Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1639–1641

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

DKA cases over the last three years: has anything changed?

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ARTICLE INFO

Article history:
Received 23 February 2019
Accepted 13 March 2019

Keywords:
Diabetic ketoacidosis
Type 1 and type 2 diabetes mellitus
Infections

ABSTRACT

Background: Diabetic ketoacidosis (DKA) has been related mainly to type 1 diabetes mellitus (T1DM). However, it is not solely related to T1DM. The purpose of this study was to assess the prevalence of DKA among type 1 and type 2 patients with diabetes mellitus, who were hospitalized in our Clinic due to DKA, as well as to determine the etiology beyond DKA.

Patients and methods: A cohort of 109 patients with DKA, 17–86 years of age, who were hospitalized in the Department of Endocrinology, Diabetes and Metabolism of our hospital between 2015 and 2017, were included in the study.

Results: Among the 109 patients, 50 (45.9%) had mild DKA, 48 (44.1%) had moderate DKA, whereas 11 patients (10%) had severe DKA. Sixty-five patients (60%) developed DKA as the first manifestation of T1DM, 30 patients (27%) developed DKA in the context of type 2 diabetes (T2DM), mainly due to the co-existence of serious infections, 11 patients (10%) had T1DM, but had omitted their insulin dosages, and 3 patients (3%) developed DKA due to unknown reasons.

Conclusions: Most patients with DKA presented with mild and moderate DKA and only a minority presented with the severe form of the disease. The etiology of DKA was mainly T1DM and less frequent uncontrolled T2DM, usually due to the co-existence of severe infections, while only in a tiny minority, the causes remained unidentifiable.

1. Introduction

In diabetic ketoacidosis (DKA), decreased insulin concentrations and increased release of hormones, such as catecholamines, cortisol, glucagon, and growth hormone result in hyperglycemia and ketosis. Hyperglycemia develops due to three main mechanisms: enhanced gluconeogenesis, increased glycogenolysis and impaired glucose utilization by peripheral tissues [1–6]. The combination of insulin deficiency and increased hormones results in increased lipolysis, ie release of free fatty acids into the circulation and to hepatic fatty acid oxidation to ketone bodies (β-hydroxybutyrate and acetoacetate), leading to ketonemia and metabolic acidosis [7].

As DKA remains the most common cause of death in children and adolescents with type 1 diabetes (T1DM) and is a life-threatening, but highly preventable complication of diabetes, clinicians should focus on prevention efforts [8,9]. In this study, we aimed to investigate the causes of DKA in order to better define preventable measures and further avoid any DKA cases.

2. Materials and methods

In this study, we collected data from 109 consecutive patients, who were admitted to the Department of Endocrinology, Diabetes and Metabolism of Evangelismos General Hospital in Athens, Greece, between 2015 and 2017, due to DKA.

DKA was defined by the presence of the triad of hyperglycemia, anion gap metabolic acidosis, and ketonemia. DKA patients were categorized in three groups according to the severity of their DKA at presentation. In particular, mild DKA was defined as blood glucose levels >250 mg/dL, pH: 7.25–7.3, HCO3: 15–18 mEq/L; moderate DKA as blood glucose levels >250 mg/dl, pH: 7.00–7.24, HCO3: 10–15 mEq/L, while severe DKA was defined as blood glucose levels >250 mg/dL, pH < 7.00 and HCO3< 10 mEq/L [1].

Initial treatment of all patients started in the Emergency Department, where vital signs were monitored and an electrocardiograph was obtained. We recorded demographic information,

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https://doi.org/10.1016/j.dsx.2019.03.022
1871-4021/

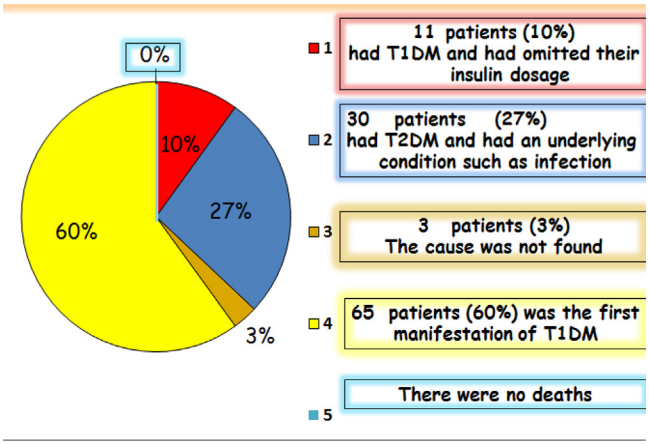

Fig. 1. In 60% of the patients who presented with DKA, this complication was the first manifestation of T1DM. 27% of the patients who presented with DKA had uncontrolled T2DM, usually due to an infection, while 10% of the patients had already known T1DM, but had omitted their insulin doses. In approximately 3% of the patient, the cause of the DKA, remained unidentifiable.

routine biochemical workup, treatment information, and clinical course from patient records, retrospectively. In general, treatment guidelines for DKA were followed in all cases, according to published guidelines [1].

3. Results

Characteristics of the participants are presented in Fig. 1. Among the 109 patients, 50 (45.9%) had mild DKA, 48 (44.1%) had moderate DKA, whereas 11 patients (10%) had severe DKA. Sixty-five patients (60%) developed DKA as the first manifestation of T1DM, 30 patients (27%) developed DKA in the context of T2DM, mainly due to the co-existence of serious infections, 11 patients (10%) had type 1 diabetes, but had omitted their insulin dosages, and 3 patients (3%) developed DKA due to unknown reasons.

4. Discussion

From 2009 to 2014, all age groups hospitalized for DKA in the United States experienced an increase of ≥6.0% annually in DKA hospitalization rates, with highest rates concerning persons aged <45 years. This increase in DKA hospitalization rates is alarming, because DKA is a life-threatening, but highly preventable complication of diabetes [10]. Despite the increase in DKA hospitalization rates, in-hospital mortality among persons with DKA decreased during the same period [10]. DKA is the most common cause of death in children and adolescents with T1DM, which is responsible for half of all deaths among patients aged <24 years [8,9]. In adults with DKA, the overall mortality is 1%; however, a mortality rate of 5% has been reported in the elderly and among patients with concomitant life-threatening illnesses [11,12]. Under these circumstances, death is rarely due to the metabolic complications of hyperglycemia or ketoacidosis, but is mainly attributable to the underlying precipitating diseases [13,14]. Identification of factors contributing to the increase in hospitalizations for DKA might help focusing on prevention measures.

Although DKA is more common among persons with T1DM, it may also occur among persons with type 2 diabetes (T2DM) [15]. DKA may be the first manifestation of unrecognized T1DM or T2DM; however, it occurs more frequently among persons with established disease [15]. Two studies in youths noted stable or decreasing rates of DKA at the time of diagnosis of diabetes, suggesting that younger persons with established disease and poor glucose control might be the group contributing most to the increase in DKA hospitalization rates [16,17]. The causes of the increase in DKA hospitalization rates are not clear, but various plausible explanations are the following: changes in case definition, new medications that might increase the risk for DKA, and higher admission rates because of lower thresholds for hospitalization (i.e., admission of persons with mild disease) [16,17]. Although the American Diabetes Association definition of DKA has not changed over the years, the 2009 publication described a "euglycemic DKA" type, characterized by metabolic acidosis and ketonemia, but with glucose levels ≤250 mg/dL, occurring in approximately 10% of patients with DKA [18]. Because SGLT2 inhibitors were only recently approved, and DKA rates increased before their introduction, they are not a main contributor to the increasing DKA cases, but do remain an ongoing concern for the future. In addition, higher admission rates for milder cases of DKA could also explain the increased trend in DKA admissions [19].

The occurrence of DKA in the context of T2DM is relatively unusual, but in the last decade several researchers have explored its characteristics. Between 13% and 21% of DKA admissions, during the last decade, involve patients with T2DM [20–22]. Discontinuation of antidiabetic medications and infection were the most common precipitating factors of DKA, and newly diagnosed T2DM was not as uncommon as one could have imagined [20,23,24]. Nevertheless, when facing a patient with DKA and probable T2DM, the presence of latent autoimmune diabetes of adults and type 1.5 diabetes should not be overlooked [25].

It is widely known that individuals with diabetes are at increased risk of infections and infection-related hospitalizations [26–29]. Indeed, infection has long been associated with hospitalizations; in fact, infections of the respiratory and urinary tract together have been reported to be responsible for more than half of these hospital admissions [26–29].

Regarding our patients, the vast majority remained patients who presented with DKA, as the first manifestation of T1DM. However, many patients also presented with DKA in the context of uncontrolled T2DM, usually due to a co-infection. This significant percentage (27%) together with patients who had DKA and T1DM (10%), but had omitted insulin administration could be highly preventable. Therefore, close monitoring of patients with diabetes, especially T1DM, as well as self-management and education, in particular under febrile circumstances, remain the cornerstone of prevention measures regarding DKA. Evidence-based and focused prevention measures, mainly diabetes self-management education and support together with intense monitoring from clinicians, especially among patients with T1DM, might help reducing this potentially life-threatening, but avoidable complication of diabetes.

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