IMJ Official Journal of the Irish Medical Organisation

Ir Med J; June 2024; Vol 117; No. 6; P976
27th June, 2024

Clinical Outcome of Type 1 and Type 2 Diabetic Patients with Diabetic Ketoacidosis

T.M. Chia[1,2], H. O'Neill[1,2], HM. Sohail[1,2], NA. Soomro[1,2]

1. Department of Internal Medicine, Portiuncula University Hospital, Ballinasloe, Co. Galway, Ireland.
2. School of Medicine, University of Galway, Newcastle Rd., Co. Galway, Ireland.

Abstract

Diabetic ketoacidosis (DKA) is one of the life-threatening complications of diabetes. It is usually associated with type 1 diabetes; however, it is increasingly being recognised in type 2 diabetes.

Aims
To analyze the difference of clinical outcomes of DKA in type 1 and type 2 diabetes patients in a Model 3 public hospital.

Method
A retrospective study was carried out between 2017 to 2022 reviewing the charts of patients diagnosed with DKA at Portiuncula University Hospital (PUH). Patients' demographics, biochemical profiles on admission and clinical outcome were analyzed.

Results
A total of 118 diabetic patients developed DKA, 89(75.4%) are Type 1 diabetes patients. Type 2 diabetic patients with DKA were older than Type 1 diabetic patients (62.3 ± 15.9 vs 39.1 ± 15.9 years, P value <0.030) and had longer duration of diabetes (15.4 ± 4.9 vs 11.3 ± 3.3, P value <0.031). There was no significant difference in biochemical profiles between patients with type 1 vs type 2 diabetes, however, those with type 2 diabetes had significantly higher lactate level (2.98 ± 1.4 vs 2.43 ± 1.1 mmol/L, P value <0.026). Overall, clinical outcomes of DKA were more severe in Type 2 compared with Type 1 diabetic patients.

Discussion
Majority of DKA cases are observed in people with type 1 diabetes, however primary outcomes was worse in DKA patients with type 2 diabetes. An innovative approach in treating this group of patients should be emphasized.

Introduction

IMJ Official Journal of the Irish Medical Organisation

Ir Med J; June 2024; Vol 117; No. 6; P976
27th June, 2024

Diabetic ketoacidosis is defined by the biochemical triad of ketonemia, hyperglycaemia and acidaemia.[1] It occurs as a consequences of absolute or relative insulin deficiency, usually accompanied by an increase in counter-regulatory hormones, leading to hepatic gluconeogenesis and glycogenolysis and resulting in severe hyperglycaemia.[2,3]

Diabetic ketoacidosis is well-known, life-threatening acute complication of type 1 diabetes. For a long time it has been considered the hallmark of type 1 diabetes; however, recently, its presence has been increasingly recognised in patients with type 2 diabetes.[4] DKA in patients with type 2 diabetes was thought to be related to ethnic minorities and specifically Afro-Caribbean populations or indigenous populations of America.[5-6] However, there was increasing number of cases documenting DKA in type 2 diabetic patients from different ethnicity such as Caucasian, Chinese and Indian. This suggests that the occurrence of DKA is not solely associated with ethnic minorities, as was once was thought.[7-9] The triggers for DKA development in type 2 diabetes patients could be due to insulin deficiency arising from long duration of hyperglycaemic state and increased lipolysis due to presence of stressors.[10]

According to published audit report of HSE in 2017, the rate of admission ketoacidosis for Type 1 was decreasing from 2003 to 2016, however the rate for Type 2 showing increasing trend.[11] Recent epidemiologic studies also shown the hospitalization for DKA have increased during the past 2 decades. Part of this increased frequency of admissions were related to the increased prevalence of type 2 diabetes.[12-13] With the changes in the frequency of DKA and the increased incidence of DKA in patients with type 2 diabetes, the question may be posed of whether there is any changes in the clinical outcome as compare to patient with type 1 diabetes. In this study, we aims to review the difference in the biochemical characteristics and clinical outcomes of patients with type 1 and type 2 diabetes admitted with DKA to Portiuncula University Hospital, Ireland.

Methods

A single centre, retrospective study of both type 1 and type 2 diabetes patients who admitted with diabetic ketoacidosis from Jan 2017 to Dec 2022 were included in this study. These DKA admission were identified from the Hospital In-Patient Enquiry (HIPE) at Portiuncula University Hospital (PUH) which is a computer-based system designed to collect demographic, clinical and administrative data on discharges and deaths from acute hospital in Republic of Ireland. Documented instances of ketosis and acidosis occurring in type 2 diabetes in the setting of excess alcohol intake, pregnancy or anorexia were excluded from this study. Patients' data was obtained through patient medical records and Winpath© (Clinisys, United Kingdom) electronic laboratory record system. Patient's demographics, duration of diabetes years,

laboratory results, time from presentation to resolution of urine ketone and clinical outcomes were reviewed retrospectively. Basic descriptive analyses were performed using Statistical Package for Social Sciences (SPSS) version 26 (International Business Machines Corporation, Armonk, New York). Comparisons between the groups were performed using the Chi square test and all data are expressed as mean ±SD unless otherwise indicated. All P value were two sided and considered as significant if less than 0.5

Results

A total of 118 diabetic patients were recruited in this 6-year study period. The patients were between the age of 16 and 98 years with mean age of (44.8±18.8). Overall, 89 (75.4%) of patients had type 1 diabetes and 29(24.6%) had type 2 diabetes (Table 1). Among patients with DKA, majority of T1DM were male (53.9%) and female in T2DM (62.1%). The mean duration of diabetes in patients diagnosed prior to admission was higher in Type 2 diabetic patients (15.4 ± 4.9 years). Table 2 lists the DKA patients' biochemical profiles upon admission and clinical outcomes in hospital. Lactate levels were higher in those with type 1 diabetes on venous blood gas (2.98 ± 1.4 vs 2.43 ± 1.1 mmol/L, P value <0.026). No significant difference was found in other biochemical parameters. HbA1c level and ventilator support were also not different significantly in both groups (P value >0.05). Mortality was also observed higher in Type 2 diabetes patients with DKA (6.9%, P value <0.007). Type 2 diabetes has higher length of stay in ICU as compared to type 1 diabetes (7.4 ± 2.5 vs 4.6 ± 1.2 days, P value <0.01). The recurrence rate of DKA was significantly higher in Type 2 diabetic patients (13.8% vs 9.0%, P value <0.04)

Table 1: Patient demographics

Demographics	Type 1	Type 2	P value
Number of patients, n(%)	89 (75.4%)	29 (24.6%)	P>0.05
Age (years)	39.1 ± 15.9	62.3 ± 15.9	<0.030*
Sex, n(%) Male Female	 48 (53.9) 41 46.1%)	 11 (37.9%) 18 (62.1%)	 P>0.05 P>0.05
Duration of diabetes (years)	11.3 ± 3.3	15.4 ± 4.9	<0.031*

Table 2: Biochemical characteristics at admission and clinical outcomes for subgroups of DKA patient by type

Characteristic	Type 1	Type 2	P value
Initial venous blood gas results pH	 7.19 ± 0.12	 7.23 ± 0.11	 P>0.05

Glucose, mmol/L	23.2 ± 16.5	25.7 ± 17.6	P>0.05
Bicarbonate, mmol/L	14.62 ± 11.7	15.91 ± 12.8	P>0.05
Lactate, mmol/L	2.98 ± 1.4	2.43 ± 1.1	<0.026*
Urine ketones, n(%)			
+2	55 (61.8%)	7 (24.1%)	P>0.05
+3	31 (34.8%)	22 (75.9%)	P>0.05
+4	3 (3.4%)	0 (0%)	P>0.05
Initial blood test results			
Urea, mmol/L	6.6 ± 5.4	9.5 ± 6.7	P>0.05
Sodium, mmol/L	138 ± 6	142 ± 8	P>0.05
Potassium, mmol/L	3.7 ± 1.2	4.2 ± 1.4	P>0.05
Creatinine, umol/L	102 ± 98	113 ± 87	P>0.05
Calcium, mmol/L	2.23 ± 0.76	2.08 ± 0.64	P>0.05
Inorganic Phosphate, mmol/L	1.04 ± 0.26	0.98 ± 0.27	P>0.05
Magnesium, mmol/L	0.63 ± 0.17	0.71 ± 0.21	P>0.05
Length of stay in ICU, days	4.6 ± 1.2	7.4 ± 2.5	<0.010*
Time of ketone resolution (hours)	36.7 ± 13.2	42 ± 15.8	P>0.05
HbA1c (%)	73.3 ± 25.4	65.6 ± 17.6	P>0.05
In-hospital mortality, n(%)	0 (0%)	2 (6.9%)	<0.007*
Mechanical Ventilation, n(%)	0 (0%)	0 (0%)	P>0.05
DKA recurrence in 1 year, n(%)			
Male	3	1	
Female	5	3	
Total	8 (9.0%)	4 (13.8%)	<0.040*

*P value <0.05

Discussion

In our study, we observed nearly two third of DKA admissions were for patients with T1DM. In addition, similar to this study, previous study conducted in Wales have also shown at least half of their DKA admissions were patients with T1DM.[14] Interestingly, we observed a higher in-hospital mortality rate in DKA patients with T2DM. The factors likely associated with the increased risk of mortality in T2DM patients are multifactorial and multidimensional, and they may be due to presence of comorbidities and higher body mass index (BMI)[15-16] Historically, DKA has been recognized as typical complication associated with T1DM. Therefore, these results highlights the importance of early recognising of DKA in T2DM patients.

High level of HbA1c level was identified in both T1DM (73.3 ± 25.4 %) and T2DM patients (65.6 ± 17.6%) in this study. HbA1c level may be useful tools to determine the current episode is due to ongoing progression in patient with undiagnosed or poor self-glycaemic control, or if it is a true acute episode in an otherwise well-managed patient.[17] In previous studies, it has shown that patient with type 2 diabetes who developed DKA has lower level of pH value and plasma glucose compared with those T1DM.[18] However, our study does not substantiate these findings. There is no significant difference of pH value and plasma glucose shown on venous blood gas in both groups of diabetes patients.

Data from several studies have identified female patients are at higher risk of developing DKA.[19,20] Our study further consolidates that both T1DM and T2DM female patients are at higher risk of DKA recurrence as compared to male patients. Depression is associated with diabetes, as evidenced by literature.[21] Several studies demonstrated that depression was more common in female, was associated with non-compliance to medication and poor blood glucose monitoring. As a result, it increases DKA readmissions and worsen overall clinical outcomes.[22-24] Therefore, well-organized, and systematically intervention is crucial to minimize likelihood of DKA reoccurrence. Diabetes education acts as a critical role in reduce recurrence rate of DKA. Consult with diabetes specialist team during hospitalization was associated with a lower risk of DKA recurrence.[25] In our facility, all admitted DKA patient will be consulted by diabetes clinical nurse specialist (CNS) to ensure adequate diabetes education and as crucial step to reduce recurrence.

Our study has some limitations. First, this study was conducted at a single center, which might restrict the external validity. Second, the sample size is relatively small which may render comprehensive overview of the disease. Third, the data only focus on hospitalized patients rather than individual patients. However, despite these limitations, this study contributed a more in-depth understanding of DKA. In conclusion, DKA is a metabolic complication which can be seen with both type 1 and type 2 diabetes patients. Doctors should be aware of this life-threatening condition and prompt management should be initiated early, ultimately leading to reduce the morbidity and mortality associated with DKA.

Declaration of Conflict of Interest:
None declared.

Corresponding author:
Tiong Ming Chia
Department of Internal Medicine,
Portiuncula University Hospital,

Co Galway,
Ireland
Email: tiongming.chia@hse.ie

References:

1. Tran TTT, Pease A, Wood AJ, Zajac JD, Mårtensson J, Bellomo R, et al. Review of Evidence for Adult Diabetic Ketoacidosis Management Protocols. Frontiers in Endocrinology. 2017 Jun 13;8(106).
2. Savage MW, Dhatariya KK, Kilvert A, Rayman G, Rees JAE, Courtney CH, et al. Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. Diabetic Medicine. 2011 Apr 12;28(5):508–15.
3. Lizzo JM, Goyal A, Gupta V. Adult diabetic ketoacidosis [Internet]. PubMed. Treasure Island (FL): StatPearls Publishing; 2023.
4. Puttanna A, Padinjakara R. Diabetic ketoacidosis in type 2 diabetes mellitus. Practical Diabetes. 2014 May;31(4):155–8.
5. Umpierrez G, Casals MMC, Gebhart SSP, Mixon PS, Clark WS, Phillips L. Diabetic Ketoacidosis in Obese African-Americans. Diabetes. 1995 Jul 1;44(7):790–5.
6. Wilson C, Krakoff J, Gohdes D. Ketoacidosis in Apache Indians with non-insulin-dependent diabetes mellitus. Archives of Internal Medicine [Internet]. 1997 Oct 13 [cited 2023 Dec 17];157(18):2098–100.
7. Tan H, Zhou Y, Yu Y. Characteristics of diabetic ketoacidosis in Chinese adults and adolescents – A teaching hospital-based analysis. Diabetes Research and Clinical Practice. 2012 Aug;97(2):306–12.
8. Seth P. Clinical Profile of Diabetic Ketoacidosis: A Prospective Study in a Tertiary Care Hospital. JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH. 2015;9(6).
9. Bagg W, Sathu A, Streat S, Braatvedt GD. Diabetic ketoacidosis in adults at Auckland Hospital, 1988-1996. Australian and New Zealand Journal of Medicine. 1998 Oct;28(5):604–8.
10. Lin MV, Bishop G, Benito-Herrero M. Diabetic Ketoacidosis in Type 2 Diabetics: A Novel Presentation of Pancreatic Adenocarcinoma. Journal of General Internal Medicine [Internet]. 2010 Apr 1;25(4):369–73.
11. Riordan F., McHugh S., Marsden P., Kearney P., Harkins V. Audit Report of the HSE Midland Diabetes Structured Care Programme. Department of Public Health, Health Service Executive Dublin Mid-Leinster. 2017.
12. Newton CA, Raskin P. Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes Mellitus. Archives of Internal Medicine. 2004 Sep 27;164(17):1925.

13. Balasubramanyam A, Zern JW, Hyman DJ, et al. New profiles of diabetic ketoacidosis: type 1 vs type 2 diabetes and the effect of ethnicity. Arch Intern Med 1999;159:2317–22.
14. Abdulrahman GO, Amphlett B, Okosieme OE. Trends in hospital admissions with diabetic ketoacidosis in Wales, 1999–2010. Diabetes Research and Clinical Practice. 2013 Apr;100(1):e7–10.
15. Almazrouei R, Siddiqua AR, Alnuaimi M, Al-Shamsi S, Govender R. Clinical and biochemical characteristics of diabetic ketoacidosis in adults with type 1 or type 2 diabetes at a tertiary hospital in the United Arab Emirates. Frontiers in Clinical Diabetes and Healthcare. 2022 Aug 8;3.
16. Umpierrez GE, Kitabchi AE. Diabetic ketoacidosis. Risk factors and management strategies. Treat Endocrinol 2003;2:95–108.
17. Kitabchi AE, Umpierrez GE, Murphy MB, et al. Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association. Diabetes Care 2006;29:2739–48.
18. Ooi E, Nash K, Rengarajan L, Melson E, Thomas L, Johnson A, et al. Clinical and biochemical profile of 786 sequential episodes of diabetic ketoacidosis in adults with type 1 and type 2 diabetes mellitus. BMJ Open Diabetes Research & Care. 2021 Dec;9(2):e002451.
19. Alourfi Z, Homsi H. Precipitating factors, outcomes, and recurrence of diabetic ketoacidosis at a university hospital in Damascus. Avicenna J Med. 2015;5(1):11– 15.
20. Barski L, Nevzorov R, Jotkowitz A, Rabaev E, Zektser M, Zeller L, et al. Comparison of Diabetic Ketoacidosis in Patients With Type-1 and Type-2 Diabetes Mellitus. The American Journal of the Medical Sciences. 2013 Apr;345(4):326–30.
21. Tabák AG, Akbaraly TN, Batty GD, Kivimäki M. Depression and type 2 diabetes: a causal association? *Lancet Diabetes Endocrinol.* 2014;2:236–45.
22. Ata F, Abdul Quaiyoom Khan, Ibrahim Khamees, Iqbal P, Yousaf Z, Mohammad B, et al. Clinical and biochemical determinants of length of stay, readmission and recurrence in patients admitted with diabetic ketoacidosis. Annals of Medicine. 2023 Feb 6;55(1):533–42.
23. Trief PM, Foster NC, Chaytor N, Hilliard ME, Kittelsrud JM, Jaser SS, et al. Longitudinal Changes in Depression Symptoms and Glycemia in Adults With Type 1 Diabetes. Diabetes Care [Internet]. 2019 May 21;42(7):1194–201.
24. Jeon EJ. Diabetes and depression. Yeungnam University Journal of Medicine [Internet]. 2018 Jun 30;35(1):27–35.
25. Burke SD, Sherr D, Lipman RD. Partnering with diabetes educators to improve patient outcomes. Diabetes Metab Syndr Obes. 2014;7:45–53