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ORIGINAL ARTICLE

Clinical outcomes of septic patients with diabetic ketoacidosis between 2004 and 2013 in a tertiary hospital in Taiwan

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Background: Infection is the most common predisposing factor for diabetic ketoacidosis (DKA); however, studies are rare that have investigated the clinical outcomes of septic patients with infection-precipitated DKA.
Methods: A retrospective cohort study was conducted at a tertiary hospital from 2004 to 2013. Patients with DKA in whom the presence of a predisposing infection was confirmed were enrolled. Characteristics at initial presentation, primary infection sources, and causative microorganisms were compared between the nonacute kidney injury (non-AKI) group and acute kidney injury (AKI) group at each stage. Risk factors for the development of failure-stage AKI and its outcomes were also analyzed.
Results: One hundred and sixty DKA episodes were assessed. The most common infection sites were the urinary and respiratory tracts. The leading causative microorganism was *Escherichia coli*, followed by *Klebsiella pneumoniae*. A complicated/severe infection state [odds ratio (OR), 15.27; $p < 0.001$] and a high level of C-reactive protein (OR, 1.012; $p < 0.001$) were independently associated with bacteremia. Corrected sodium (Na; OR, 1.062; $p = 0.039$), initial

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plasma glucose (OR, 1.003; $p = 0.041$), severe grade of DKA (OR, 13.41; $p = 0.045$), and the Acute Physiology and Chronic Health Evaluation (APACHE) II score (OR, 1.08; $p = 0.033$) were identified as independent risk factors for the development of failure-stage AKI among septic patients with infection-precipitated DKA. Patients with failure-stage AKI had a higher frequency of incomplete recovery of renal function (20.4% of patients in failure vs. 5.9% of patients in risk and injury, $p = 0.009$). Bacteremia independently predicted the absence of complete recovery of renal function (OR, 5.86; $p = 0.038$).

Conclusion: For patients with infection-precipitated DKA, the clinician should aggressively monitor renal function if a patient presents with risk factors associated with failure-stage AKI. Furthermore, bacteremia predicts a poor renal prognosis.

Introduction

Infection is the most common predisposing factor for the development of hyperglycemic crises, diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state; it has an estimated range of 32—60%.[1] Among the predisposing factors for hyperglycemic crises, infection is the most common cause of death. However, previous studies are lacking that address in detail the infection source and microbiological characteristics of septic patients with infection-precipitated DKA. Potential complications of diabetic ketoacidosis (DKA) include electrolyte imbalance, dehydration, cerebral and peripheral venous thrombosis, rhabdomyolysis, and acute renal failure.[2] Diabetic ketoacidosis can result in severe fluid depletion that is accompanied by marked metabolic disturbance, although a low incidence of acute renal failure in patients with DKA was reported in a previous study.[3] However, acute kidney injury (AKI) is an independent risk factor for mortality in critically ill patients.[4—7] Furthermore, a more severe stage of AKI—as classified by Risk, Injury, Failure, Loss, End-stage Kidney Disease (RIFLE) criteria or by the Acute Kidney Injury Network (AKIN) criteria—is associated with increased hospital mortality.[4,6,8]

To further our understanding of the relationship between the infection site or the causative microorganism in septic patients with DKA and renal involvement, especially with regard to the severity stage of AKI in which renal replacement therapy may be necessary or a higher mortality is expected, we conducted a retrospective cohort study to investigate the risk factors and clinical outcomes of patients with infection-precipitated DKA that develops into failure-stage AKI.

Materials and methods

Study design and setting

This retrospective cohort study was conducted at a tertiary hospital in southern Taiwan—Kaohsiung Medical University Hospital (Kaohsiung, Taiwan)—in which medical records were reviewed of patients who developed DKA from January 2004 to December 2013. The protocol for this study was reviewed and approved by the Institutional Review Board of Kaohsiung Medical University Hospital (approval number KMUH-IRB-980057). Diabetic ketoacidosis was diagnosed in accordance with the diagnostic criteria of the American Diabetes Association: hyperglycemia (i.e., plasma glucose $>$ 250 mg/dL) and high anion gap metabolic acidosis (i.e., arterial pH $<$ 7.30, serum bicarbonate $<$ 18 mEq/L, and an anion gap $>$ 10) with positive serum or urine ketones.[1] In the event that a patient developed multiple DKA episodes during the study period, each episode was evaluated. Patients under the age of 18 years were excluded. Precipitating factors of DKA were extracted. Two infectious disease specialists confirmed the infection state and the primary infection source with the recovered causative microorganism, based on specific symptoms and signs, imaging study results, and microbiologic results from the appropriate specimen. In the event of a disagreement, a third specialist participated in the adjudication. To further identify a complicated or severe infection state, we defined complicated urinary tract infection in accordance with the guidelines of the Association of Medical Microbiology and Infectious Diseases Canada.[9] We also defined pneumonia with parapneumonic effusion or empyema, severe skin and soft tissue infection with systemic inflammatory response syndrome or deeper infection, and complicated intra-abdominal infection, based on the clinical practice guidelines of the Infectious Diseases Society of America.[10—13] Patients who were confirmed as having infection-precipitated DKA were enrolled and then evaluated for whether AKI developed in the first 48 hours after admission. Patients in the AKI group were further divided into three stages (i.e., "risk", "injury", and "failure") on the basis of the RIFLE classification. Demographic characteristics and physiologic and laboratory data at the initial presentation were compared between the non-AKI and AKI groups at each stage. For investigation of the risk factors associated with the development of severe AKI, for which renal replacement therapy may be necessary or which may have a higher than expected mortality, we compared AKI in the failure stage and other infection-precipitated DKA episodes (non-AKI group and AKI in the risk and injury stages). Also investigated were the clinical outcomes of patients in failure-stage AKI, which included the length of hospital stay, recovery of renal function at discharge, and hospital mortality.