Letter to Editor

Misleading Presentation of Euglycemic Diabetic Ketoacidosis: Implication for Low-Mid-Income Communities

Dear Editor,

In a recent Case Study article, Thawabi and Studyvin reported two cases of euglycemic diabetic ketoacidosis (euglycemic DKA) that were misleading at initial presentation.[1] The authors meticulously attended to the patients, including performing physical examinations and requesting robust pathology tests.

It is established that DKA is a complex metabolic disorder and that understanding the pathophysiology is essential for optimal management.[2,3] It is important to mention that DKA is a clinical condition that has recently generated debate over its dysfunctional metabolic basis,[4,5] and it is pertinent to highlight that ketonuria can be absent or masked by alkalosis in some cases.[6] Therefore, there could be false negative ketonuria with normoglycemia, and without other biochemistry criteria it is possible to miss a diagnosis of DKA.

It has been recommended that "careful search for the precipitating cause … and that patient education incorporating a variety of healthcare beliefs and socioeconomic issues are critical to an effective prevention program,"[3] and the significance and success of preventive mechanisms have been reported.[7,8] The pathophysiology of DKA is comprised of four causes, which are dehydration, fasting, insulin deficiency, and stress hormone excess; and it needs to be emphasized that "stress in any form can lead to metabolic decompensation."[9] What is being brought to the fore is the apparent difficulty to adopt guidelines and the need for careful search for the precipitating cause, especially in the low-mid-income communities (LMIC). In other words, it is pertinent to appreciate in the report of Thawabi and Studyvin the following:

1. Some of what was done may be difficult to do in LMIC.
2. What can be done, which is feasible in LMIC?

What was done, which may be difficult to do in LMIC: For instance, the clinical biochemistry profile for diagnosis of DKA shows blood glucose greater than 200 mg/dL, blood ketone level greater than 3 mmol/L with positive ketonuria, and venous bicarbonate <15 mEq/L or pH <7.3.[6,10] The authors assessed arterial pH, perhaps as part of blood investigations including partial pressure of carbon dioxide (pCO_2). It is easier to collect venous samples and it is known that arterial and venous pH compare well.[11,12] Thus, where collection of arterial blood is a challenge, venous pH can be measured.

Reports of this nature have implications for LMIC: It is arguable that clinical practice guidelines are neither rules nor procedures to comply with and, by default, clinicians in the LMIC may not have the resources to implement such guidelines. Hence, some communities lack access to modern health-care services such as blood gas analyzers. The implication is that if a patient presents with euglycemia, where the resources to perform blood gas analysis as well as ketonemia tests are unavailable, a clinician may be subjected to make diagnosis of DKA based on ketonuria alone or without a pathology evidence-base. Thus, the apparent difficulty to diagnose euglycemic DKA in LMIC using the current recommended clinical biochemistry profile for diagnosis of DKA lies in the lack of (1) real compliance with the recommendations, and/or (2) facilities to perform the tests.

What else could have been done, which may be feasible to do in LMIC? Given insulin deficiency as a hyperglycemic factor that underpins the diabetes, medication aims to regulate blood glucose levels. On one hand, compliance with medication plus fasting additively counters diabetes, but also leads to the hypoglycemia complication. On the other hand, stress signals from the hypothalamic-anterior pituitary-adrenocortical gland axis tend to potentiate hyperglycemia, which would counter the hypoglycemic state to euglycemia [Figure 1].[13,14] At this juncture, it is noteworthy that the patients in the Thawabi and Studyvin case presentation have abstained from food; i.e., the fasting and medications were apparently having impact. Case 1 also had stress from infection, while Case 2 had stress from severe epigastric abdominal pain. Such stress induces ketoacidosis because stress hormones precede generation of ketone bodies,[15] just as starvation is also a factor.[14]

What this means is that health education equipping diabetics to avoid fasting as well as management of stress are alternative management options that possibly prevent euglycemia and/or ketoacidosis. In the Case Presentations reported, Thawabi and Studyvin have

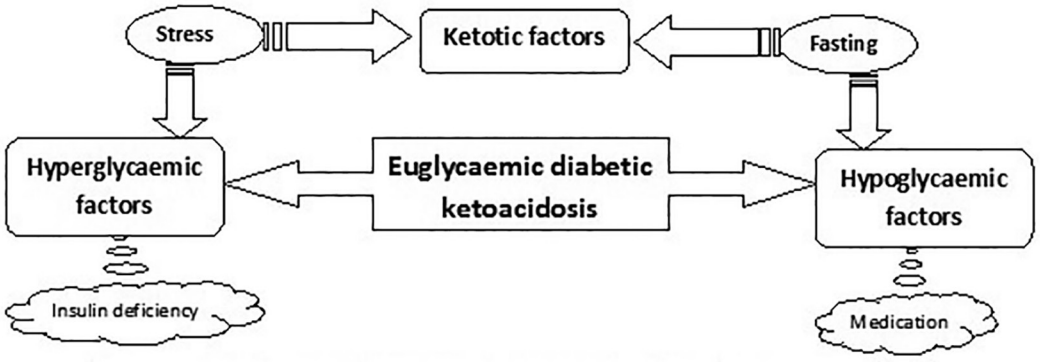

Figure 1: Misleading presentation of euglycemic DKA, illustrated

dutifully assessed starvation and stressors, but it is not clear if the patients were referred to diabetic health educators and/or other relevant community health workers for physical and health education. Such education may involve choice of foods and the implications of fasting and infection in managing DKA. The implication of this in LMIC is that there may not be the necessary health education, but that if this is available the outcomes are obvious and include possible benefits in terms of cost of health services and avoidance of hospitalization.

It is highly likely, albeit hypothetical, that many euglycemic DKA are undiagnosed and misleading, because blood gas analysis and ketonemia tests are unavailable, while ketonuria could be falsely reported as negative. We present two implications for LMIC and the first is that assessment of euglycemic DKA should diversify beyond the usual clinical biochemistry profile to include the roles of starvation and stress. The second is that management of euglycemic DKA should be delimited to primary health-care professionals and diversify to include allied health professionals, and to educate diabetes patients on the significance of avoiding fasting and stress.

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Conflicts of interest

There are no conflicts of interest.

Ezekiel Uba Nwose, Phillip Taderera Bwititi[1]

School of Community Health, [1]School of Biomedical Sciences, Charles Sturt University, New South Wales, Australia

Address for correspondence:
Dr. Ezekiel Uba Nwose, School of Community Health, Charles Sturt University, Leeds Pde, Orange 2800, New South Wales, Australia.
E-mail: enwose@csu.edu.au

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