



CLINICAL MANIFESTATIONS AND PRECIPITATING FACTORS IN PATIENTS WITH DIABETIC KETOACIDOSIS AT CALMETTE HOSPITAL, CAMBODIA

Health Sciences

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is a serious and potentially life-threatening acute complication of Diabetes Mellitus. It occurs mainly in patients with Type 1 Diabetes (T1D), although it can also occur in patients with Type 2 Diabetes (T2D) under certain conditions such as severe stress or infection. **Objective:** The objective of this research is to determine the clinical signs and causes of diabetic ketoacidosis, as well as Sociodemographic of DKA patients, their type of diabetes. **Methods:** This retrospective study was carried out at Calmette Hospital between April 1, 2021, and March 31, 2023, among patients with diabetic ketoacidosis. Upon reviewing the patients' medical records, it was discovered that they had diabetic ketoacidosis. **Results:** Among 51 participants. The most frequent clinical manifestations were abdominal pain (60.78%), dyspnea (52.94%), and nausea/vomiting (50.98%). The most common precipitating factor was infection (54.90%), while 47.06% of cases represented the first presentation of diabetes. When comparing precipitating factors for diabetic decompensation between T1D and T2D, no significant between-group differences were detected. **Conclusion:** The results draw attention to the important clinical signs and risk factors of DKA in this study of 51 patients, whose mean age was 39.90 years. Infections, especially pneumonia and pyelonephritis, were the main cause, and the most prevalent symptom was abdominal pain. No significant differences were observed in precipitating factors for diabetic decompensation between T1D and T2D.

KEYWORDS

Diabetic Ketoacidosis; Infection; Non-Adherence to Medication; Pyelonephritis; Pneumonia

INTRODUCTION

Diabetic ketoacidosis (DKA) is the most common hyperglycemic emergency in patients with diabetes mellitus. DKA most often occurs in patients with type 1 diabetes (T1D), but patients with type 2 diabetes (T2D) are susceptible to DKA under stressful conditions, such as trauma, surgery, or infections. DKA is reported to be responsible for more than 100 000 hospital admissions per year in the US, and accounts for 4-9% of all hospital discharge summaries among patients with diabetes [1].

Worldwide, infection is the most common precipitating cause for DKA, occurring in 30-50% of cases. Urinary tract infection and pneumonia account for the majority of infections. Other precipitating causes are intercurrent illnesses (i.e., surgery, trauma, myocardial ischemia, pancreatitis), psychological stress, and non-compliance with insulin therapy [2].

Diabetic ketoacidosis and the hyperglycemic hyperosmolar state (HHS) are the two most serious, acute, and life-threatening hyperglycemic emergencies in individuals with T1D and T2D. Global reports clearly show an increase in the number of DKA and HHS admissions during the past decade, with recent data reporting a 55% increase in the rate of DKA hospitalizations, especially in adults aged < 45 years [3].

DKA is characterized by the triad of hyperglycemia, increased ketone concentration in the blood and/or urine, and metabolic acidosis.

The earliest symptoms of marked hyperglycemia are polyuria, polydipsia, and weight loss. As the degree or duration of hyperglycemia progresses, neurologic symptoms, including lethargy, focal signs, and obtundation, can develop. This can progress to coma in later stages. Neurologic symptoms are most common in HHS, while hyperventilation and abdominal pain are primarily limited to patients with DKA.

MATERIALS AND METHODS

This retrospective study was conducted at Medical Ward A, A1-A6 of Calmette Hospital from 1 April 2021 to 31 March 2023. The study included adult patients hospitalized with diabetic ketoacidosis. Medical records of patients diagnosed with DKA were reviewed. A total of 51 cases that met the inclusion criteria were included in the study using convenience sampling.

Inclusion Criteria

- Adults aged ≥ 18 years
- Both sexes
- T1D
- T2D
- Serum glucose ≥ 200 mg/dL (11.1 mmol/L) OR prior history of diabetes
- β -hydroxybutyrate concentration ≥ 3.0 mmol/L or urine ketone strip 2+ or greater
- pH < 7.3 and/or a serum bicarbonate < 18 mEq/L (18 mmol/L)

Exclusion Criteria

- Lactic acidosis
- Hyperglycemic hyperosmolar state
- Alcoholic ketoacidosis
- Starvation ketosis

Data were collected from patient medical records using a structured questionnaire. The collected information was checked for completeness and accuracy before being entered into Microsoft Excel 2016 and later analyzed using Stata version 18.

Ethical approval for the study was obtained from the National Ethics Committee for Health Research and the University of Health Sciences. Patient confidentiality was strictly maintained. A limitation of this study is the small sample size and the use of non-probability sampling, which may limit the generalizability of the findings.

RESULTS

In a study assessing eligibility for participation, a total of 54 patients were evaluated. Out of these, 3 patients were excluded based on specific criteria: 2 patients had pancreatitis with ketonuria but without acidemia, and 1 patient was excluded due to known pregnancy with ketonuria but without acidemia. The exclusion criteria included conditions such as lactic acidosis, hyperglycemic hyperosmolar state, alcoholic ketoacidosis, starvation ketosis, and lack of criteria for DKA. Consequently, the total number of patients included in the study was 51 cases, after employing the inclusion and exclusion criteria.

In our study among 51 patients, the sample included 27 females (52.94%) and 24 males (47.06%), indicating a slightly higher representation of females. Among those with T1D, 11 women (40.47%) were included, while 16 individuals (59.25%) had T2D.

The mean age was 39.9 years (± 15.27 ; range 18–80). The cohort was relatively young, reflecting the inclusion of both T1D and T2D. Mean age differed by diabetes type: 28.36 years in T1D and 46.81 years in

T2D. Age distribution showed that most participants were 21–40 years old (29; 57%), followed by 41–60 years (13; 25%) and 61–80 years (7; 14%); only 2 participants (4%) were aged 18–20 years.

The evaluation of clinical manifestations revealed that abdominal pain was the most common symptom, reported by 31 individuals (60.78%). Dyspnea and nausea/vomiting were also prevalent, with 27 participants (52.94%) and 26 participants (50.98%) respectively. Other notable symptoms included polyuria and polydipsia (18 participants, 35.29%), and loss of consciousness (17 participants, 33.33%). Weight loss was reported by 6 participants (11.76%), while headache occurred in 4 participants (7.84%). Seizures were noted in 2 participants (3.92%), and both polyphagia and blurred vision were reported by 1 participant each (1.96%). This data highlights the diverse range of clinical manifestations experienced by the participants (Table 1).

Table 1: Distribution of Clinical Manifestations

Clinical manifestations	Patient (51)	Percentage (%)
Abdominal pain	31	60.94
Dyspnea	27	52.94
Nausea and vomit	26	50.98
Polyuria and polydipsia	18	35.29
Loss of consciousness	17	33.33
Weight loss	6	11.76
Headache	4	7.84
Seizure	2	3.92
Polyphagia	1	1.96
Blurred vision	1	1.96

The precipitating factors among the 51 participants revealed that infections were the most common precipitating factor (28/51; 54.9%), followed by first presentation of diabetes mellitus (24/51; 47.1%). Medication non-adherence was reported in 10/51 (19.6%), while pregnancy and prior pancreatitis were each reported in 4/51 (7.8%). Acute kidney injury occurred in 3/51 (5.9%), and non-adherence to diet was least common (1/51; 2.0%), highlighting infections and initial diabetes presentation as key triggers.

When comparing precipitating factors for diabetic decompensation between T1D (n=19) and T2D (n=32), no significant between-group differences were detected. First presentation of diabetes occurred in 10/19 (T1D) and 14/32 (T2D) participants (P=0.58). Infections or wounds were more common in T2D (22/32) than in T1D (8/19), but the difference was not statistically significant (P=0.08). Medication non-adherence was infrequent and similar across groups (4/19 vs 6/32; P=1.00). Pregnancy showed comparable frequencies (2/19 vs 2/32; P=0.58), as did acute kidney injury (2/19 vs 1/32; P=0.56). Non-adherence to diet was rare, occurring in 1/19 T1D participants and none in the T2D group (P=0.37). Pancreatitis was uncommon in both groups (1/19 vs 3/32; P=1.00). Overall, the results indicate broadly similar precipitating patterns between T1D and T2D in this cohort (Table 2).

Table 2: Precipitating Factors of DKA

Precipitation factors	T1D (19)	T2D (32)	P value
First presentation of DM	10	14	0.58
Infections or wounds	8	22	0.08
Non-adherence to medications	4	6	1
Pregnancy	2	2	0.58
Acute kidney injury	2	1	0.56
Non-adherence to diet	1	0	0.37
Pancreatitis	1	3	1

The distribution of infection types was as follows: pyelonephritis was the most common, affecting 53.57% (15 individuals). Pneumonia was the second most prevalent infection, accounting for 32.14% (9 individuals). Other infections included melioidosis, foot infection, skin infection, and pansinusitis, each representing 3.57% (1 individual) of the cases. This data indicates a significant prevalence of pyelonephritis among the studied population compared to other infection types (Table 3).

Table 3: Type of Infection

Type of infection	Patient (28)	Percentage (%)
Pyelonephritis	15	53.57
Pneumonia	9	32.14

Melioidosis	1	3.57
Foot infection	1	3.57
Skin infection	1	3.57
Pansinusitis	1	3.57

DISCUSSION

The five most common clinical symptoms reported were abdominal pain, dyspnea, nausea, vomiting (digestive problems), and coma. When compared to studies conducted in Pakistan [4], which found similar symptoms such as nausea, vomiting, and abdominal pain. By the way the fainting symptom was reported less frequently.

Infections were the most prevalent precipitating factor among the 51 participants in our study, as reported by 28 people (54.90%). Furthermore, 24 individuals (47.06%) reported that their illness was a first manifestation of diabetes mellitus. Ten participants (19.61%) were found to have not taken their medications as prescribed, four (7.84%) reported being pregnant, and four more had a history of pancreatitis. Three participants (5.88%) had acute kidney injury, and one participant (1.96%) had non-adherence to diet. These results highlight how important infections and the onset of diabetes are as precipitating factors in this population.

Moreover, the precipitating factors for patients with T2D are usually linked to infections such as urinary infection, diabetic foot and pneumonia which are found to be more prevalent in this group compared to those with T1D, where the primary precipitating factor is typically identified at the time of diagnosis.

Consistent with previous studies [5-7], our findings indicate that the precipitating factors were broadly similar to those reported in the literature. In addition, global evidence suggests that infection is the most frequent precipitant of diabetic ketoacidosis (DKA), occurring in 14–58% of cases [7]. Overall, infection remains the predominant trigger, in line with our results.

When comparing our study to a study done in the emergency room of a tertiary care hospital in rural Sindh, Pakistan [4], infections were the most frequent causes (69.0%) and treatment non-compliance (53.5%). It is evident that our study's common precipitating factors are comparable to those found in other studies.

In the evaluation of infection types among 28 patients with DKA, pyelonephritis was the most frequently observed infection, affecting 15 patients (53.57%). Pneumonia was the second most common, reported in 9 patients (32.14%).

In contrast, pneumonia (38.7%) and urinary tract infections (30.6%) were the most frequently reported infections in the emergency room of a tertiary care hospital in rural Sindh, Pakistan [4]. Compared to our study, the most frequent infections that caused diabetic patients to develop DKA were urinary tract infections and pneumonia.

CONCLUSIONS

In conclusion, our study of 51 patients with DKA revealed a relatively young average age of 39.9 years, with significant differences in age between those with T1D and T2D. The prevalence of DKA was comparable between genders, and a notable portion of patients were unaware of their diabetes and most of the cases were also associating with the infection of pulmonary and/or urinary tract, indicating a critical need for improved health education and monitoring in Cambodia.

The five most common clinical symptoms reported were abdominal pain, dyspnea, nausea, vomiting (digestive problems), and coma.

The primary precipitating factors for DKA were infections and initial diabetes presentations, aligning with findings from international studies. Our results highlighted those infections, particularly pyelonephritis and pneumonia, were common among these patients, which underscores the importance of infection management in preventing DKA. No significant differences were observed in precipitating factors for diabetic decompensation between T1D and T2D.

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Conflict of Interest

The author declares no conflict of interest.

REFERENCES

- [1] Weinstock RS, Xing D, Maahs DM, Michels A, Rickels MR, Peters AL, et al. Severe hypoglycemia and diabetic ketoacidosis in adults with type 1 diabetes: results from the T1D Exchange clinic registry. *J Clin Endocrinol Metab.* 2013 Aug;98(8):3411-9. Epub 2013 Jun 12.
- [2] Ehrmann D, Kulzer B, Roos T, Haak T, Al-Khatib M, Hermanns N. Risk factors and prevention strategies for diabetic ketoacidosis in people with established type 1 diabetes. *Lancet Diabetes Endocrinol.* 2020 May;8(5):436-446.
- [3] Feig DS, Donovan LE, Corcoy R, Murphy KE, Amiel SA, Hunt KF, et al. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. *Lancet.* 2017 Nov 25;390(10110):2347-2359. Epub 2017 Sep 15.
- [4] Sukharani N, Kumar J, Makheja K, Bai P, Sharma S, Subash K, Kamawal Y, et al. Gastrointestinal Manifestation of COVID-19 in Hospitalized Patients. *Cureus.* 2021 Sep 16;13(9):e18024.
- [5] O'Reilly JE, Jeyam A, Caparrotta TM, Mellor J, Hohn A, McKeigue PM, et al. Rising Rates and Widening Socioeconomic Disparities in Diabetic Ketoacidosis in Type 1 Diabetes in Scotland: A Nationwide Retrospective Cohort Observational Study. *Diabetes Care.* 2021 Sep;44(9):2010-17. Epub 2021 Jul 8.
- [6] McCoy RG, Herrin J, Lipska KJ, Shah ND. Recurrent hospitalizations for severe hypoglycemia and hyperglycemia among U.S. adults with diabetes. *J Diabetes Complications.* 2018 Jul;32(7):693-701. Epub 2018 Apr 24.
- [7] Dhatriya KK, Nunney I, Higgins K, Sampson MJ, Iceton G. National survey of the management of Diabetic Ketoacidosis (DKA) in the UK in 2014. *Diabet Med.* 2016 Feb;33(2):252-60. Epub 2015 Oct 8.