

11-Year Review of Hyperglycemic Hyperosmolar Syndrome in Diabetics in the Medical Emergency Department of the University Hospital of Bouaké

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Abstract

Background: In addition to its pandemic nature, diabetes mellitus presents potentially fatal complications such as hyperglycemic hyperosmolar syndrome. The lack of data on this complication in Côte d'Ivoire over the past 20 years motivated this study. **Methods:** This is a retrospective descriptive study conducted in the emergency department of the Bouaké University Hospital from 2010 to 2020. It included diabetic patients aged 15 years and over suffering from hyperosmolar hyperglycemic syndrome. **Results:** The prevalence of hyperglycemic hyperosmolar syndrome was 2.1%. The mean age was 58.8 ± 13.9 years (range 29 - 91 years), and the male-to-female ratio was 1.15. This syndrome was associated with diabetes in 69.6% of cases, of which 87.5% were type 2 diabetes. The main triggering factor was infection (57.1%). Hospitalizations were primarily due to altered mental status (51.8%), dehydration (71.4%), and fever (48.2%). Ketoacidosis was present in 32.1% of cases. The mean blood glucose level was 7.7 g/L (range 6.01 - 18.37), and the mean osmolality was 339.6 mOsm/L (range 320.72 - 389.35). Treatment consisted primarily of rehydration, insulin therapy, and management of precipitating factors. The mean observation period was 2.4 days (range 1 - 5 days). The mortality rate was 51.8%. **Conclusion:** In Africa, hyperglycemic hyperosmolar syndrome has a high mortality rate, and infections are by far the main triggering factor, highlighting the importance of early diabetes screening and patient education.

Keywords

Hyperosmolar Hyperglycemic Syndrome, Diabetes Mellitus, Emergency Medicine, Bouaké University Hospital, Ivory Coast

1. Introduction

Diabetes mellitus, a veritable and constantly evolving pandemic, stands out due to its mortality and complications, both globally and in sub-Saharan Africa [1]-[3]. Beyond its pandemic nature, its progression is marked by numerous formidable complications of an infectious, degenerative, and metabolic nature, including hyperglycemic hyperosmolar syndrome (HHS). The latter is a hyperglycemic emergency, which is serious, common in elderly people with type 2 diabetes, and associated with significant mortality, ranging from 15 to 20% according to several Western studies [4]. In Sub-Saharan Africa, particularly in Ivory Coast, Apart from Lokrou, which had a prevalence of this complication of 5.9% in diabetic patients, few studies have been conducted [5]. It is this scarcity of data that motivated this study in Ivory Coast, the objective of which was to describe the epidemiological, clinical, paraclinical, therapeutic and evolutionary aspects of hyperglycemic syndrome hyperosmolar, in diabetics patients admitted in medical emergencies.

2. Patients and Methods

1) Patients

Our study involved a population of 2761 patients Diabetics, admitted to the emergency department of the University Hospital Center of Bouaké, 56 of whom were diagnosed with hyperosmolar hyperglycemic syndrome. The patients included were: diabetics of any type, sex, with an age ≥ 15 years, a blood glucose level ≥ 6 g/l and a plasma osmolarity > 320 mOsm/l. Patients whose medical records were unusable for the parameters studied were excluded.

2) Methods

This was a retrospective, descriptive, cross-sectional study of the medical records of diabetic patients during the period from January 1, 2010, to December 31, 2020 (11 years). Data were recorded on a pre-established questionnaire for each patient. The parameters studied were:

- **Socio-demographic parameters:** age, sex, occupation, marital status, rural origin or urban.
- **Clinical and paraclinical parameters:** reason for admission, history and comorbidities (duration of diabetes, type of diabetes, other revealed), triggering factors of HHS, clinical signs; blood glucose on admission, serum potassium, serum sodium, plasma osmolarity, functional renal failure (*diagnostic criteria: ratio* $(1000 \times \text{plasma urea [in mmol/l]} / \text{serum creatinine } [\mu\text{mol/l}]) > 100$ and *slightly elevated serum creatinine: < 34 mg/l or 300 $\mu\text{mol/l}$*) [6].
- **Therapeutic and evolutionary parameters:** treatments implemented, dura-

tion of observation, outcome of patients.

The diagnosis of HHS-associated ketoacidosis was based on the presence of 2, 3, or 4 crosses of ketonuria on the urine dipstick. The data were entered and analyzed using Excel 2019 and Epi-info 7.2.2.6 software. Quantitative variables are presented as means with standard deviation and extreme values, and qualitative variables as proportions.

Strengths and limits of the study

The limitations of our study are twofold. First, certain tests used to diagnose HHS, such as ionograms, which enable more accurate calculation of osmolarity, were unavailable, leading to the hypothesis of underdiagnosis. Second, the diagnosis of ketoacidosis associated with HHS is semi-quantitative due to the absence of blood gas analysis and biochemical measurement of ketonemia. However, the size of the population and the long period concerned component constituting the main strengths of this study, allow us to interpret our results.

3. Results

1) Socio-demographic parameters

Of the 2761 diabetic patients observed during the study period, 56 presented hyperglycemic hyperosmolar syndrome that is a prevalence of 2.1%.

The mean age of patients with HHS was 58.8 ± 13.9 years (range 29 - 91). The age groups were as follows: 16.1% were between 29 and 44 years, 37.5% between 45 and 60 years, 35.7% between 61 and 76 years, and 8.9% between 77 and 92 years. The sex ratio was 1.15 (males: 53.6%, females: 46.4%). Housewives represented 35.7% of cases, followed by shopkeepers at 23.2%. 64.3% of patients came from urban areas, and 64% were married.

2) Clinical and paraclinical parameters

Altered mental status, polyuria-polydipsia syndrome, and fever accounted for 51.8%, 35.7%, and 28.6% of patient admissions, respectively. The mean duration of diabetes was 6.4 years (range: 3 months-38 years), and HHS was the initial clinical presentation that led to a new diagnosis of diabetes in 69.6% patients. Type 2 diabetes was present in 87.5% of cases. Comorbidities included hypertension (26.8%), alcoholism (23.2%), and smoking (14.3%). The mean osmolarity was 339.6 ± 14.26 mOsm/L, with a range of 320.72 mOsm/L to 389.35 mOsm/L. The average blood glucose level was $7.7 \text{ g/L} \pm 2.12$ with extremes of 6.01 g/L and 18.37 g/L.

3) Therapeutic and evolutionary parameters

The average duration of observation was 2.4 ± 0.9 days, with a range of 1 to 5 days. The duration average of putting in observation before the death was 2.5 ± 1.1 days with extremes of 1 and 5 days.

4. Discussion

Socio-demographic parameters

The prevalence of HHS was 2.1% (56/2761). Our low results were also observed in Africa by Sow (2.4%) and Kerekou (0.5%), whereas the prevalence of HHS

found by Lokrou was significantly higher (5.9%) [5] [7] [8]. Like Kerekou, we believe that the prevalence of HHS, which varies between 0.5% and 5.9%, is underestimated, especially since there is no shortage of triggering factors in diabetic subjects. Furthermore, the diagnosis takes into account parameters such as blood ionograms, which are often unavailable for financial or technical reasons. In Europe, this complication is most often seen in type 2 diabetics over the age of 75 years [9]-[11]. In our study, the mean age was 58.8 ± 13.9 years, similar to other studies: Ivorian (55.4 ± 16.63) and Cameroonian (59.2 ± 13.5) [2] [5]. Although age is more advanced in HHS, due to the particularity of elderly people, who feel little thirst (hence the importance of regular hydration), the high age observed in Europe in this condition is also due to the aging of the population. However, in our African context, hyperosmolar state should never be ruled out in a diabetic patient admitted to the emergency department, regardless of age. The sex ratio in our study (1.15) shows a male predominance, but the varying data from one study to another prove that HHS is not exclusive to men [5] [12] [13]. The socio-professional categories were mainly represented by low-income patients from the informal economic sector, an aspect known to constitute a significant risk of diabetes imbalance [5] [14].

Clinical and paraclinical parameters

The main reason for admission was impaired consciousness (51.8%), as found by Drabo in Burkina Faso (40%), followed by polyuria-polydipsia syndrome (35.7%) which falls within the framework of common dehydration in HHS [15]. Patients with HHS predominantly had type 2 diabetes (87.5%), similar to the 2004 Ivorian study (89%) [5]. However, HHS is not exclusive to type 2 diabetes, because any intercurrent condition predisposing to dehydration or decreased insulin action in a diabetic can cause HHS, even in young people, as is the case in our study [9] [16] [17]. SHH was revealed in 69.6% of cases by diabetes in our study, hence the lack of awareness of Status of the patients, the lack of screening of the population, especially that of the parents of type 2 diabetic patients. Regarding clinical signs upon admission (**Table 1**), dehydration was by far the most prevalent (71.4%). This condition is frequently observed in several studies [13] [18]. It can be explained by fluid loss. Firstly, there are digestive losses, particularly diarrhea and vomiting, present in nearly 20% of patients in our study, associated with abdominal pain well described in the literature, which can lead to misdiagnosis [19]. Secondly, there is intracellular dehydration caused by fever (48.2% in our study), found in 32% to 60% of cases reported in the literature [20] [21]. Thirdly, water is lost through respiration (26.8% dyspnea). This dehydration is partly responsible for the 58.9 % of consciousness disorder of our study with an average of Glasgow Coma Scale value was 12.5 ± 2.7 , as found by Klouche (11 ± 3) [9]. Coma thus appears as a sign of consultation late, as shown by studies linking vigilance disorders and depth of hyperosmolarity [18] [22] [23]. In addition to neurological consequences, this fluid depletion was responsible for 69.6% of functional renal failure in our patients (**Table 2**). This condition observed was prerenal azotemia secondary to severe dehy-

dration, and is reversible if fluid resuscitation is rapid and adequate. Ketoacidosis associated with HHS was observed in 32.1% of patients (Table 2), unlike in Lokrou's study, where there was no association between these two metabolic complications (0%; n = 53) [5]. Ketonuria, a consequence of hyperketonemia, is generally absent or low in HHS on the one hand, due to the inhibition of lipolysis secondary to hyperglycemia itself, and on the other hand, by the persistence, at the start of the process, of peripheral insulin levels that are insufficient to allow glucose to enter cells, but sufficient to inhibit lipolysis. Our results thus highlight the depth of insulinopenia in diabetic patients, even those with type 2 diabetes. Among the triggering factors, infection was responsible for the HHS in 57.1 % of the cases. The most common causes were pneumonia (46.9%), malaria (15.6%), and superinfection of diabetic feet (12.5%). Our results are consistent with the literature, which identified infections as the most frequent factor in 28% to 60% of cases [5] [24]. Organic causes such as myocardial infarction, stroke (16.1% in our study) or any other acute medical condition (causing an increase in counter-regulatory hormones), combined with a drop in fluid intake due to an inability to move or a reduced sense of thirst, can lead to dehydration in older people (35.7% in our study), which will worsen and lead to hyperosmolar decompensation [10]. Blood sugar average of patients was 7.7 ± 2.12 g/L according to the literature data from the American Diabetes Association [25]. The mean serum sodium level in our study was 145.1 ± 5.3 mEq/L (136 - 158.5). It is known to be variable during HHS depending on fluid loss and the stage of this decompensation [26]. As for serum potassium, it can be normal, offspring or augmented, but in any case a hypokalemia severe can appear during treatment if potassium supplementation was not initiated early upon the start of insulin therapy [27]. This explains the hypokalemia (23.2%) and hyperkalemia (17.8%) found in our study (Table 2). Regarding osmolarity blood, it was on average 339.6 ± 14.26 mOsm/L with a value maximum of 389.35 mOsm/L. Our result is close to that found in the African works of Lokrou (322.5 ± 21.7 mOsm/L), but is below that of European authors in whose osmolarity average varied from 370 ± 8 mOsm/l to 384 ± 27 mOsm/L [11] [28].

Table 1. Distribution of the 56 patients according to clinical signs admission.

	n	%
Neurological signs		
Alertness disorders	29	51.8
<i>Glasgow score</i> [10 - 14]	21	72.4
<i>Glasgow score</i> [7 - 9]	6	20.7
<i>Glasgow score</i> [3 - 6]	2	6.9
Headaches	14	25
Motor deficits	11	19.6
Convulsions	6	10.7

Continued

Facial paralysis	3	5.3
Respiratory signs		
Dyspnea	15	26.8
Cough	14	25
Chest pain	5	8.9
Expectorates	3	5.3
Digestive symptoms		
Vomiting and nausea	8	14.3
Abdominal pain	4	7.1
Diarrhea	3	5.4
Other clinical signs		
Dehydration	40	71.4
Fevers	27	48.2
Tachycardia	26	46.4
Cardiovascular collapse	12	21.4
Fetid leukorrhea	3	5.3
Oligo-anuria	2	3.6

Table 2. Distribution of the 56 patients according to the type of hyperglycemic hyperosmolar syndrome, triggering factors and biological characteristics.

	n	%
Type of hyperglycemic syndrome hyperosmolar		
Isolated (without ketoacidosis)	38	67.9%
Associated with ketoacidosis	18	32.1%
Triggering factors		
Serious infections	32	57.1
<i>Pneumonia</i>	15	46.9
<i>Malaria access</i>	5	15.6
<i>Superinfected diabetic feet</i>	4	12.5
<i>bacterial gastroenteritis</i>	3	9.5
<i>Tonsil phlegmon</i>	1	3.1
Dehydration (digestive losses)	20	35.7
Stroke	9	16.1
Non-compliance with treatment	4	7.1
Long-term corticosteroid therapy	1	1.8
Osmolarity (mOsm/L)		
[320 - 330[17	30.4

Continued

[330 - 340[14	25
[340 - 350[11	19.6
≥350	14	25
Blood glucose (g/L)		
[6 - 8[40	71.4
[8 - 10[11	19.6
≥10	5	8.9
Ionic disturbances		
Hypernatremia	27	48.2
Hypokalemia [<3]	13	23.2
Hyperkalemia [>5]	10	17.8
Functional renal failure	39	69.6%

Therapeutic parameters and evolving

Management of HHS should take place in the emergency department, ideally in an intensive care unit [29]. In our study, almost all of our patients (98.2%) received parenteral rehydration and rapid-acting intravenous insulin therapy (Table 3). However, in 7.8% and 1.8% % of our patients, insulin therapy and rehydration have not summer carried out due to the deaths of his patients while awaiting medication. Potassium intake must be systematic (if diuresis is good) and guided by serum potassium levels to prevent frequent hypokalemia, as it is highly lethal according to Menon [20]. Potassium supplementation was administered in only 14.3% of cases in our study. This rarity of potassium supplementation, as reported in our study, could be explained by the fact that blood ionograms were not performed urgently due to technical reasons. Antithrombotic prophylaxis was also rare in our study (only 14.3% of patients received anticoagulants). Overall, patient care in our study had numerous weaknesses. These included the lack of use of auto-pulse syringes for insulin administration (due to a shortage of technical equipment), and emergency medical prescriptions being the responsibility of the parents and filled with considerable delays, highlighting the importance of implementing an emergency cart. Indeed, the lack of auto-injecting syringes for insulin administration complicates glycemic control due to the irregularity of injections, which can lead to either delays in injections that are ineffective in correcting hyperosmolarity due to hyperglycemia, or overdosing errors that can cause cerebral edema. Duration average of putting in observation was of 2.4 days (1 - 5) in our study (Table 3). This figure was lower than that reported in the study by Klouche (5.8 ± 0.8 days) and in the study by Lokrou (8.3 ± 7.0 days) [5] [9]. HHS has a poor prognosis, especially in Africa, with a mortality rate in our series of 51.8% (Table 3), including 48.2% of cases after a 2-day observation period; this is close to most studies in Africa. In African series, the mortality rate ranged from 2% to 34.8% of cases [5] [8] [30]. In contrast to this lethal metabolic emergency,

a similar study in Ivory Coast reviewed nine years of care for 737 patients admitted with ketoacidosis and reported only 5.1% mortality (N = 2400), making HHS the deadliest metabolic emergency in diabetes [31]. The high mortality rate of HHS observed in sub-Saharan Africa, and particularly in our study, could be explained by: the delay in seeking medical advice for patients with metabolic disorders, the low capacity of the service resuscitation, the lack of therapeutic education among our diabetics' patients, the lack of emergency trolleys and hospital technical facilities, the existence of comorbidities. This mortality could reach up to 28% in European series with shock as the main cause of death [9] [32]-[34].

Table 3. Distribution of the 56 patients according to therapeutic and evolutionary parameters.

	n	%
Institutionalized treatments		
Rehydration with saline solution	55	98.2
Insulin therapy	52	92.8
Antibiotic therapy	45	80.3
Painkillers	20	35.7
Potash ports	8	14.3
Anticoagulation	8	14.3
Antimalarials	7	12.5
Macromolecule infusions	5	8.9
Blood transfusion	5	8.9
Dressings	3	5.3
Diazepam	3	5.3
Antihypertensives	2	3.6
Implementation time observation		
1 day	7	12.5
2 days	27	48.2
3 days	14	25
4 days	6	10.7
5 days	2	3.6
Patient outcomes		
Death	29	51.8
<i>Time before death</i>		
1 day	4	13.8
2 days	13	44.8
3 days	7	24.1
4 days	3	10.4
5 days	2	6.9

Continued

Exeats	13	23.2
Discharged against medical advice	8	14.2
Transfer to internal medicine	5	8.9
Transfer to neurology	1	1.8

5. Conclusion

Hyperglycemic hyperosmolar syndrome is an uncommon reason for hospitalization in diabetic patients. Affected patients were around 60 years old, male, of low socioeconomic status, and had type 2 diabetes. This complication often marked the onset of diabetes. The main signs on admission were impaired consciousness, dehydration, and fever. Infections were by far the most common triggering factor. Treatment was based mainly on rehydration, intravenous insulin therapy, and treatment of the triggering factors. Mortality was high. This study highlights the importance of early screening for diabetes, efficient management of diabetic patients, and therapeutic education.

Authors Contributions and Acknowledgments

- *Title development:* Koné Salifou
- *Study design:* Koné Salifou
- *Literature review:* Koné Famoussa, Kouassi Lauret
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- *Analysis and synthesis of results:* Acho Jean Kévin
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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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