mg/dL, mean ± SD	2.2 ± 1.7	2.33 ± 1.94	1.97 ± 0.86	2.6 ± 2.0
HbA1c %, mean ± SD	12.2 ± 2.8	11.9 ± 3.51	11.9 ± 2.38	13 ± 1.76
Leucocytes $10^3/\mu L$, mean ± SD	14,259 ± 7978	17,014 ± 9350	11,491 ± 5883	11,520 ± 4553
Neutrophil $10^3/\mu L$, mean ± SD	11,965 ± 6855	14,761 ± 7292	8868 ± 5583	9531 ± 4888
Lymphocyte $10^3/\mu L$, mean ± SD	1779 ± 1057	1907 ± 1158	1845 ± 902	1419 ± 1012
Monocyte $10^3/\mu L$, mean ± SD	896 ± 858	1055 ± 841	983 ± 1117	439 ± 186
Eosinophil $10^3/\mu L$, mean ± SD	95.3 ± 152	115 ± 172	62 ± 95	90 ± 167
Band $10^3/\mu L$, mean ± SD	38,1 ± 253	72 ± 358	0	0
GCS, mean ± SD	13 ± 3	13 ± 3	13 ± 3	13 ± 3
Weight in Kg, mean ± SD	67 ± 15	65.6 ± 13.7	66.4 ± 16.7	71.3 ± 16.3
Height in meters, mean ± SD	1.65 ± 0.08	1.65 ± 0.08	1.63 ± 0.11	1.69 ± 0.05
BMI Kg/m^2, mean ± SD	24.5 ± 5.1	24.1 ± 5.3	25.6 ± 4.7	24.5 ± 5.5
Systolic pressure mmHg, mean ± SD	131 ± 35	131 ± 34	134 ± 36	129 ± 41
Diastolic pressure mmHg, mean ± SD	73 ± 19	73 ± 18	78 ± 12	69 ± 27
Heart rate, beats per minute, mean ± SD	99 ± 21	101 ± 22	94 ± 19	101 ± 22
Temperature in °C, mean ± SD	36.6 ± 0.9	36.8 ± 0.4	36.7 ± 0.8	36.2 ± 1.6
Respiratory frequency, breaths per minute, mean ± SD	19 ± 4	21 ± 5	16 ± 2	19 ± 3

DKA Diabetic ketoacidosis, *HHS* hyperglycemic hyperosmolar state, *DM* diabetes mellitus, *SD* Standard deviation, *HbA1c* Glycated hemoglobin, *GCS* Glasgow coma scale, *BMI* Body mass index

of HbA1c obtained at the time of the crisis suggests that even those who admitted being adherent to the therapy had poor ambulatory glycemic control and this could contribute, especially in addition to other factors such as infections, trauma or cardiovascular events to DKA or HSS. DKA as the first manifestation of DM is a frequent scenario reported in the literature [25], however it was infrequent in our cohort, probably because our hospital is not a primary care center but a referral institution or because in Latin-American countries the prevalence of T1DM is very low [5, 26] and it is in this population where this type of presentation would be expected. In T2DM DKA usually is associated with some other factors as we found in our cohort and as reported before by other authors in similar conditions [26].

During the evaluated period, a low number of hyperglycemic crisis was found compared to that reported in the literature [27], this could be explained by only considering patients with ketone measurement, which left some patients with possible hyperglycemic crises with insufficient data outside the analysis. Additionally, despite serving a population of around 5 million, most of our patients are referred from centers of low and medium complexity in which some crises can resolve, or the patients can be referred to other specialized centers of the hospital network.

Prolonged HLS was an interesting and unexpected finding of our study, it is much longer that the one reported in some clinical trials and surveys [23, 28, 29] and it was especially long in patients with DKA. Insulin noncompliance among patients with DKA is reported as a variable associated with a shorter length of hospital stay [30] however, none of the variables collected in our study influence the HLS, this could be explained by the low number of events, the presence of others comorbidities such as chronic renal disease and in the opinion of the authors in some cases it could also be related to some aspects of the health system that hinder the discharge due to delays in the delivery of supplies and medications necessary for the treatment of DM or other conditions, however, we have no way of proving this.

Mortality rate, one of the outcomes that we intended to explore, is similar to the data found in the literature for DKA

Table 2 Diagnostic criteria for diabetic ketoacidosis (DKA) hyperglycemic hyperosmolar state (HHS)

	DKA			HHS
	Mild	Moderate	Severe	
Plasma glucose	>250 mg/dL	>250 mg/dL	>250 mg/dL	> 600 mg/dL
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10	>18
Urine ketone	Positive	Positive	Positive	Small
Serum ketone	Positive	Positive	Positive	Small
Effective serum osmolality*	Variable	Variable	Variable	>320 mOsm/kg
Anion gap‡	>10	>12	>12	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

Adapted from ref. [8]

†Effective serum osmolality: 2[measured Na^+ (mEq/l)] + glucose (mg/dl)/18

‡Anion gap: $(Na^+) - [(Cl^- + HCO_3^-$ (mEq/l)]

[31], It is peculiar that no death was reported in the HHS group, this could be related to the fact that in our cohort patients with HHS were younger that in other studies or to the precipitating factors. It is unlikely that it relates to the treatment since a clearly established protocol is followed [7] and the process is frequently audited. In none of the patients who died the mortality scores predicted a high mortality risk.

In other report in Latin-America that only evaluated patients with T2DM presenting with DKA. The investigators reported some findings like ours. The main precipitating factors were infections (30%) and discontinuation of treatment (40%), the patients were relatively young (45 ± 12 years) and a high HbA1c suggested long-standing hyperglycemia. However, 42% of their patients had new onset diabetes and the authors proposed that this might show the inadequate availability of primary health care services and a delayed diagnosis of T2DM which suggest that some of the conditions of the health care system can influence the epidemiology of hyperglycemic crises.

This study has several limitations, the data was obtained retrospectively in a documentary form in a single institution that provides highly specialized care to which the patients are more likely to arrive in a more critical state, therefore our findings cannot be extrapolated to the general population and some patients may have been excluded due to lack of data for analysis.

Conclusions

In Latin America, the reports of hyperglycemic crisis characteristics are scarce, this work contributes to the knowledge of these conditions that are relatively frequent, additionally not only includes data on DKA, but also HHS and mixed state that are rarely described in the literature probably due to the low frequency of HHS and not all authors agree on the existence of mixed states.

Table 3 Hyperglycemic crisis precipitating factors

Factor	Population (%) ($n = 44$)	DKA (%) (n = 22)	HHS (%) $n = 12$	Mixed state (%) $n = 10$
Infection	14 (32%)	9 (41%)	5 (41.7%)	–
Inadequate therapy*	12 (27%)	5 (23%)	2 (25%)	5 (50%)
DM debut	6 (13%)	2 (9%)	0	4 (40%)
Pancreatitis	1 (2%)	1 (4.5%)	0	0
Medications	2 (4%)	1 (4.5%)	1 (12.5%)	0
Acute myocardial infarction	3 (7%)	0	2 (25%)	1 (10%)
Trauma	1 (2%)	0	1 (12.5%)	0
Others	5 (11%)	4 (18%)	1 (12.5%)	0

DKA Diabetic ketoacidosis, *HHS* hyperglycemic hyperosmolar state, *DM* Diabetes mellitus

*Whether omitted or inadequately prescribed

Compliance with ethical standards

Conflict of interest The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Source of financial resources Own resorces.

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