Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 06, 2023

ORIGINAL RESEARCH

Clinical Profile, Precipitating Events and Metabolic Abnormalities in Patients with Diabetic Ketoacidosis

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is one of the most common medical emergencies in the world. The patient can present with manifestations like ketosis, ketoacidosis, ketoacidosis precoma and coma, but often these manifestations are submerged in the clinical presentation of precipitating illnesses. Objective: To assess the clinical profile and biochemical characteristics in diabetic ketoacidotic patients and to assess the precipitating factors triggering diabetic ketoacidosis.

Methods: This cross sectional study conducted in Mandya Institute of Medical Sciences, Mandya was done from January 2019 to December 2019 involving 50 patients who presented with Diabetes Ketoacidosis. Method of data collection was done by history taking, clinical examination, laboratory and radiological investigations. SPSS V22 was used for statistical analysis. P <0.05 was considered as statistically significant.

Results: Out of 50 patients admitted for diabetic ketoacidosis; 30 were type 2 diabetes (60%) and 20 (40%) were type 1 diabetes mellitus. Average age at the time of presentation was 45 $\pm$ 18.45 years. The most common clinical features at the time of presentation were vomiting (72%), abdominal pain (42%), acidotic breathing (84%) and dehydration (88%). The commonest precipitating factor was infection (50%) followed by irregular treatment (26%) and other factors (26%). The mean values for RBS, HCO3 and pH was 432.9 $\pm$ 88, 13 $\pm$ 3.57 and 7.18 $\pm$ 0.96 respectively. Mortality rate was 8% and factors found to be predict the high mortality were high RBS, low pH, low HCO3, altered sensorium at the time of presentation and comorbid conditions.

Conclusion: Most common precipitating factors are infection and irregular treatment. Most common clinical features at the time of presentation are vomiting, abdominal pain, dehydration, acidotic breathing. There is no significant difference in the clinical and biochemical profile of patients with type 1 and type 2 diabetes. Mortality rate in diabetic ketoacidosis is 8% and the predictors of poor prognosis are; high RBS, low pH, low HCO3, altered sensorium at the time of presentation and comorbid conditions.

Keywords: Clinical and biochemical profile; Diabetic ketoacidosis; Predictors of poor prognosis; Precipitating factors

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INTRODUCTION

Diabetic ketoacidosis (DKA) is one of the most common medical emergencies in the world. The patient can present with manifestations like ketosis, ketoacidosis, ketoacidosis precoma and coma, but often these manifestations are submerged in the clinical presentation of precipitating illnesses.[1] Diabetic ketoacidosis (DKA) is characteristically associated with type 1 diabetes. It also occurs in type 2 diabetes under conditions of extreme stress such as serious infections, trauma, cardiovascular or other emergencies and less often as a presenting manifestation of type 2 diabetes, a disorder called ketosis-prone diabetes mellitus. DKA is more common in young (<65 years) patients, whereas hyperosmolar hyperglycemic state (HHS) most commonly develops in individuals older than 65 years.[2]

Majority of the patients presenting with diabetic ketoacidosis are known diabetics on treatment and the commonest precipitating factors are infections and omission of insulin[3]. The presenting complaints are nausea, vomiting, polydipsia, polyuria and main clinical findings include dehydration, acidotic respiration and confusion or coma.[4] Neurological status in such patients correlates statistically significantly with mean random blood glucose, pH and osmolality. [1]

DKA diagnosis was made by the presence of hyperglycemia (Blood sugar > 250 mg/dl), acidosis (Arterial pH<7.3) serum bicarbonate (<15mEq) and ketonemia[5]. Parameters related to mortality include mainly a) duration of diabetic ketoacidosis prior to admission b) severity of acidosis and c) severity of peripheral vascular insufficiency and d) comorbid conditions. [3]

Therefore, this study was taken to look into the present scenario of clinical presentation of diabetic ketoacidosis, precipitating factors and biochemical abnormalities in the hospitalised patients.

MATERIALS AND METHODS

This Cross sectional study was conducted among patients presenting with diabetic ketoacidosis admitted in Medicine Department Mandya Institute of Medical Sciences (MIMS), Mandya who fulfill the inclusion and exclusion criteria during the study period i.e 12 months (June 2019 - May 2020). Sample size was 50 .

Based on retrospective data of previous year statistics in Medicine department of our hospital average of 4 Diabetic ketoacidosis cases per month admitted identified, hence sample size was considered to be 50 cases.

Sampling Method

All the patients who are diagnosed to have DKA and give consent to participate in the study will be included.

Inclusion Criteria

1. Patients presenting with diabetic ketoacidosis.
2. Patients with accidental detection of diabetic ketoacidosis but primarily admitted for other diseases.

Method of Collection of Data

All patients admitted and diagnosed to have DKA in the hospital explained about this study and informed consent obtained. A detailed history like name, age, gender and presenting complaints are taken and physical examination was performed on the patients on admission. All the points mentioned in the proforma were recorded. The information regarding lab parameters were carried out like haemoglobin, total leukocyte count and differential leukocyte count, random blood sugar estimation, serum electrolytes, renal function test, blood pH analysis, HbA1C, urine

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 06, 2023

ketone bodies, routine and cultures of urine, blood and throat and USG (ultrasound-if clinically indicated), chest x ray PA view and ECG.

Statistical Analysis

All the data collected was entered in an excel sheet and the data statistically analyzed. Descriptive studies (Like percentage, proportion, central tendency, variation) chi-square test, t-test and other suitable statistics were used. A *P* value of <0.05 was considered to indicate statistical significance.

RESULTS

Out of 50 cases of diabetic ketoacidosis, 30 (60.0) were classified as type 2 diabetes mellitus and 20 (40.0) were as type 1 diabetes mellitus. Out of 50 patients, 25 were male (50%) and 25 were female (50%). Male (M) and female (F) ratio M: F was 1:1.

In our study, the minimum age was 16 years and the maximum age was 80 years and the mean age 45 $\pm$ 18.45 yrs. Maximum number of cases 11 (22.0%) observed in the age group 61-70 years. Majority number of cases in type 1 DM were in age group of 20- 40 years, that is 19 (95%). Majority of cases in type 2 DM were in 40-70 years, that is 24 (80.1%).

In our study, DKA can be presenting manifestation in newly detected diabetes mellitus patients. The maximum duration is 25 years.

Table 1: Distribution of patients according to the duration of diabetes in diabetic ketoacidosis

Duration of diabetes (years)	Number n=50 (%)
0-1	12 (24.0%)
2-5	15 (30.0%)
6-10	13 (26.0%)
>10	10 (40.0%)
Total	50

In our study, maximum number of patients were advised on both insulin and oral hypoglycemic drugs (OHD) were 18 (36.0%), 14 (28.0%) were on only OHDs, 10 (20.0%) were on insulin and 8 (16%) were newly detected DM, were not on any prior medications.

Table 2: Precipitating factors in Diabetic Ketoacidosis

Precipitating factors	Type 1 (%) n = 20	Type 2 (%) n =30	Total (%) n =50
Irregular treatment	**10 (50.0)**	**3 (10.0)**	**13 (26.0)**
Infection	**5 (25.0)**	**20 (26.7)**	**25 (50.0)**
UTI	1 (5.0)	5 (16.7)	6 (12.0)
LRTI	3 (15.0)	8 (26.7)	11 (22.0)
Sepsis	1 (5.0)	5 (16.7)	6 (12.0)
Acute pancreatitis	0 (0.0)	1 (3.3)	1 (2.0)
Seizures	0 (0.0)	1 (3.3)	1 (2.0)
Others	**5 (25.0)**	**7 (23.3)**	**12 (24.0)**
MI	0 (0.0)	3 (10.0)	3 (6.0)
Stroke	0 (0.0)	3 (10.0)	3 (6.0)
Fracture	0 (0.0)	1 (3.3)	1 (2.0)

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Newly detected	5 (25.0)	0 (0.0)	5 (10.0)

Pearson Chi square value is 24.35; df is 9 and p <0.004.

In our study, the commonest precipitating factor was found to be infection in 25 (50%) patients. Amongst infections, majority that is 11 (22%) patients had respiratory tract infections and 6 (12%) had urinary tract infections. 13 (26%) were non compliant to medications. 5 (10%) type 1 DM patients presented as DKA. CVA and MI in 3 (6%) and 3 (6%) patients respectively. In 1 (2%) patient surgery was found to be the precipitating factor.

Table 3: Clinical profile in diabetic ketoacidosis before and after treatment

Clinical features	Before treatment N=50 (%)	After treatment N=46 (%)	Chi-square value	P value
Fever	18 (36.0)	5 (10.9)	9.395	<0.001
Dehydration	44 (88.0)	5 (10.9)	57.037	<0.001
Abdominal pain	21 (42.0)	-	24.729	<0.001
Vomiting	36 (72.0)	5 (10.9)	36.590	<0.001
Mental status			17.664	<0.001
Conscious	34 (68.0)	46 (100.0)		
Drowsy	7 (14.0)			
Stupor	9 (18.0)			
Acidotic breathing	42 (84.0)	-	68.693	<0.001

In our study, out of 50 patients 44 (88%) were dehydrated and 42 (84%) had acidotic breathing at the time of admisssion. 21 (42%) patients had abdominal pain and 36 (72%) had vomiting. 9 (18%) were stuporous, 7 (14%) were drowsy and 34 (68%) were fully conscious at the time of admisssion. Out of which 46 patients who survived regained conscious post treatment. After treatment fever, dehydration and vomiting were present in 5 (10.9%) each patients. In our study, urine ketone bodies of majority of patients were 3+ i.e., 18 (36.0%).

Table 4: Comparison of biochemical profile before and after treatment

Measurement	Before treatment		After treatment		P value
	Range	Mean±SD	Range	Mean± SD	
RBS	269- 600	432.9±88	122 - 259	162.6±32.6	<0.001
pH	6.4 - 7.3	7.18±0.96	7.27 -7.38	7.34 ± 0.27	<0.001
HCO_3	7 -18	13 ± 3.57	20 -25	22.9 ± 1.5	<0.001

In our study, at admission Mean ± SD of RBS, pH and bicarbonate values were 432.9 ± 88 mg/dL, 7.18 ± 0.96, 13 ± 3.57 respectively. Following treatment, Mean ± SD of RBS, pH and bicarbonate values were 162.6 ± 32.6 mg/dL, 7.34 ± 0.27, 22.9 ± 1.5 respectively.

In our study, Mean ± SD of RBS, pH in type 1 and 2 DM are similar. No significant difference found. However in our study Mean ± SD of HCO3 in type 1 DM were low compared to type 2 DM.

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Table 5: Comparison of mild, moderate, severe DKA in Type 1 and Type 2 diabetes mellitus based on pH

pH	Type1 (%)	Type 2 (%)	Total (%)
7.25 - 7.30	1 (5.0)	3 (10.0)	4 (8.0)
7.24 - 7.0	16 (80.0)	15 (50.0)	31 (62.0)
< 7.0	3 (15.0)	12 (40.0)	15 (30.0)
Total	20	30	50

Chi-square value is 4.616; p value is 0.099

In our study, out of 50 patients maximum number of patients had moderate acidosis pH 7.24 -7.0 i.e., 31 (62%) and minimum patients 4 (8%) had mild acidosis pH 7.25- 7.30.
There is no significant difference in pH in type 1 and type 2 DM. Among admitted cases, majority 22 (44%) had moderate depletion of bicarbonate levels.

Table 6: Comparison of Biochemical profile of patients who survived and expired

Measurements	Survived	Expired	P value
RBS	432 $\pm$ 88	550 $\pm$ 51.8	0.012
pH	7.18 $\pm$ 0.09	6.57 $\pm$ 0.17	<0.001
HCO_3	13 $\pm$ 3.57	8 $\pm$ 0.82	0.007

Independent sample t test (significance level at $p<0.005$)

In our study, we found to have significant difference in the biochemical parameters like RBS, pH and bicarbonate levels between the patients who survived and expired.
Mean $\pm$ SD of RBS high in expired patients compared to survived patients. Severe acidosis and severe loss of bicarbonate noticed in expired patients.

Table 7: Clinical and biochemical profile of patients who expired

Parameters	Patient 1	Patient 2	Patient 3	Patient 4
Age	28	66	70	58
Sex	M	F	F	M
Duration of DM (years)	0.5	0	15	3
Type	T1	T2	T2	T2
Compliance	No	newly detected	No	No
Fever	Absent	Absent	Present	Absent
Dehydration	Present	Present	Present	Present
Mental status	Stupor	Drowsy	Drowsy	Stupor
UKB	4+	4+	3+	4+
RBS	600	590	507	504
PH	6.8	6.4	6.6	6.5
HCO_3	7	8	8	9
Precipitating Factor	Irregular treatment	MI	LRTI	STROKE

In our study patients who expired, we found severe acidosis (pH - 6.57 $\pm$ 0.17), bicarbonate was (8 $\pm$ 0.82) and high RBS (550 $\pm$ 51.8) found at the time of presentation. Patients were drowsy and

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 06, 2023

stuporous and were severely dehydrated. Many were non compliant to medications. After starting insulin infusion, persisting urine ketone bodies were present.

DISCUSSION

In our study, minimum age is 16 years and maximum age is 80 years. Mean age of distribution is 45 ± 18.45 years. Males were 25 and females were 25. Male: Female ratio was 1:1. This is similar to the study conducted by Tuba Zia et al[6]., at Multan Institute of Kidney Diseases Indus Hospital in 2017. In this study, the mean age was 42.9 ± 12.9 years and Male: Female ratio was 1:180.

Incidence of DKA in Correlation with Type of DM

In our study, among 50 patients type 1 DM were 20 (40%) and type 2 DM were 30 (60%). This result was correlating with studies conducted by Pankaj Seth et al[7]., at Kasturba Medical College, Manipal in 2015. DKA was more common in type 2 DM.

Correlation of Duration of the Diabetes and the Incidence of DKA

In our study, the percentage of freshly diagnosed diabetes as presenting DKA are 5 (10%). All of them are type 1 DM. Maximum duration of DM was 25 years.

The incidence of DKA was more in early period of DM (0 - 1 yr:12 (24%); 2 - 5 yr:15 (30%); 6 - 10 yr:13 (26%); >10 yr: 10 (20%). This shows that the incidence of DKA was more in 0 - 5 years of diabetes duration.

This is similar to the study conducted by Muhammed Kashif et al[8]., at Mayo hospital in 2018. In this study incidence of DKA was 0 - 1 yr:18%; 2 - 5 yr:32%; 6 -10 yr:30%; >10 yr: 20%.

Clinical Profile of DKA

In our study, vomiting (72%) and abdominal pain (42%) were common presenting symptoms. The most common signs were dehydration (88%) and acidotic breathing (84%).

Altered sensorium (32%) was present at the time of presentation.

These findings are consistent with study conducted by Pankaj Seth et al[7]. in Kasturba Medical College, Manipal , 2015. In this study clinical features were vomiting (63%), pain abdomen (43%), dehydration (33.5%) and altered sensorium (30%).

Precipitating Factors of DKA

In our study, infections (50%) were most common precipitating factors. Among infections, respiratory tract infections (22%), urinary tract infections (12%) were more common. Non compliance to medications accounts for about 26%. CVA and MI in 6% and 6% patients respectively.

These results were comparable with study conducted by Sreena Sreekumar T et al[9], at Government Medical College, Kozhikode in 2017. In this study, more common precipitating factors were infections followed by omission of drugs.

In contrast another retrospective study by S.P.Efstathiou et al[10]. conducted from 1992 to 2002 at Greece, reported treatment non-compliance, new diagnosis and infection were 63.7%, 5.8% and 30.5% respectively contributing factors in the overall disease onset.

Biochemical Profile

In our study RBS values ranged from 269 - 600 mg/dL with mean 432.9 ± 88, pH ranged from 6.4 - 7.3 with mean 7.18 ± 0.96 and bicarbonate ranged from 7 - 18 with mean 13 ± 3.57.

In our study, Mean ± SD of RBS, pH in type 1 and 2 DM are similar. No significant difference found. However in our study Mean ± SD of HCO3 in type 1 DM were low compared to type 2 DM.

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In other study done by S.P.Efstathiou et al[10]., at Greece, the study showed there were no significant differences in biochemical parameters in type 1 DM and type 2 DM.
We noted there was severe acidosis, high RBS and severe bicarbonate loss in expired patients. Around 8% patients expired. All fell in to the severe DKA criteria.

Predictors of Mortality

In our study, we noted 4 (8%) mortality occurred. Out of which one death is due to severe DKA with severe hypokalemia. One had Acute MI with cardiogenic shock. Other two patients had LRTI and CVA with aspiration ending up in septicaemic shock.
All 4 patients at the time of presentation had altered sensorium, severe dehydration, high RBS, severe acidosis and persisting UKB for longer time and other comorbities.
In a study conducted by S.P. Efastathiou et al[10]., at Greece concluded that coexisting diseases, severe acidosis pH <7.0, units of insulin required in first 12 hrs >50 and serum glucose >16.7 mmol/L after 12 hrs, depressed mental state and fever after 24 hrs as mortality predictors.

CONCLUSION

In our study most common precipitating factors are infection and omission of insulin or irregular treatment. Altered sensorium, low pH, high RBS, low bicarbonate, coexisting illnesses were associated with increased risk of mortality. Mortality mainly depends on the general condition of the patient, as well as the coexistent medical illness and time of onset of therapy. Preventing DKA with effective communication and proper patient education about warning symptoms of ketosis such as vomiting, abdominal pain and drowsiness are mandatory for early diagnosis and treatment. In conclusion, measures should be taken to rule out DKA in any diabetic and comatose patient to prevent complications and mortality.

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