ORIGINAL ARTICLES

CLINICAL CHARACTERISTICS OF DIABETIC KETOACIDOSIS IN TYPE 2 DIABETES MELLITUS IN BANGLADESHI ADULT PATIENTS

HOSSAIN MZ[1], MUHAMMAD A[2], AZAD KAK[3], DEB SR[4], RAHMAN MM[5], ANWAR ASMT[6], KARMAKER M[7], AMIN R[8]

Abstract

A cross-sectional observational study on 50 patients of diabetic ketoacidosis (DKA) was conducted in the Medicine Department of Dhaka Medical College Hospital from January 2011 and December 2011 to find out the clinical, biochemical and hematological features of these patients. DKA can no longer be considered pathognomonic of type 1 DM alone. Substantial numbers of adult DKA episodes occur in patients with a history of type 2 DM. The aim of this study was to review the clinical characteristics, precipitating factors, short-term outcome in terms of mortality and factors influencing mortality of DKA in Type 2 DM patients among the Bangladeshi population. Significant statistical difference between male and female subjects of the study in terms of hemoglobin level, ESR, serum creatinine, serum potassium, urinary ketone body levels and in clinical features like increased rate and depth of respiration, air hunger, fatigue and weight loss. Patients with lower consciousness had more severe hypotension, tachycardia and pyrexia. Non-adherence to antidiabetic medication (especially insulin) for previous diagnosis of DM and infection was found to be the most important precipitant of DKA and were present in most of the cases. Pattern of infection in DKA patients were sought and associated organism identified. Mortality remained at 6% in our series within first five days of admission with DKA. Statistically significant difference in pulse, blood pressure, fasting blood sugar, ESR, GCS score, shock and coma were noted in patients with and without mortality within 5 days. Despite the mentioned limitations of our study, it provides substantial insight regarding DKA in type 2 DM in Bangladeshi adult population. Type 2 DM can present as DKA in majority of adult patients in Bangladesh as well as in South Asia. Physicians should be aware of this complication and adopt early aggressive management.

Keywords: *Diabetic ketoacidosis, type 2 diabetes mellitus, gender-related differences, clinical characteristics, mortality, Bangladesh.*

J Dhaka Med Coll. 2012; 21(2) : 131-139.

Introduction

Diabetic ketoacidosis (DKA) is a common and serious acute complication of diabetes mellitus (DM). DKA was formerly considered a hallmark of type 1 DM, but also occurs in individuals who lack immunologic features of type 1 DM and who can sometimes subsequently be insulin independent.[1] They are more likely to be obese and have an absence of autoimmune markers.[2] Patients with type 2 diabetes are susceptible to DKA under stressful conditions as their relative insulin deficiency is worsened by metabolic decompensation resulting from the insulin-resistance enhancing effect of counter-regulatory hormones, dehydration, and metabolic acidosis.[2, 3]

Recent epidemiologic studies[4] estimate that hospitalizations for DKA have increased during the past two decades. Part of this increased frequency of admissions may be related to the increased prevalence of type 2 diabetes.[5]

1. Dr. Mohammad Zaid Hossain, Assistant Professor, Department of Medicine, Dhaka Medical College, Dhaka.
2. Dr. Ali Muhammad, Honorary Medical Officer, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
3. Prof. Khan Abdul Kalam Azad, Professor of Medicine, Dhaka Medical College
4. Dr. Sudip Ranjan Deb, Resident Physician, Dhaka Medical College Hospital, Dhaka
5. Dr. Md. Mostafizur Rahman, Assistant Registrar, Department of Medicine, Dhaka Medical College
6. Dr. ASM Tanim Anwar, IMO, Department of Medicine, Dhaka Medical College
7. Dr. Madhabi Karmaker, HMO, Department of Medicine, Dhaka Medical College
8. Dr. Robed Amin, Assistant Professor, Department of Medicine, Dhaka Medical College, Dhaka.

Correspondence: Dr. Mohammad Zaid Hossain, Assistant Professor, Department of Medicine, Dhaka Medical College, Dhaka.

DKA results from relative or absolute insulin deficiency combined with counter-regulatory hormone excess (glucagon, catecholamines, cortisol, and growth hormone). Both insulin deficiency and glucagon excess, in particular, are necessary for DKA to develop.[1] This leads to increased production of ketone bodies and glucose in the liver.[6] The cardinal biochemical features are hyperglycemia, hyperketonemia and metabolic acidosis.[7]

DKA is often precipitated by increased insulin requirements, as occurs during a concurrent illness.[7] In general, the common precipitating factors include infections, treatment non-compliance and concomitant cardiovascular disease.[2,8]

In South Asian population, the prevalence of Type 2 DM is high and expected to increase significantly over the next 20 years[9], while rates of Type 1 DM remain low. In this population, more patients presenting with DKA appear to have a clinical picture of Type 2 DM rather than autoimmune Type 1 DM. Patients with Type 2 DM are generally considered to have some circulating insulin and are therefore able to avoid excessive lipolysis and ketogenesis.[1, 10] The perception that DKA is rare in the South Asian population or carries a better prognosis in Type 2 DM patients, needs to be addressed.

To our knowledge, there has been a paucity of population-specific data focusing on clinical characteristics of DKA patients for Bangladesh. The prevalence, precipitating factors and mortality of DKA among indigenous Bangladeshi population classified as having Type 2 DM have not been extensively described. The aim of this study was to review the clinical characteristics, precipitating factors, short-term outcome in terms of mortality and factors influencing mortality of DKA in Type 2 DM patients among the Bangladeshi population.

Methods

The study was carried out in Dhaka Medical College Hospital in Dhaka, Bangladesh, between January and December of 2011. All Bangladeshi patients admitted with a clinical diagnosis of DKA in the medicine wards as assessed by attending physician were recruited into the study. DKA was defined as a capillary blood glucose level of >13.9 mmol/L, and plasma bicarbonate level of <15 mmol/L and presence of ketone in urine strip test with no prior history of intake of captopril or penicillamine or any other drugs that may cause false-positive reactions with urinary ketone assay. All patients included in the study had phenotypic features of type 2 diabetes (such as obesity, acanthosis nigricans, or a family history of type 2 diabetes) and none of them had a previous diagnosis of type 1 DM. None of the patients had any other comorbidity or taking any medications other than antidiabetic medications by those who were diagnosed previously as diabetic. A total of fifty subjects (34 males and 16 males, age range 21–80 years) satisfied the inclusion criteria. The participants were informed about the nature of the study and written informed consents were taken.

Data for male and female patients with DKA were collected, analyzed, and compared. Information on the patients' demographic characteristics, compliance with previously instituted antidiabetic medications, precipitating factors of DKA, and clinical and laboratory data were obtained. Mortality of DKA patients included in the study was noted within a period of 5 days of admission.

Blood glucose levels were initially measured on admission using glucometer. The fasting blood glucose and other biochemical and hematological investigations were performed in the laboratory with automated analyzer. Ketonuria was determined by the nitroprusside reaction through strip test at bedside or in the laboratory. Calculated osmolality was measured by adding two times of serum sodium and potassium concentration in mmol/L with random blood sugar value in mmol/L obtained on admission. All laboratory data for analysis were obtained on the day of admission to the medicine department. Statistical analysis was performed by using SPSS version 20.0 (IBM Corporation, USA). Continuous data were expressed as mean±SD and median with minimum and maximum values present in the data. Independent-Samples T Test was used for comparison of the continuous variables. The results for categorical data are presented as count and percentage of total patients. Pearson Chi-Square Test was used to compare categorical data. A two sided P value <0.05 was considered to indicate statistical significance.

Results

Demographical profile of patients is shown in figure 1. Clinical and investigation profile of male and female patients in our study are listed in table-I and table-II. No statistically significant difference was noted for age, vital parameters, consciousness level and most of the biochemical and hematological investigations between male and female DKA patients (P>0.05). However, male patients had higher hemoglobin level (P<0.001), serum creatinine (P<0.001) and serum potassium (P=0.034) when compared to the female patients. On the other hand, female patients presented with higher Erythrocyte Sedimentation Rate (ESR) when compared to their male counterpart (P=0.002). There was also statistically significant difference (P=0.047) between urinary ketone body levels of male and female patients with male more commonly having higher levels.

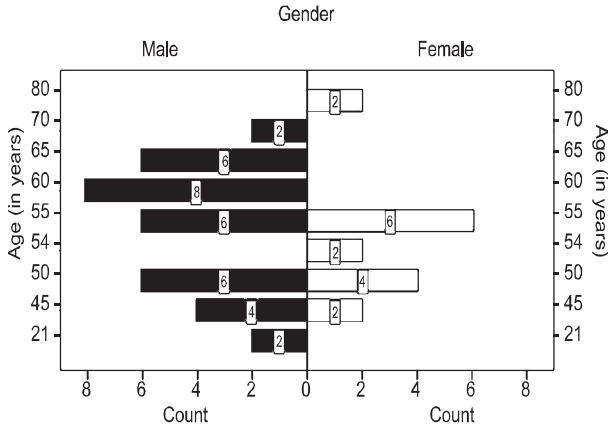

Fig.-1: *Age distribution of patients.*

Table-I

Comparison of clinical and investigation profile of male and female patients with diabetic ketoacidosis (continuous variables)

	Gender	Mean ± Standard Deviation	Median (minimum; maximum)	P value
Age (in years)	Male	54.76 ± 11.16	55 (21; 70)	.824
	Female	55.50 ± 10.16	54.50 (45; 80)	
Pulse (beats/min)	Male	105.38 ± 13.41	100 (86; 142)	.942
	Female	105.06 ± 16.57	98 (85; 138)	
Systolic blood pressure (mmHg)	Male	85.44 ± 7.11	85 (75; 100)	.261
	Female	88.13 ± 9.11	90 (70; 100)	
Diastolic blood pressure (mmHg)	Male	55 ± 8.53	55 (35; 70)	.452
	Female	57.19 ± 11.40	60 (30; 70)	
Core temperature (°F)	Male	100.847 ± 1.75	101 (98; 104)	.302
	Female	100.281 ± 1.89	100.45 (97; 103.60)	
Haemoglobin (mg/dl)	Male	12.7206 ± .95	12.45 (11.60; 15.24)	<.001
	Female	11.7463 ± .52	11.62 (10.98; 12.55)	
Total count of WBC (cells/cmm)	Male	11684.71 ± 4858.43	12750 (4500; 20000)	.373
	Female	13006.25 ± 4827.35	13000 (5500; 20000)	
Erythrocyte Sedimentation Rate (mm in 1st hour)	Male	50.56 ± 17.25	42.50 (30; 81)	.002
	Female	71.31 ± 20.66	82 (42; 95)	
Serum sodium (mmol/L)	Male	134.06 ± 4.83	135 (125; 144)	.750
	Female	134.50 ± 3.83	134 (130; 140)	
Serum potassium (mmol/L)	Male	4.2888 ± 1.19	3.80 (2.70; 6.80)	.034
	Female	3.7875 ± .41	3.83 (2.94; 4.20)	
Serum bicarbonate (mmol/L)	Male	12.29 ± 3.54	12 (8; 20)	.104
	Female	14.38 ± 4.29	14 (9; 20)	
Fasting blood sugar (mmol/L)	Male	14.1753 ± 6.20	11.80 (8.85; 28)	.513
	Female	13 ± 5.12	10.50 (8.90; 24.90)	
Random blood sugar (mmol/L)	Male	22.6829 ± 11.37	20.60 (12.40; 60.70)	.282
	Female	19.4250 ± 5.32	16.55 (14.30; 29.40)	
Calculated osmolality of plasma (mmol/L)	Male	299.3982 ± 15.76	295.56 (282.60; 346.10)	.571
	Female	296.9925 ± 8.57	299.70 (281.96; 307.28)	
Serum creatinine (mg/dl)	Male	1.9768 ± 1.51	1.40 (1; 7.10)	<.001
	Female	.8444 ± .14	.83 (.65; 1.18)	

*Derived from Independent-Samples T Test

When clinical profile of the male and female patients was compared, male patients were found to have higher frequency of increased rate and depth of respiration (P = .001), air hunger (P = .034), fatigue (P=0.001), weight loss (P=0.006). No difference of statistical significance was noted in other clinical parameters between genders.

As shown in table-III, vital parameters (e.g. pulse, blood pressure and temperature) were more away from normal range in DKA patients with lower consciousness level documented with Glasgow Coma Scale (GCS). Patients having poorer GCS level presented with more severe hypotension, tachycardia and pyrexia.

It has been reported that up to 25% of cases of DKA do not have an identified precipitating event.[11, 12] Fortunately, in our study, we were able to identify a precipitant in all our cases. As shown in table-IV, non-adherence to antidiabetic medication (especially insulin) for previous diagnosis of DM was the single most important factor precipitating DKA (52.9% of male and 50% of female).

Table-II

Comparison of clinical and investigation profile of male and female patients with diabetic ketoacidosis (categorical variables)

Clinical features		Gender				P value*
		Male		Female		
		Count	% in male	Count	% in female	
Hypoxia		6	17.6%	0	0.0%	.073
History of excessive physical activity		6	17.6%	0	0.0%	.073
Shock		5	14.7%	4	25.0%	.377
Coma		5	14.7%	3	18.8%	.716
Dehydration		18	52.9%	6	37.5%	.308
Increased rate and depth of respiration		16	47.1%	0	0.0%	.001
Air hunger		8	23.5%	0	0.0%	.034
Fruity breath		6	17.6%	0	0.0%	.073
Fatigue		26	76.5%	4	25.0%	.001
Weight loss		18	52.9%	2	12.5%	.006
Anorexia		20	58.8%	8	50.0%	.558
Vomiting		22	64.7%	8	50.0%	.322
Diarrhoea		4	11.8%	0	0.0%	.153
Abdominal pain		14	41.2%	6	37.5%	.804
Excessive thirst		12	35.3%	6	37.5%	.880
Polydipsia		8	23.5%	4	25.0%	.910
Polyuria		12	35.3%	6	37.5%	.880
Postural hypotension		8	23.5%	2	12.5%	.363
Hypothermia		2	5.9%	2	12.5%	.421
Urinary Ketone Body	Trace	4	11.8%	6	37.5%	
	1+	4	11.8%	4	25.0%	.047
	2+	14	41.2%	2	12.5%	
	3+	12	35.3%	4	25.0%	

*Derived from Pearson Chi-Square Test

Table-III

Vital parameters in relation to consciousness level in patients with diabetic ketoacidosis at presentation

Glasgow Coma Scale (GCS) score	Vital parameters	Mean±SD	Median (minimum; maximum)
<7	Pulse (beats/min)	131±10	130 (112; 142)
	Systolic blood pressure (mmHg)	77±4	78 (70; 80)
	Diastolic blood pressure (mmHg)	43±10	40 (30; 60)
	Core temperature (°F)	102±2.2	102.3 (97; 104)
7-10	Pulse (beats/min)	104±9	103 (86; 120)
	Systolic blood pressure (mmHg)	84±7	80 (80; 100)
	Diastolic blood pressure (mmHg)	55±7	50 (50; 70)
	Core temperature (°F)	101.4±1.5	101.8 (98; 104)
>10	Pulse (beats/min)	97±7	97 (85; 120)
	Systolic blood pressure (mmHg)	92±5	90 (80; 100)
	Diastolic blood pressure (mmHg)	61±6	60 (50; 70)
	Core temperature (°F)	99.5±1.2	99.2 (97.5; 102.3)

Infection was present in 80% of cases with urinary tract infection predominating in male (29.4%) and pneumonia in female (25%). Urinary tract infection (UTI) was diagnosed when urinary tract infection symptoms, pyuria were present and urine or blood culture was positive. Lung infections in forms of pneumonia, empyema or pulmonary tuberculosis (PTB) were diagnosed when respiratory infection symptoms (productive cough, high fever etc.) and relevant clinical signs were present along with consistent history (e.g. persistent or recurrent pyrexia despite suitable antibiotic therapy in patients with empyema, relevant history for PTB) and identification of organism through sputum smear microscopy or sputum, effusion fluid or blood culture in suitable medias. Cellulitis was diagnosed when cutaneous infection symptoms with swab from wound or pustule positive on microscopy or culture or a positive blood culture in more extensive cases. Acute otitis externa (AOE) was diagnosed when acoustic channel discharge was present and microscopy or culture revealed likely bacteria. Septicemia with no known focus was diagnosed when positive culture in both of two subsequent blood samples from different sites or only one positive culture with significant bacteria, e.g., Gram-negative bacilli without an apparent clinical infectious focus.

Table-IV

Comparison of precipitating factors of diabetic ketoacidosis in male and female patients

		Gender				P value*
		Male		Female		
	Count	Column N %		Count	Column N %	
Adherence to hypoglycaemic therapy	Previously not diagnosed as diabetic	4	11.8%	6	37.5%	
	Non-adherent	18	52.9%	8	50.0%	.060
	Adherent	12	35.3%	2	12.5%	
Precipitating infection	Absent	6	17.6%	4	25.0%	
	Urinary tract infection	10	29.4%	2	12.5%	
	Empyema	4	11.8%	2	12.5%	
	Pneumonia	4	11.8%	4	25.0%	
	Pulmonary tuberculosis	1	2.9%	2	12.5%	.581
	Acute otitis externa	1	2.9%	0	0.0%	
	Cellulitis	3	8.8%	1	6.2%	
	Septicemia with no known focus	5	14.7%	1	6.2%	

*Derived from Pearson Chi-Square Test

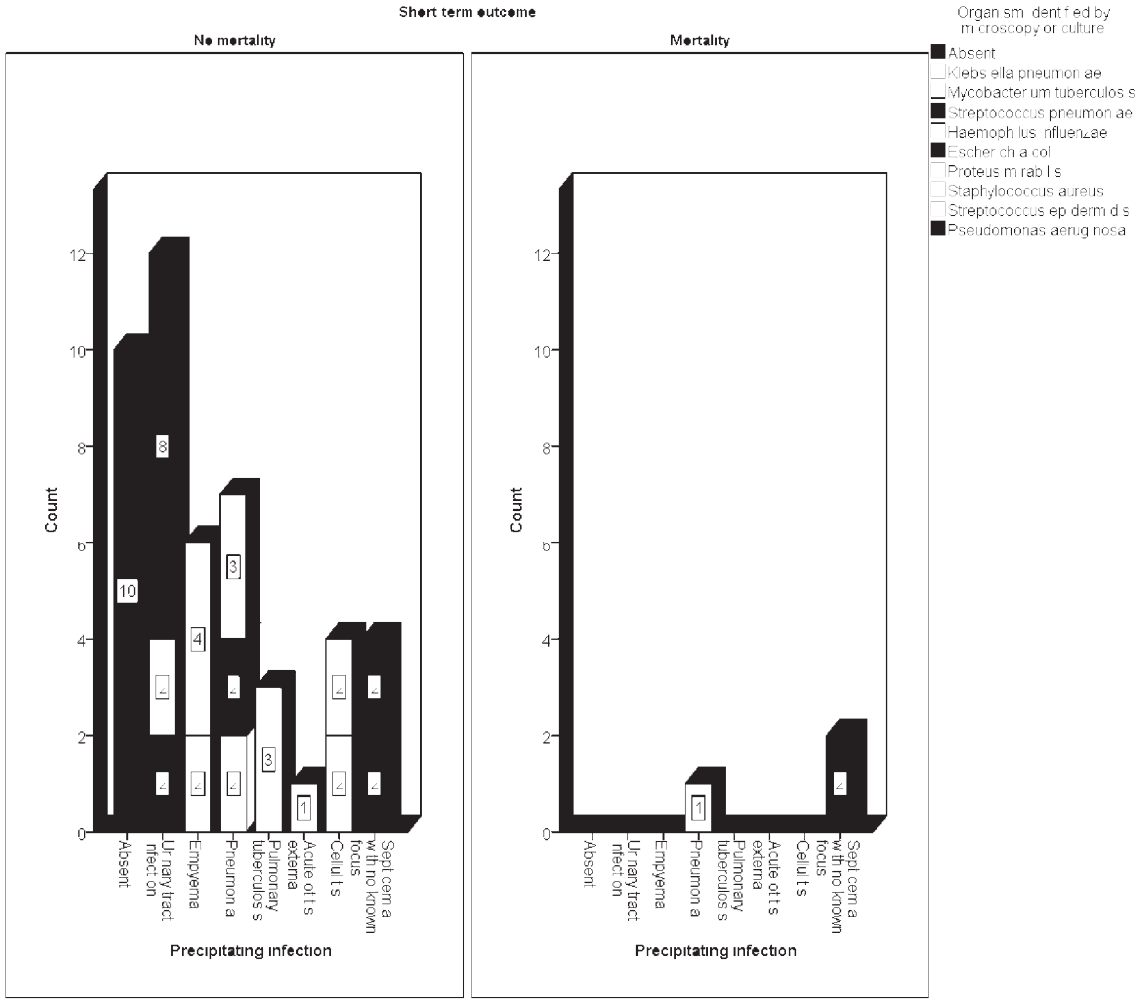

Fig.-2: *Graphical correlation between precipitating infection and organism identified by microscopy or culture with respect to different short-term outcomes in patients with diabetic ketoacidosis*

Figure 3 depicts distribution of organisms identified by microscopy or culture in cases with mortality and without mortality within a short-term (5 days). Septicemia with *Pseudomonas aeruginosa* and bacterial pneumonia with *Klebsiella pneumoniae* comprised the cases with mortality. The major organism causing specific infections include *Escherichia coli* for UTI (in 66.67% of all cases of UTI in our series), *Mycobacterium tuberculosis* for PTB and empyema (in 100% cases of PTB and 66.67% of empyema), *Klebsiella pneumoniae* for pneumonia (in 50% pneumonia cases), *Staphylococcus aureus* for AOE (100% AOE cases), *Staphylococcus aureus* and *Streptococcus epidermidis* for cellulitis (each of them caused 50% cellulitis cases) and Pseudomonas aeruginosa for septicemia with unknown focus (66.67% of septicemia cases).

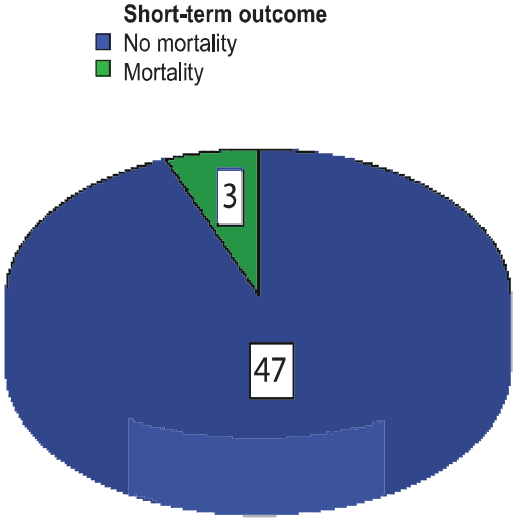

Fig. 3. *Graphical presentation of short-term outcome in terms of mortality in patients with diabetic ketoacidosis*

The mortality rate for DKA varies from less than 5% to 13% in different series.[13, 14] As shown in Figure 3, in our series, it remained at 6% within first five days of admission with DKA.

Due to the limitation of the nature of our study (cross-sectional observational) we were not able to determine independent predictors of mortality of DKA cases in our series. Nevertheless, when comparing different clinical and bedside or laboratory investigation variables in cases with and without mortality within the 5-day period, we did manage to identify variables that were significantly different statistically in the patients with and without mortality. These variables are compared in Table 5 and Table 6 between the patients with and without mortality. Influence on prognosis, at least to some extent, can be attributed to these variables, which include pulse, blood pressure, fasting blood sugar, ESR, GCS score, shock and coma.

Table-V

Comparison of clinical and investigation variables of statistically significant differences in DKA patients with separate short-term outcomes (continuous variables)

	Short-term outcome				P value*
	No mortality		Mortality		
	Mean ± Standard Deviation	Median (minimum; maximum)	Mean ± Standard Deviation	Median (minimum; maximum)	
Pulse (beats/min)	103 ± 12	100 (85; 140)	137 ± 6	138 (130; 142)	<.001
Systolic blood pressure (mmHg)	87 ± 7	85 (75; 100)	75 ± 5	75 (70; 80)	.008
Diastolic blood pressure (mmHg)	57 ± 8	60 (35; 70)	35 ± 5	35 (30; 40)	<.001
Erythrocyte Sedimentation Rate (mm in 1st hour)	56 ± 20	55 (30; 95)	80 ± 19	90 (58; 92)	.047
Fasting blood sugar (mmol/L)	13.24 ± 5.39	10.80 (8.85; 28)	22.53 ± 6.96	24.90 (14.70; 28)	.006

*Derived from Independent-Samples T Test

Table-VI

Comparison of clinical variables of statistically significant differences in DKA patients with separate short-term outcomes (categorical variables)

		Short-term outcome				P value*
		No mortality		Mortality		
		Count	Column N %	Count	Column N %	
Glasgow Coma Scale	<7	5	10.6%	3	100.0%	<.001
(GCS) score	7-10	20	42.6%	0	0.0%	
	>10	22	46.8%	0	0.0%	
Shock	Absent	41	87.2%	0	0.0%	
	Present	6	12.8%	3	100.0%	<.001
Coma	Absent	42	89.4%	0	0.0%	
	Present	5	10.6%	3	100.0%	<.001

*Derived from Pearson Chi-Square Test

Discussion

Type 2 DM arises from alteration in insulin sensitivity and secretion. DKA may occur in Type 2 DM when there is a substantial loss of â-cell function such that the patient needs long-term insulin administration.[15] Our data demonstrate that DKA is not uncommon and can be associated with Type 2 DM in the Bangladeshi population. Forty patients (80%) in our series had a prior diagnosis of Type 2 DM. 34 patients (68%) in our series were male (male:female = 2.13:1). This can be correlated to the evidence that in United States, 60% of urban African American patients with DKA are men.[5] Male predominance in DKA cases is also demonstrated for other populations.[16]

Presence of higher hemoglobin level in men compared to that of women can be attributed as a constitutional feature. ESR can relate to that and also the observation that female had lower infection rate (75%) when compared to male (82.35%) in the study. However, male patients presenting in higher rates with clinical and laboratory evidence of chronic renal failure when compared with female patients is consistent with other studies on DKA.[3] In our series, male patients developed more severe clinical and laboratory evidence of DKA as compared to female patients, although mortality was more in female (12.5% in female as compared to 2.94% in male).

Patients presenting with poorer consciousness level had a poor short-term outcome in our series, as all the cases with mortality had a GCS score <7 on admission.

Non-adherence to antidiabetic therapy, especially insulin therapy in previously diagnosed type 2 DM (omission or inadequate insulin therapy, discontinuation of insulin use) and infection in different forms were the most common precipitators of DKA in our series. These results are consistent with previous studies.[17, 18, 19]

Pattern of organism causing specific infections in our data can be correlated to different series.[20]

Advanced age, mechanical ventilation, and bedridden state were independent predictors of mortality in one series.[3] However, there was no statistically significant difference in age between cases with and without mortality in our series.

Limitations of our study are that it was a cross-sectional observational study and was carried out in only 1 institution. The sample size was rather small to draw inference regarding the whole population in the catchment area of the hospital. Also being a tertiary referral center, the hospital may have missed cases with milder or less severe presentation of DKA. Data collected on the same sample at a later point of time could enable us to make further assumption regarding factors affecting outcome and predicting mortality and optimal management for DKA cases. Poorer economic status of the patients and unavailability of facilities in our institute hindered us to reach a conclusive diagnosis of the type of DM by means of more sophisticated laboratory tests like markers of islet cells autoimmunity pathognomonic of type 1 DM, plasma C peptide level, which is lowered in type 1 DM and compelled us to resort to phenotypic features of type 2 diabetes only to exclude possible type 1 DM cases. We also could not confirm ketonemia by serum or plasma assays for â-hydroxybutyrate level for the same reason.

Conclusion

Despite our limitations, our study provides substantial insight regarding DKA in type 2 DM patients in Bangladeshi adult population. Type 2 DM can present as DKA in majority of adult patients in Bangladesh as well as in South Asia. Physicians should be aware of this complication and adopt early aggressive management.

References

1. Powers AC. Diabetes mellitus. In: Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J. eds. Harrison's principles of internal medicine. 18th ed. New York: McGraw-Hill; 2011: p.2109-37.

2. Kitabchi AE, Umpierrez GE, Murphy MB, Barrett EJ, Kreisberg RA, Malone JI, et al. Management of hyperglycemic crises in patients with diabetes. Diabetes Care 2001; 24: 131–53.

3. Barski L, Harman-Boehm I, Nevzorov R, Rabaev E, Zektser M, Jotkowitz AB, et al. Gender-related differences in clinical characteristics and outcomes in patients with diabetic ketoacidosis. Gend Med 2011; 8(6): 372-7.

4. Centers for Disease Control, Division of Diabetes Translations. 1999 Diabetes Surveillance Report. Available at: http://www.cdc.gov/diabetes/ statistics/survl99/ hap7/contents.htm. Accessed May 7, 2012.

5. Umpierrez GE, Kelly JP, Navarrete JE, et al. Hyperglycemic crises in urban blacks. Arch Intern Med 1997; 157: 669–75.

6. Laffel L. Ketone bodies: a review of physiology, pathophysiology and application of monitoring to diabetes. Diabetes Metab Res Rev 1999; 15: 412-26.

7. Frier BM, Fisher M. Diabetes mellitus. In: Boon NA, Colledge NR, Walker BR. eds. Davidson's principles & practices of medicine. Edinburgh: Churchill Livingstone; 2010: p.809-12.

8. Westphal SA. The occurrence of diabetic ketoacidosis in non-insulin dependent diabetes and newly diagnosed diabetic adults. Am J Med 1996; 101: 19–24.

9. O'Rahilly S, Savill J. Science, medicine, and the future non-insulin dependent diabetes mellitus: the gathering storm. BMJ 1997; 314: 955.

10. Bennett P. Definition, diagnosis, and classification of diabetes mellitus and impaired glucose tolerance. In: Kahn C, Weirr G. eds. Joslin's Diabetes Mellitus. Philadelphia: Lea & Feibiger; 1994: p.193–200.

11. Kitabchi AE, Fisher JN, Murphy MB, Rumbak MJ. Diabetic ketoacidosis and the hyperglycemic, hyperosmolar non-ketotic state. In: Kahn CR, Weir GC, eds. Joslin's Diabetes Mellitus. 13th ed. Philadelphia: Lea & Febiger; 1994: p.738-70.

12. Jabbour SA, Miller JL. Uncontrolled diabetes mellitus. Clin Lab Med 2001; 21: 99-110.

13. Efstathiou SP, Tsiakou AG, Tsioulos DI, Zacharos ID, Mitromaras AG, Mastorantonakis SE, et al. A mortality prediction model in diabetic ketoacidosis. Clin Endocrinol (Oxf) 2002; 57: 595–601.

14. Freire AX, Umpierrez GE, Afessa B, Latif KA, Bridges L, Kitabchi AE. Predictors of intensive care unit and hospital length of stay in diabetic ketoacidosis. J Crit Care 2002; 17: 207–11.

15. Westphal SA. The occurrence of diabetic ketoacidosis in non-insulin dependent diabetes and newly diagnosed diabetic adults. Am J Med 1996; 101: 19–24.

16. Thewjitcharoen Y, Sunthornyothin S. Clinical characteristics of diabetic ketoacidosis in newly diagnosed adult patients. Diabetes Res Clin Pract 2010; 90(2): 43-5.

17. Kitabchi AE, Umpierrez GE, Murphy MB, Kreisberg RA. Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association. Diabetes Care 2006; 29: 2739–48.

18. Hardern RD, Quinn ND. Emergency management of diabetic ketoacidosis in adults. Emerg Med J 2003; 20: 210–3.

19. Wachtel TJ, Tetu-Mouradjian LM, Goldman DL, et al. Hyperosmolarity and acidosis in diabetes mellitus: a three-year experience in Rhode Island. J Gen Intern Med 1991; 6: 495–502.

20. Lin SF, Lin JD, Huang YY. Diabetic Ketoacidosis: comparisons of patient characteristics, clinical presentations and outcomes today and 20 years ago. Chang Gung Med J 2005; 28(1): 24-9.