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PREVALENCE OF ACUTE KIDNEY DAMAGE SECONDARY TO DIABETIC KETOACIDOSIS IN A POPULATION BELONGING TO THE ISSSTE CLINICAL HOSPITAL CELAYA, MEXICO

Clinical Research

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ABSTRACT

Mexico is on the list of the 10 countries with the highest number of people living with Diabetes Mellitus. This disease causes blindness, chronic kidney problems, non-traumatic amputations, and is one of the 10 most frequent causes of hospitalization in adults. On the other hand, diabetic ketoacidosis is one of the acute complications of Diabetes Mellitus, and it is caused by insulin deficiency, characterized by a metabolic disorder, consisting of three concurrent abnormalities: hyperglycemia, hyperketonemia, and metabolic acidosis, which commonly leads to deterioration of kidney function and death. In this research, 24 patients (15 female, 9 male) were observed, and related to the prevalence of acute kidney injury secondary to diabetic ketoacidosis. The results show that female patients were the most prevalent, with 15 cases (62.5%), while males made up a total of 9 cases (37.5%). The median age for females is 67.5 years, with a minimum age of presentation of 50 years; for males the median age is 71.5 years, with a minimum age of presentation 45 years. It should be noted that in 100% of these, with adequate fluid therapy, they achieved remission of AKIN, without evolving into chronic kidney disease.

KEYWORDS

Chronic kidney disease, Diabetes mellitus, Acute kidney injury, Diabetic ketoacidosis, osmotic polyuria.

INTRODUCTION

The diabetes mellitus (DM) epidemic is recognized by the World Health Organization (WHO) as a growing global threat. It is estimated that there are currently more than 180 million people with diabetes in the world and this number is likely to more than double by 2030. Acute complications of diabetes represent almost 30% of hospitalizations in the emergency room and up to 10% of mortality in said service. Mexico is on the list of the 10 countries with the highest number of people living with diabetes and it is one of the 10 most frequent causes of hospitalization in adults [1].

DM occupies first place among the main causes of mortality and has an upward increase of approximately 400,000 new cases per year and 60 thousand deaths. Diabetic ketoacidosis is one of the most common complications of diabetes mellitus. It was described in 1886 by Derescheld, it is more common in patients with type 1 DM, but in recent years, it has been a very common reason for hospitalization in patients with type 2 DM. It is a state of metabolic severity, which has a profound impact. directly in the mortality of the patient who is diagnosed, as well as in their quality of life, most of the time, establishing sequelae, after management, in which AKI stands out in the first instance, progressing chronic kidney disease [2].

DKA is a syndrome caused by absolute or relative insulin deficiency, and the activation of counterregulatory hormones that favor the formation of ketone bodies, and acidosis; characterized by hyperglycemia, severe dehydration, electrolyte imbalance, and metabolic acidosis, it primarily affects insulin-dependent diabetics, but it is not exclusive. It is characterized by the biochemical triad of hyperglycemia > 250 mg/dL; metabolic acidosis, pH < 7.3, HCO_3 (bicarbonate) < 15; and ketonemia with ketonuria > 3 mmol/L or 150 (+++) on general urine examination. This causes hydrolysis in adipose tissue, increasing the supply to the liver of free fatty acids, which serve as a ketogenic substrate. Ketones include β-hydroxybutyrate, aceto-acetate, and acetone, with β-hydroxybutyrate being the predominant one in DKA [3, 4].

The symptomatic process of diabetic ketoacidosis occurs rapidly, it begins with polyuria, polydipsia, anorexia, vomiting, and abdominal pain. Rapid and deep breathing (Kussmaul) represents compensatory hyperventilation, and is accompanied by the classic fruity breath. Infections are the most important precipitating factors for its development, followed by lack of insulin administration, others: cerebral vascular events, mesenteric ischemia, acute pancreatitis, use of steroids, thiazides, calcium channel blockers, propranolol, and phenytoin. [5].

The objective of treatment is to correct the hydroelectrolyte deficit, stop the formation of ketone bodies, reduce glucose through the use of insulin (which prevents secretion or formation of counterregulatory hormones), and correct the severe dehydration suffered by the patient. The American Diabetes Association recommends using 0.9% saline solution in initial resuscitation, starting at 15-20 ml/kg in the first hour, then evaluating its continuity at an infusion rate of 250-500 ml. /hr, until serum glucose levels normalize; if serum Na levels above 145 mEq or serum Cl over 100 mEq are documented during resuscitation, the use of half molar solutions, 0.45% NaCl solution, is recommended. Rapid correction of the metabolic disorder should be avoided, thus avoiding cerebral edema, fluid overload, and acute kidney injury, which, if not treated adequately, can progress to chronic kidney injury, directly impacting quality of life of the patient, days of hospital stay, and mortality [6].

Traditionally, acute kidney injury (AKI) has been defined as the acute loss of kidney function that occurs over a period of hours to days, which causes accumulation of creatinine, urea, and other metabolic products (azotemia), and is associated with decreased urinary volume (oliguria), and water retention. The prevalence of AKI varies widely, because the studies that report it use a large number of different definitions, ranging from quantitative alterations in creatinine, and changes in urinary volume to requirements for replacement therapy [7].

Previously, the most used systems for staging and diagnosing AKIN were RIFLE and AKIN. However, in 2012, a system to diagnose and classify AKIN was published by the Kidney Disease Improving Global Outcomes (KDIGO) working group [9]. It is defined as any of the following: 1) creatinine increase >0.3 mg/dl within 48 hours; or 2) increase in serum creatinine >1.5 times the baseline value, known or assumed to have occurred within 7 days of the initial insult; or 3) urine volume <0.6 ml/kg/hr during the last 6 hours [8].

Diagnosis of ARF in hospitalized patients increased 4.9% in 1983, 20% in 2012, and 7.2% in 2022; this difference in increments is associated with the advent of classifications (RIFLE, AKIN AND KDIGO), which allowed a timely diagnosis in daily practice [9].

In 2007, adjustments were made that resulted in the AKIN definition, defining AKI in three risk phases: injury and failure, using stages I, II and III, respectively. The increase in serum creatinine of 0.3 mg/dl was added to the stage I, but without specifying creatinine clearance or biomarkers, and automatically III to patients who start renal replacement therapy (RRT) [10]. The AKIN classification is based solely on serum creatinine, and not on changes in glomerular filtration rate. AKIN does not require a baseline creatinine value and requires at least two creatinine measurements, obtained within a 48-h period; therefore, acute kidney injury is defined by a sudden decrease (within 48 hours) in kidney function, with an increase in creatinine of at least 26.5 mol/L (0.3 mg/dL) or a decrease in urinary output. (documented oliguria) <0.5 ml/kg/h for more than 6 hours) [11].

In Mexico, it is an important reason for consultation, estimating that 5-7% of hospitalized patients suffer from acute kidney injury, with the second most important cause being conditions that present with moderate to severe dehydration [12]. Recently, in a study published in 2019, 30% of patients with diabetic ketoacidosis will develop acute kidney injury [13].

It should be noted that when acute kidney injury is severe and renal function replacement therapy is required, mortality may exceed 50%. AKIN is irreversible in 5% of patients, but in elderly patients this percentage can rise to 16%. It is currently known that even a subtle decrease in kidney function (slight decrease enough to be classified as organ failure) is associated with an increase in morbidity and mortality, ranging between 20 and 40% [14].

In the ISSSTE Celaya, México hospital clinic, to date there are no studies that have evaluated the prevalence of acute kidney injury in patients with diabetic ketoacidosis; that establish the same in terms of type of diabetes, sex and age; Some research articles and theses were reviewed, where by knowing these data, the mortality rate, the days of hospital stay and the costs for the health sector were reduced by up to 10%; it also highlights that it is a preventable and reversible pathology.

From the above, the main purpose of this medical research is to improve preventive, diagnostic and therapeutic procedures, as well as to understand the etiology and pathogenesis of these diseases, directly impacting the mortality rate, sequelae and days of hospitalization of patients.

Methodology

An observational, cross-sectional, correlational, and retrospective study was carried out on 24 records of an adult population between 18 and 100 years of age, from the ISSSTE Celaya Clinic-Hospital in México, who entered the emergency service or another specialty with a diagnosis of diabetic ketoacidosis, which present with acute kidney injury.

The research protocol was submitted to evaluation by the honorable local ethics and research committee of the ISSSTE Clinic-Hospital, Celaya, Guanajuato, Mexico, obtaining a positive result for the initiation of research. Authorization was also obtained from the hospital's governing authorities to collect the user's clinical record, the following information: age, sex, type of diabetes mellitus, clinical and biochemical criteria for CAD, according to the guidelines of the American Diabetes Association, and criteria for acute kidney injury according to the Acute Kidney Injury Network (AKIN) and Kidney Disease Improving Global Outcomes. (KDIGO). Preparing during and at the end of the research a complete analysis of the data obtained, in order to directly impact the prognosis and functionality of the patients.

Ethical Principles

It was a risk-free investigation; since no clinical intervention was carried out; Only clinical and biochemical determinants were obtained that did not interfere with medical management.

According to the Declaration of Helsinki, the present study considered the recommendations for biomedical research in humans, which were adapted at the 64th general assembly, Fortaleza Brazil, in the Declaration of Helsinki in 2013. In accordance with the official research standard, was subject to its ethical regulations and the confidentiality of the data recorded in the protocol was respected [15].

The study represented low risk for patients, since the information was obtained from medical notes and laboratory results obtained during their hospitalization. This work adheres to the provisions of the general health law published on 06/01/2021, in its fifth title, sole chapter, article 100, therefore this research protocol was developed in accordance with the following:

- Adaptation to the scientific and ethical principles that justify medical research, especially with regard to its possible contribution to the solution of health problems and the development of new fields of medical science.
- The same was carried out, since it does not expose the experimental subject to unnecessary risks or damage [16].

The research protocol was reviewed by the local medical research and ethics committee for prior authorization and validation.

The confidentiality of the information obtained from the clinical record NOM-004-SSA3-2012 will be guaranteed [16].

RESULTS

Tables 1 and 2 show the results of the general patient information, as well as the measurements of the CAD, creatinine and GFR criteria.

Table 1. Information on the measurements of the CAD, creatinine, and GFR criteria of the MALE patients.

Identification	Age Years	Type Diabetes Mellitus	CAD Criteria (Diabetic Ketoacidosis)	Creat-inine	TFG ml
1.SORV760508/10	45	1	GAUZE: pH 7.25 HCO3: 11 mEq Glucose: 422 Ketones: +++	1.2	72.2
2.CAJN970301/50	47	2	GAUZE: pH 6.94. HCO3: 4 mEq Glucose: 477 Ketones: +++	1.26	67.5
3.EARL711228/10	50	2	GAUZE: pH 7.12 HCO3: 7 mEq Glucose: 566 Ketones: +++	1.31	63.6
4.EAML520410/10	70	2	GAUZE: pH 7.23 HCO3: 10 mEq Glucose: 450 Ketones: +++	1.29	59
5.SAMM740110/50	73	2	GAUZE: pH 7.15 HCO3: 12 mEq Glucose 361 Ketones: +++	2.10	32
6.GOCN690412/50	76	2	GAUZE: pH 7.22 HCO3: 9 mEq Glucose: 408 Ketones: +++	1.34	53
7.OIMN770504/50	76	2	GAUZE: pH 7.22 HCO3: 11 Glucose: 375 Ketones: +++	1.7	41
8.GOHH441202/90	77	2	GAUZE: pH 7.27 HCO3: 12 mEq Glucose: 353 Ketones: +++	1.4	48
9.GAHJ640730/50	86	2	GAUZE: pH 7.25 HCO3: 11 mEq Glucose: 482 Ketones: +++	1.5	45

Tabla 2. Information on the measurements of the CAD, creatinine, and GFR criteria of the FEMALE patients.

Identification	Age Years	Type Diabetes Mellitus	CAD Criteria (Diabetic Ketoacidosis)	Creat-inine	TFG Ml
1.FOSD720513/20	50	2	GAUZE: pH 7.17 HCO3: 8 mEq Glucose: 540 Ketones: +++	1.4	43
2.ZALA620219/30	55	2	GAUZE: pH 7.22 HCO3: 10 mEq Glucose: 405 Ketones: +++	1.7	33.5

3.PARR590607/30	56	2	GAUZE: pH 7.19 HCO3: 8 mEq Glucose: 559 Ketones: +++	1.5	40
4.RANJ600218/30	62	2	GAUZE: pH 7.18 HCO3: 11 mEq Glucose: 438 Ketones: +++	1.6	36
5.LAHS900510/60	59	2	GAUZE: pH 7.20 HCO3: 10 mEq Glucose: 572 Ketones: +++	1.4	45
6.TIPG510409/90	64	2	GAUZE: pH 7.17 HCO3: 10 mEq Glucose: 562 Ketones: +++	1.7	36
7.SAAJ471015/30	65	2	GAUZE: pH 7.24 HCO3: 12mEq Glucose: 658 Ketones: +++	1.5	38
8.AIPE520317/90	70	2	GAUZE: 7.21 HCO3: 8 mEq Glucose: 560 Ketones: +++	1.6	32
9.MEGM511008/90	70	2	GAUZE: pH 7.18 HCO3: 9 mEq Glucose: 345 Ketones: +++	1.7	32
10.COSC511005/70	71	2	GAUZE: pH 7.22 HCO3: 9 mEq Glucose: 515 Ketones: +++	1.4	37
11.DOMA821030/60	76	Tipo 2	GAUZE: pH 7.15 HCO3: 9 mEq Glucose: 501 Ketones: +++	1.7	30
12.LIHE400417/70	80	2	GAUZE: pH 7.22 HCO3: 11 mEq Glucose: 578 Ketones: +++	1.5	32
13.MEPA840226/60	81	2	GAUZE: pH 7.21 HCO3: 12 mEq Glucose: 471 Ketones: +++	1.8	28
14.MEMM661116/60	83	2	GAUZE: pH 7.22 HCO3: 9 mEq Glucose: 445 Ketones: +++	1.7	29
15.MOMR350617/90	87	2	GAUZE: pH 7.20 HCO3: 9 mEq Glucose: 712 Ketones: +++	1.8	24

As can be observed, of these 24 patients, it was found that the female sex was the most prevalent, with a total of 15 cases (62.5%), while the male sex made up a total of 9 cases (37.5%) of the total sample. The median age for females is 67.5 years, with a minimum age of presentation of 50 years, maximum of 87 years; whereas for males the median age is 71.5 years, with a minimum age of presentation of 45 years old, and maximum 86 years old.

For the female sex, the total sample corresponding to 15 patients (100%) has the established diagnosis of Diabetes Mellitus 2, while for the male sex, of the total of 9 patients that made up the study, 1 patient (11.11%) has with Diabetes Mellitus type 1, the remaining 8 patients representing (88.88%) have the diagnosis of Diabetes Mellitus 2.

Regarding acute kidney injury secondary to CAD, the 24 patients who entered the study (100%) had some degree of AKIN, according to AKIN and KDIGO criteria, for females 13/15 patients (86.6%) had an AKIN 1 or KDIGO 1, while 2/15 patients (13.3%) had an AKIN 2 or KDIGO 2, it is notable that 100% of these achieved remission of AKIN, with adequate fluid therapy, without progressing to chronic kidney disease.

For the male sex, AKIN occurred in 9 patients, which represents (100%) of the total sample, of these; 8 patients (88.8%) presented AKIN; KDIGO 1 or AKIN 1, while 1 patient (11.1%) presented a KDIGO 2 or AKIN 2, it is notable that of the total of 9 patients, no progression to chronic kidney disease was documented.

In relation to international statistics, this study found agreement with them, which reveals that CAD has a more significant prevalence in females than in males.

CONCLUSIONS

From this medical research carried out in the ISSSTE Celaya, México hospital clinic, to evaluate the prevalence of acute kidney injury in patients with diabetic ketoacidosis, the following conclusions are derived:

The 24 patients who entered the study (100%) had some degree of AKIN, according to AKIN and KDIGO criteria, for females 13/15 patients (86.6%) had an AKIN 1 or KDIGO 1, while 2/15 patients (13.3%) had an AKIN 2 or KDIGO 2.

100% of the patients who achieved AKIN remission, with adequate fluid therapy, did not progress towards chronic kidney disease.

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