A Prospective Study of Risk Factors, Clinical Profile and Outcome in Patients of Diabetic Ketoacidosis (DKA) in Type II Diabetes Patients

Srishti Sonwani[1], Anita Arya[2], Rita Singh Saxena[3]

ABSTRACT

Introduction: Diabetic ketoacidosis (DKA), a well-known and major acute metabolic complication, classically occurs in young patients with type 1 diabetesmellitus (T1DM). However, it may also occur in patients with type 2 Diabetes Mellitus (T2DM). Hence, this study was planned to assess and find out the association between clinical profile, laboratory profile and clinical outcome of DKA patients in T2DM. Study aimed to assess the clinical profile and outcome of DKA in patients of T2DM.

Material and Methods: Hundred T2DM patients, admitted with DKA were studied at Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal. Data on demography (age, sex, diabetes duration), co-morbidities, precipitating factors, presenting complaints, body mass index (BMI), hemoglobin (Hb), random blood sugar (RBS), glycated hemoglobin (HbA1c) and arterial pH were recorded for each patients. Nature of treatment and outcome was also recorded.

Results: Most of the our patients with DKA had age between 51-55 years (21%), were male (72%) and were obese (46%). Most of them were on oral hypoglycemic drugs (70%). Mean duration of diabetes, BMI, Hb, RBS, HbA1c and pH was 7.28±3.81 years, 29.00±3.58 kg/m2, 9.8±1.42 gm%, 351.72±22.32 mg/dl, 9.3±1.23%, 7.14±0.10 respectively. Out of 100 patients, 86% were discharged, 7% succumbed to death while 7% left the study. Most common co-morbidity, clinical symptoms and precipitating factor in DKA patients were hypertension (60%), obesity (47%), nausea vomiting (86%), abdominal pain (58%), poor compliance (53%) and infection mainly pneumonia (24%). Patients who died, majority of them were having diabetes duration >10 years (23.1%) (p=0.012), poor compliance (10.2%) (0.028), had CVD (40%) (p=0.004) and ACS (40%) (p=0.004).

Conclusion: DKA is a fatal acute metabolic complication even in T2DM with heterogeneous clinical presentation. Early diagnosis and treatment can avoid morbidity and mortality.

Keywords: Diabetic Ketoacidosis, Infection, Abdominal Pain, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetic ketoacidosis (DKA) is serious acute metabolic complication in diabetes patients. It is characterized by absolute or relative insulin deficiency with an overall mortality rate of up to 5% in experienced healthcare centers.[1,2] Insulin deficiency, increased insulin counter-regulatory hormones and peripheral insulin resistance can lead to hyperglycemia, dehydration, ketosis, and electrolyte imbalance which is the underling pathophysiology of DKA.[3]

For a long time, it has been considered the hallmark of type 1 diabetes; however, it's presence has been increasingly recognised in patients with type 2 diabetes when severe insulin resistance occurs with co-existing illnesses like septicaemia, acute myocardial infarction or disseminated tuberculosis.[4] Several studies have reportedthat patients with T2DM accounted for 12–56% of the DKA cases. Author also reported that these patients had longer hospital stays, and higher mortality which may be due to advanced age and comorbidities compared to patients with type 1 diabetes mellitus (T1DM).[2,5]

The incidence of DKA in T2DM also depends upon age, sex, race/ethnicity, diabetes duration, different geographic locations etc. DKA can be the initial presentation of diabetes mellitus or precipitated in known patients with diabetes mellitus by many factors, most commonly infection.[6] Other precipitating factors include acute myocardial infarction, any cerebrovascular accident or any postoperative stress.[7] The present study was performed to assess the clinical profile and outcome of DKA in patients of T2DM.

MATERIAL AND METHODS

A prospective observational study was done including 100 T2DM patients with DKA admitted at Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal

All patients of T2DM with DKA who had onset of diabetes mellitus after 25 years of age were included in the study. Patients of Type 1 Diabetes Mellitus with DKA, patients with hyperosmolar state and hyperglycemia without ketoacidosis, pregnancy, alcohol abuse and chronic kidney disease with serum creatinine>3 mg/dl were excluded from the present study.

Information was collected through preapproved proforma for each patient and informed consent was obtained from each patients. The study protocol was approved by Institutional Ethics Committee of Gandhi Medical College,Bhopal.

Data on patient's demography, co-morbidities, characteristics of the diabetes, presenting complaints at admission including systemic, respiratory, gastrointestinal and neurological

[1]PG 3rd Year Student, [2]Associate Professor, [3]Assistant Professor, Department of Medicine, Gandhi Medical College, Bhopal, India

Corresponding author: Dr. Srishti Sonwani, PG 3rd Year Student, Department of Medicine, GMC, Bhopal, India

How to cite this article: Srishti Sonwani, Anita Arya, Rita Singh Saxena. A prospective study of risk factors, clinical profile and outcome in patients of diabetic ketoacidosis (DKA) in type II diabetes patients. International Journal of Contemporary Medical Research 2018;5(4):D21-D24.

DOI: 10.21276/ijcmr.2018.5.4.15

symptoms, bedside blood and urine dipstick quantification of glycemia, glycosuria, and ketonuria, precipitating factors, vital signs, BMI, biochemical profile and events and treatments during the first 24 hour after admission were recorded.

Data concerning clearance of ketonuria was evaluated at 6-hour intervals with use of reagent strips (graded with 0-5 plus signs). Follow up of all the patients was done till discharge or death.

The diagnosis of DKA was made in the emergency department by the presence of 4 laboratory findings; a plasma glucose level of 250 mg/dl or higher, a serum bicarbonate level of 15mEq/L or lower, an arterial blood pH of 7.35 or lower and presence of urinary ketones with Dipstick.[8]

Intravenous Insulin was administered according to the standard institutional treatment algorithm.Additional hydration and electrolyte replacement were left to the discretion of the treating physicians, although American Diabetes Association (ADA) practice guidelines were followed. The insulin infusion was discontinued 2 hours after the administration of subcutaneous insulin once patients had resolution of their metabolic status, including a ketone-free urine sample, and were able to tolerate oral feedings.

All patients were investigated with complete hemogram, urine analysis, blood urea levels, serum creatinine levels, serum electrolytes, lipid profile (Total cholesterol, Triglycerides and HDL), plasma glucose (mg/dl), HbA1c, arterial pH and serum bicarbonate (mmmol/L). ECG was done before administration of potassium.

Parameters		Percentage
Co-morbidities	Hypertension	60
	CKD	2
	CVA	7
	Obesity	47
	CVD	6
Clinical Symptoms	Nausea vomiting	86
	Abdominal Pain	58
	Weakness	20
	Polyurea, polydypsea	42
	Fever	35
	Altered Sensorium	18
	Shortness of breath	28
Precipitating factor	Pneumonia	24
	UTI	22
	Pleural Effusion	6
	Diabetic foot	3
	Unidentified	4
	Poor compliance	53
	Stroke	7
	ASC/MI	6

Data is expressed as percentage, CKD; chronic kidney disease, CVA; cerebro vascular accidents, CVD; cardiovascular disease, UTI; urinary tract infection

Table-1: Showing co-morbidities and clinical symptoms in DKA patients with T2DM

Parameters		Outcome		Total	P value
		Died	Survived		
Duration of DM (DD) (years)	≤10	4 (5)	76 (95)	80	0.012
	>10	3 (23.1)	10 (76.9)	13	
HbA1c (%)	6.5-10	4 (4.9)	77 (95.1)	81	NS
	>10	3 (25)	9 (75)	12	
pH	Mild(7.25-7.30)	0 (0)	7 (100)	7	NS
	Moderate(7.00-7.24)	3 (3.7)	79 (96.3)	82	
	Severe(<7.00)	4 (100)	0 (0)	4	
Compliance	Poor	5 (10.2)	44 (89.8)	49	0.028
	Proper	2 (4.5)	42 (95.5)	44	
HTN	Yes	2 (4.7)	41 (95.3)	43	NS
	No	5 (10)	45 (90)	50	
Obesity	Yes	2 (4.7)	41 (95.3)	43	NS
	No	5 (10)	45(90)	50	
Stroke	Yes	1 (14.3)	6 (85.7)	7	NS
	No	6 (7)	80 (93.)	86	
CVD	Yes	2 (40)	3 (60)	5	0.004
	No	5 (5.7)	83 (94.3)	88	
CKD	Yes	2 (100)	0 (0)	2	NA
	No	5 (5.5)	86 (94.5)	91	
Infection	Yes	5 (9.4)	48 (90.6)	53	NS
	No	2 (5)	3 (95)	40	
ACS	Yes	2 (40)	3 (60)	5	0.004
	No	5 (5.7)	83 (94.3)	88	

Data is expressed as number of patients (percentage), DD; diabetes duration, HbA1c; glycated hemoglobin, HTN; hypertension, CVD; cardiovascular disease, CKD; chronic kidney disease, ACS; Acute Coronary Syndrome, NA; not available, NS; not significant, p Value of <0.05 is considered as significant.

Table-2: Association of different parameters with clinical outcome in study cohort

STATISTICAL ANALYSIS

Data was entered in M.S. excel 2010. Data was presented in the form of frequency and percentage and wherever required appropriate statistical test of significance was applied. Data was analyzed using IBM SPSS ver. 20 software.

RESULTS

Most common age group of patients presented with DKA was in the range of 51-55 years (21%) (mean age being 56.10±10.40 years), were male (72%) and were obese (BMI >30) (46%).Most of the patients were on OHAs (70%) and only 10% were taking insulin.

Most of the patients had diabetes for 6-10 years (56%), hemoglobin between 8-10 gm % (47%), RBS between 351-400 mg/dl (43%), HbA1c between 8.6- 10% and pH between 7.00-7.24 (89%).

Mean duration of diabetes, BMI, Hb, RBS, HbA1c and pH was 7.28±3.81 years, 29.00±3.58 kg/m2, 9.8±1.42 gm%, 351.72±22.32 mg/dl, 9.3±1.23%, 7.14±0.10 respectively.

Blood and urine culture was positive in 17% and 26% DKA patients respectively. Out of 100 patients, 86% were discharged, 7% succumbed to death while 7% left the study.

DISCUSSION

In developing country like India poor socio-economic status in patients with T2DM incline to have poor compliance and poor glycemic control so any precipitating factor tends to land them in a state of DKA.[9,10]

A study including 138 consecutive admissions for DKA observed that 21.7% patients were having T2DM.[11] Another study from Taiwan also reported that the patients attacked with DKA were predominant type 2 DM (98 vs. 39 patients).[12] Mishra et al has reviewed the pathophysiology of DKA prone T2DM in his recent article and shown that DKA is not just the feature restricted to T1DM but can also be a complication of T2DM usually with a precipitating factor.[13,14] Wang et al in their study also supported similar findings of DKA in T2DM patients.[3]

Mean age of patients in present study was 56.10±10.40 years. In present study, T2DM was most commonly first appeared in adult cohort.[15] The statement is supported by many other studies. Adhikari et al[9] reported mean age of 44.78 years. Faich et al and Kreisberg et al mean age of DKA patients with T2DM to be 40-50 years.[16,17] In further agreement to present study Beigelman et al reported 47 years as the mean age of presentation for DKA.[18]

Among clinical symptoms nausea and vomiting were most common (86%) followed by abdominal pain in 58% DKA patients which is in agreement to the study done by Seth et al[7] who reported that nausea and vomiting was reported in 63.33% and abdominal pain in43.33% DKA patients. Altered sensorium was seen in 30% of patients, 26.66% patients were complaining of polyuria and polydipsia, 16.66% of patients had kussmaul breathing and 13.33% had hypotension as reported by Seth et al.[7] Similarly in present study altered sensorium, complaining of polyuria and polydipsia and shortness of breath was reported in 28%, 42% and 28% DKA patients respectively. A similar incidence of symptoms has been reported in previous studies done by Munro et al, Umpierrez et al, and Adhikari et al.[9,19,20] A similar study from Bangladesh on 200 DKA T2DM patients also reported nausea and vomiting (63%), polyuria (43%), polydypsia (42.5%), fever (29%) and abdominal pain (28%) as the most common presenting symptoms.[21]

Present study has revealed that DKA patients were having more than one precipitating factor like 53% who had poor compliance also had infection like pneumonia (24%) and UT I(22%). DKA patients also presented with stroke (7%) and MI (6%) as the precipitating factors. Hence, it can be said that presence of non-compliance to treatment is an important precipitating factor which indicates that prevalence of DKA can be reduced by proper education of patients about their illness and harm of non-compliance. Welch et al[22] studied T2DM patients presenting with DKA and reported that multiple precipitating factors are required in diabetic patients to develop DKA, which is in agreement to the present study findings.

Pneumonia was the most common (24%) infection in our study precipitating DKA, which is lower than the reports of a similar study by Seth et al.[7] Urinary Tract Infection was the precipitating infection in 22% of cases, pleural effusion in 6% patients and diabetic foot was reported in 3% patients. Similar to present study Adhikari et al[9] also reported diabetic foot as the infection precipitating DKA in 30.23% of patients. Other factors such as hyperglycemia, leukocyte dysfunction, macrovascular disease and acidosis predispose the diabetic with ketoacidosis to common and rare infections. This is agreement with the other's which showed that infection of any site is an important precipitating factor in causing DKA.[23-25] Rahim et al reported infection in 45.5% patients which is higher than what is revealed by present study. Author also showed that infection was the commonest precipitating cause of DKA.[21]

A mortality rate in present study was 7% which is almost similar to the reports of other studies. Westphal found mortality of 5.1%[25], while Beigelman and Faich et al., found mortality rate of 9%.[16,18] Adhikari et al., found mortality of 16.3% and Matoo et al., reported mortality of 23.7%.[9,24] Chaisson et al.,[26] revealed the estimated mortality rates in DKA patients as 4-10%. This indicates that DKA in T2DM patients should be considered as more severe disease compared to DKA in T1DM patients. Barski et al did a comparative study in diabetic patients presented with DKA and reported that T2DM patients who were presented with DKA had significantly severe presentation and worse outcome than those who have Type 1 DM.[27] Many Indian studies still report mortality figures in the range of 20-30%. The possible reason for such a high mortality rates in Indian patients may be due to delayed presentation and poor socio-economic conditions which influence the selection of better antibiotics for the treatment. Present study has showed that the clinical profile of T2DM patients presented with DKA is similar to the reports from West and other Indian

studies.

CONCLUSION

There is need of taking active measure to rule out DKA in T2DM and comatose patients in order to prevent further complication and mortality. Mortality mainly depends on the general condition of the patients, as well as the co-existent medical illness and time of onset of therapy. Hence, education is the key in T2DM patients regarding the warning symptoms of DKA such as weakness, abdominal pain, vomiting and drowsiness which can be the reason for early diagnosis and treatment.

REFERENCES

1. Gosmanov AR, Gosmanova EO, Dillard-Cannon E. Management of adult diabetic ketoacidosis. Diabetes Metabolic Syndrome. Obes Targ Ther 2014; 7:255–64.
2. Xu Y, Bai J, Wang G, Zhong S, Su X, Huang Z et al. Clinical profile of diabetic ketoacidosis in tertiary hospitals in China: a multicentre, clinic-based study. Diabet Med: J Br Diabet Assoc 2016;33:261–8.
3. Wang Y, Desai M, Ryan PB, DeFalco FJ, Schuemie MJ, Stang PE et al. Incidence of diabetic ketoacidosis among patientswith type 2 diabetes mellitus treated with SGLT2inhibitors and other antihyperglycemic agents. diabetes research and clinical practice 2017; 128: 83–90.
4. Kitabchi AE, Umpierez GE, Miles JM, Fisher JN. Diabetes care 2009; 32:1335-43.
5. Barski L, Nevzorov R, Harman-Boehm I, Jotkowitz A, Rabaev E, Zektser M, et al. Comparison of diabetic ketoacidosis in patients with type-1 and type-2 diabetes mellitus. Am J Med Sci. 2013;345:326-30.
6. Wilson JF. Diabetic Ketoacidosis- The Clinics. Ann Int Med. 2010;152:ITC 1-1.
7. Seth P, Kaur2 H, Kaur M. Clinical Profile of Diabetic Ketoacidosis: A Prospective Study in a Tertiary Care Hospital. Journal of Clinical and Diagnostic Research 2015; 9: OC01-4.
8. Kitabchi AE, Umpierrez GE, Murphy MB, KreisbergRA.Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American DiabetesAssociation. Diabetes Care 2006;29:2739–48.
9. Adhikari PM, Mohammed N, Pereira P. Changing profile of diabetic ketosis. J Indian Med Assoc. 1997;95: 540-42.
10. National Center for Health Statistics. National hospital discharge and ambulatory surgery data. [article online]. Available from http://www.cdc.gov/nchs/about/major/hdasd/nhds.htm. Accessed 9 March 2018.
11. Newton CA, Raskin P. Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes: Clinical and Biochemical differences. Arch Intern Med. 2004;164:1925-31.
12. Chu CH, Lee JK, Lam HC, Lu CC. The Occurrence of Diabetic Ketoacidosis in Type 2 Diabetic Adults. www.tsim.org.tw/journal/jour10-6/P10_230.PDF.
13. Misra S, Oliver N, Dornhorst A. Diabetic ketoacidosis: not always due to type 1 diabetes. BMJ. 2013;346:f3501.
14. Umpierrez GE, Woo W, Hagopian WA, Isaacs SD, Palmer JP, Gaur LK, et al. Immunogenetic analysis suggests different pathogenesis for obese and lean African-Americans with diabetic ketoacidosis. Diabetes Care. 1999;22:1517- 23.
15. Alberti KG, Zimmer PZ. Definition,diagnosis and classification of diabetes mellitus and its complications. Part 1:diagnosis and classification of diabetes mellitus provisional report of a WHO consultation.Diabet Med,1998.15:p.539-53
16. Faich GA, Fishbein HA, Ellis SE. The epidemiology of diabetic acidosis: A population based study. Am J Epidemiol. 1983;117:551-58.
17. Kreisberg R. Diabetic ketoacidosis. In: Rifkin H, Porte D (eds). Diabetes mellitus: [26] Theory and practice. 4th edn. New York: Elsevier Science, 1990: 591-603.
18. Beigelman PM. Severe diabetic ketoacidosis (diabetic "coma"). 482 episodes in [27] 257 patients; experience of three years. Diabetes. 1971;20:490–500.
19. Munro JF, Campbell IW, McCuish AC, Duncan LJ. Euglycaemic diabetic ketoacidosis. Br Med J. 1973;2:578–80.
20. Umpierrez G, Freire AX. Abdominal pain in patients with hyperglycaemic crises. [11] J Crit Care. 2002;17:63-67.
21. Rahim MA, Rouf R, Ahmed AU, Mitra P, Zaman S, Uddin KN et al. Clinical Characteristics and Outcome of Diabetic Ketoacidosis: Experience at BIRDEM, Dhaka, Bangladesh. Bangladesh Crit Care J September 2015; 3: 53-56
22. Welch BJ, Zib I. Case Study: Diabetes Ketoacidosis in Type 2 Diabetes: "Look Under the Sheets". Clinical Diabetes. 2004;22:198-200.
23. Vignati L, Asmal AC, Black WL, Brink SJ, Hare JW. Coma in diabetes. In: Marble A, Krall LP, Bradley RF, et al (eds). Joslin's Diabetes Mellitus. 12th edn. Philadelphia: Lea and Febiger, 1985: 526-48.
24. Matoo VK, Nalini K, Dash RJ. Clinical profile and treatment outcome of diabetic [14] ketoacidosis. J Assoc Physicians India. 1991;39:379-81.
25. Westphal SA. The occurrence of diabetic ketoacidosis in non-insulin dependent [15] diabetes and newly diagnosed diabetic adults. Am J Med. 1996;101:19-24.
26. Chiasson JL, Jilwan NA, Belanger R, et al. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycaemic hyperosmolar state. CMAJ. 2003;168:859-66.
27. Barski L, Nevzorov R, Harman-Boehm I, Jotkowitz A, Rabaev E, Zektser M, et al. Comparison of diabetic ketoacidosis in patients with type-1 and type-2 diabetes mellitus. Am J Med Sci 2013;345:326–30.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 03-03-2018; **Accepted:** 21-04-2018; **Published:** 05-05-2018