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Original Research Article

Biochemical profile of diabetic ketoacidosis in type 2 diabetes patients: an observational study

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ABSTRACT

Background: The present study was conducted to assess the clinical profile of type 2 diabetes patients presenting with diabetic ketoacidosis and review their biochemical parameters at the time of presentation.
Methods: The present study was an analytical, cross-sectional study conducted over the period of two years. All the type 2 diabetes patients with diabetic ketoacidosis admitted during the study period constituted the study population, after being subjected to prefixed selection criteria. All the participants were subjected to detailed clinical examination and biochemical analysis during hospitalization and parameters were monitored.
Results: Out of the total 60 type 2 DM patients with DKA studied, 53.3% patients belonged to 51 to 60 years age group and 55% were males. One patient died and 59 survived (mortality rate-1.6%). Comparatively higher mean RBS, higher mean serum osmolality and lower pH were observed in the death case in comparison with those who survived. The patient who died had no statistically significant difference in serum sodium, potassium, calcium and magnesium but had lower serum HCO_3^- than alive patients on admission.
Conclusions: DKA is a serious metabolic complication even in cases of type 2 diabetes and higher RBS, higher Sr Osmolality and lower pH at the time of presentation correlate directly with poorer outcomes.

Keywords: Diabetes ketoacidosis, Type 2 diabetes, Biochemical profile

INTRODUCTION

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate.[1] In India, type 2 diabetes is said to account for more than 90 percent of all diabetes cases.[2] Diabetic ketoacidosis (DKA) remains one of the most frequently encountered diabetes related emergencies and, despite updates in management and increasing standardisation of care, still has an appreciable morbidity and mortality.[3] "Ketosis-prone type 2 diabetes" was discovered as an entity in the 80's.[3,4] Diabetic ketoacidosis occurs most commonly as a result of absolute or relative insulin deficiency; and whilst DKA occurs frequently in those with type 1 diabetes, it can occur in people with type 2 diabetes and other relatively uncommon variants of diabetes as well.[4] In fact, the "expert committee on the diagnosis and classification of diabetes mellitus (2003)" had estimated that the hospitalizations for DKA have increased during the past 2 decades and the major reason of this may be related to the increased prevalence of type 2 diabetes.[5] Available evidence points towards differences in the biochemical parameters of DKA in type 1 and type 2 diabetes cases.[6,7] With the changes in the frequency of DKA and the increased incidence of it in patients with type 2 diabetes mellitus, the question may be posed as to whether there has been any change in the biochemical characteristics of the type 2 diabetes mellitus patients with DKA when they present to the emergency department. This study was therefore undertaken to find out the clinical profile of type 2 diabetes patients presenting with diabetic

ketoacidosis and review their biochemical parameters at the time of presentation.

METHODS

The present study was an analytical, cross-sectional study conducted at Government medical college & hospital, Nagpur (a tertiary care government, teaching hospital in Central India) over the period of two years (from November 2017 to October 2019). Due approval from the Institutional Ethics Committee was taken before commencement of the study. All the type 2 diabetes patients with diabetic ketoacidosis admitted during the period at the study hospital constituted the study population. Following selection criteria were adopted for the selection of study sample: Patients less than 18 years in age, those with alcoholic ketoacidosis, starvation ketoacidosis, lactic acidosis, Ethylene Glycol poisoning along with those not willing to participate were excluded from the study. Informed written consent was elicited from all the enrolled participants (or legal guardian- if the patient is not in a state to give consent). A total of 60 such patients were part of final study sample and were enrolled sequentially from the hospital OPD/emergency.

Those >18 years and previously diagnosed as having diabetes and at some time in their disease, other than a time consistent with the "honeymoon period", were managed with diet and exercise alone or with hypoglycemic drugs, or were noncompliant with their insulin regimen for more than 3 weeks preceding admission were considered as Type 2 Diabetic for the study purpose (operational definition). Detailed history was recorded and clinical examination was conducted. All the basal parameters of diabetic ketoacidosis (random plasma glucose, urea, electrolytes, creatinine, and white blood cell count) were recorded on admission. HbA1C and blood culture and sensitivity (in selected cases) were also investigated. Urine sugar, ketone bodies, routine & microscopy were also undertaken, along with urine culture and sensitivity (in selected cases). Chest X-ray & ECG were undertaken on the basis of clinical requirement.

Standard protocol was used for management of patients with DKA. Random capillary blood glucose was checked every one hourly using a glucose meter. Venous blood samples were drawn at the 0, 1, 6, 12 hours, along with Serum electrolytes, ABG, vitals & urine output and thereafter daily once and the results were charted. Following criteria were adopted for the diagnosis of Diabetes Ketoacidosis: Plasma glucose >250 mg/dl, arterial blood pH <7.3, serum bicarbonate <15 mEq/l and urine positive for ketones.[8] The data were analysed using Statistical Program for Social Science statistical software (SPSS) (version 16) and were presented as frequency and percentage distribution. Association between parameters was analysed using Pearson's Chi-square test. Comparison of mean between parameters was done using unpaired t test and ANOVA. A level of significance of $p<0.05$ was considered as statistically significant.

RESULTS

Out of 60 type 2 DM patients with DKA in the study, 53.3% patients belonged to 51 to 60 years age group, followed by 23.3% belonging to 41 to 50 years. With respect to gender, 55% were males and 45% were females (ratio 1.2:1). (Table 1).

Table 1: Age and gender distribution of the participants (n=60).

Parameters	N	%
Age group (years)		
Up to 40	6	10.0
41 to 50	14	23.3
51 to 60	32	53.3
>60	8	13.3
Total	60	100.0
Gender		
Female	27	45.0
Male	33	55.0
Total	60	100.0

Major precipitating factors of DKA in type 2 DM patients were poor compliance to treatment in 51.7%, pneumonia in 25%, while 21.7% had UTI. Past history of similar illness was present in 18.3% patients; 58.3% were on anti-hypertensive treatment, 5% had IHD, 8.3% had history of stroke while obesity was present in 48.3% patients. Duration of DM in patients of DKA was for 0 to 5 years in 48.3%, 40% had duration of 6 to 10 years and 11.7% had duration within 11 to 15 years. There was family history of DM in 68.3% patients and HTN in 41.7% patients. Out of 60 Type 2 DM patients with DKA, 18.3% were smokers, 16.7% were tobacco chewers while 20% were alcoholics. Around 2/3rd (68.3%) were on OHA, 10% were on OHA and insulin, while 21.7% were newly diagnosed. Omission of treatment of DM was noted in 46.7% type 2 DM patients with DKA. Mean BMI of type 2 DM patients with DKA was 29.0±4.35 kg/m2, pulse was 114.1±11.03 beats/min, SBP /DBP was 119.9±8.8/74.37±8.03 mm of Hg and RR was 21.53±2.8/min. Blood examination revealed that mean Hb was 11.04±0.78 gm/dl, TLC was 9278.9±4081.8 cells/mm^3, BUN was 16.6±9.5mg/dl, Sr Creatinine was 1.4±0.86 mg/dl. Mean urine output of patients was 1126.83±542.05 /day. Mean RBS in type 2 DM patients with DKA was 498.33±175.89 mg/dl and mean HbA1C was 9.15±0.78 %. RBS in type 2 DM patients with DKA was within 330 to 940 range and HbA1C was in 7 to 11 range (Table 2).

In the present study, the mean pulse rate at time of admission was 114.1/min, at 1hour it was 110.1/min, at 6 hours from admission it was 105.6/min, at 12 hours it changed to 103.5/min. On Day 2 mean pulse was 91.63/min, on Day 3 it decreased to 80.93/min, Day 4 it was 76.27/min and on Day 5 it was 80.14/min; indicting a consistently decreasing trend.

Table 2: Broad variables in type 2 DM patients with DKA.

Parameters	N	Minimum	Maximum	Mean	SD
BMI	60	22.49	38.08	29.0	4.35
Pulse	60	97	134	114.10	11.03
SBP	60	90	136	119.90	8.80
DBP	60	52	88	74.37	8.03
RR	60	14	28	21.53	2.80
Hb	60	9	13	11.04	.78
TLC	60	5398	24500	9278.9	4081.8
BUN	60	7.6	40	16.6	9.5
Sr. Creatinine	60	0.7	3.8	1.4	0.86
Urine output	60	100	2100	1126.83	542.05
RBS	60	330	940	510.8	153.5
HBA1c	60	7	11	9.15	0.78

Table 3: Serum electrolytes levels in type 2 DM patients with DKA.

Parameters	N	Minimum	Maximum	Mean	SD
Sr. Na	60	122.0	149.0	131.40	6.42
Sr. K	60	2.8	6.5	4.75	0.67
Sr. HCO3	60	4.6	14.5	11.20	1.91
Sr. Ca	60	8.3	10.8	9.60	0.71
Sr. Mg	60	1.3	2.5	1.83	0.35
Sr. Osmolality	60	267.3	332.2	291.2	15.5
Anion Gap	60	20.8	69.6	44.61	10.32
Arterial pH	60	6.90	7.29	7.23	0.07

The mean SBP at time of admission was 119.9 mmHg, at 1hour it was 119.9 mmHg, at 6 hours it was 121.7 mmHg, at 12 hours it changed to 121.3 mmHg. On Day 2 mean SBP was 122.01 mmHg, on Day 3 it decreased to 123.5 mmHg, Day 4 it was 122.7 mmHg and on Day 5 it was 124.54 mmHg. The mean DBP at time of admission was 74.37 mmHg, at 1hour it was 74.4 mmHg, at 6 hours it was 73.8 mmHg, at 12 hours it changed to 73.7 mmHg. On Day 2 mean DBP was 74.3 mmHg, on Day 3 it changed to 74.28 mmHg, Day 4 it was 73.9 mmHg and on Day 5 it was 75.22 mmHg. The mean RBS at time of admission was 510.8 mg/dl. After treatment there was reduction of RBS so that at 1hour it was 406.92 mg/dl, at 6 hours it was 394.92 mg/dl, at 12 hours it reduced to 364.92 mg/dl. On Day 2 mean RBS was reduced to 322.92 md/dl, on Day 3 it decreased to 258.38 mg/dl, Day 4 it was 193.3 mg/dl and 174.1 mg/dl on Day 5; showing an obvious & expected downward trend. Out of 60 type 2 DM patients with DKA 41.7% had 1+urine ketone bodies, 36.7% had 2+ketone bodies, 3+ketone bodies were in 15% patients while 6.7% had 4+urine ketone bodies in the study. HbA1C was within 6.5 to 7.5 in 5% patients, 21.7% had it within 7.6 to 8.5, 28.3% had it within 8.6 to 9.5 range and 45% patients had HbA1C above 9.5. Out of 60 type 2 DM patients with DKA 8.3% needed less than 100 units insulin, 40% patients had 101 to 150 units of insulin, 11.7% were treated with 151 to 200 units total insulin, while 18.3% were given total insulin between 201 to 250 units. There were 21.7% DKA patients needing more than 250 units of insulin for the management of DKA in the study. Maximum patients i.e. 45% needed 13 to 24 hours of insulin therapy. IV potassium was given to 60% and IV bicarbonates to 3.3% of type 2 DM patients with DKA. With regards to the electrolytes, the levels were as given in table 3. The Serum Osmolality was 291.2 with 15.5 (SD) and in the range of 267.3 to 332.2. Mean Anion gap was in 20.8 to 69.6 range with mean of 44.61 and 10.32 (SD). In type 2 DM patients with DKA mean blood pH was 7.23 with 0.07 (SD) and was in 6.9 to 7.29 range.

With regards to observations regarding monitoring of electrolytes levels in the present study, the Sr Sodium increased with treatment over the 5 days period (from 131.4 to 143.7mEq/l). The mean Serum Potassium concentration in mEq/l at time of admission was 4.75, at 1 hour it was 4.6, at 6 hours from admission it was 4.4, at 12 hours it changed to 4.32. On Day 2 mean Sr K was 4.12, on Day 3 it increased to 4.45, Day 4 it was 4.53 and at Day 5 it was 4.58. The mean Serum Bicarbonate levels (Sr HCO3) showed a slow, consistent rise from 11.2 to 14.69 mEq/l. Mean Serum Calcium concentration in mg/dL at time of admission was 9.6, at 1 hour it was 9.4, at 6 hours & 12 hours it was 9.5. On Day 2 mean Sr Ca was 9.4, on Day 3 it was 9.6, Day 4 it was raised to 9.7 and on Day 5 it was 9.6; indicating a fluctuating pattern. The mean Serum Magnesium concentration indicated a rapid fall in initial hour of treatment (from 1.88 to 1.72 mEq/l, followed by slow rise over next 5 days (1.78 mEq/l). In present study of type 2 DM patients with DKA patients were hospitalized for duration of 3 to 6 days with mean

duration of hospitalization of 4.31 days and 0.77 (SD). With regards to the treatment outcome, all the mild and moderate DKA patients recovered after treatment while one patient i.e. 11.1% in severe DKA had expired in the study. There was statistically no significant difference in outcome of management in patients with severity of DKA in the study. Comparison of mean findings of crucial parameters according to outcome of DKA revealed mean age of alive patients to be 54.25 years as compared to 58 years of the ones who died. Mean RBS in alive patients was 503.6 and 940 in expired patient, at time of admission. HbA1C in alive DKA patients was 10.48 compared to 10 in expired patient. Sr osmolality at time of admission in alive patients was 290.5 compared to 332.2 in expired patient. Anion Gap in alive was 44.29 compared to 63.4 in expired and blood pH was 7.24 in alive and 6.9 in expired patients at time of admission. There was statistically no significant ($p>0.05$) difference of mean age, HbA1C, and anion gap at time of admission with outcome of the patients. There was statistically significant ($p<0.05$) difference of decreased RBS, lower Sr Osmolality and high pH in alive patients compared to the one patient who had died (Table 4).

Table 4: Comparison of mean findings of crucial parameters according to outcome of DKA.

Outcome	Alive (N=59)	Died (N=1)	P value
Age	54.25±8.113	58.00	0.649
RBS	503.6±144.1	940.0	0.004
HbA1c	10.48±10.55	10.00	0.964
Sr. Osmolality	290.5±14.6	332.2	0.006
Anion gap	44.29±10.11	63.4	0.066
Arterial pH	7.24±0.05	6.90	<0.001

DISCUSSION

The present study was conducted to analyse the clinical profile of type 2 diabetes patients presenting with diabetic ketoacidosis and review their biochemical parameters at the time of presentation. A total of 60 type 2 DM patients with DKA were selected and data were analyzed and reviewed. Maximum participants were found in the age group 51 to 60 years i.e. 53.3%. Out of 60 total patients in the present study, 33 (55%) were male & 27 (45%) were female; i.e. slight male preponderance; much in line with available literature. In our study, among the 60 patients 27 (45%) patients were having the HbA1c level more than 9.5 % and 17 patients (28.3%) were having HbA1c level in between 8.6-9.5 %. In fact, poor compliance to treatment (51.7%) was observed to be the single largest precipitating factor towards occurrence of DKA in type 2 DM patients; followed by pneumonia in 25%, urinary tract infection in 21.7%. Sonawani et al reported poor compliance (45%) as the commonest precipitating factor followed by pneumonia (24%) & UTI (22%); much like our observations.[9] Adhikari et al & Welch et al stressed upon the requirement of multiple precipitating factors to be required in diabetic patients to develop DKA.[10,11] Matoo et al reported infection (30%) to be the commonest precipitating factor in DKA, out of other multiple factors.[12] Many patients who were non-compliant to treatment also had infection or other precipitating conditions.

In present study of type 2 DM patients with DKA, obesity was present in 48.3% patients with mean BMI of 29±4.35 kg/m^2. Newton et al had noted that 25% patients to be having BMI >27 at the time of discharge.[6] Narasimham et al described in their study that majority of the patients with type 2 diabetes who experience ketoacidosis were obese; whereas the type 1 patients with DKA were observed to be predominantly lean.[13] Systolic & diastolic blood pressure and respiratory rate were observed to be on the expected lines in DKA. The blood examination revealed mean RBS to range between 510.8±153.5 mg/dl in the present study; also similar to observations of previous studies. The mean urine output of patients was 1126.83±542.05 /day was slightly on the higher side for reasons unknown. Increased mean RBS and mean HBA1C values were observed to be associated with increased amount of ketone bodies in urine. This was in agreement with findings of Sobngwi et al who observed increased ketonuria with increasing hyperglycemia and HBA1C.[14] In present study it was observed that in severe DKA 55.6% patients needed 201 to 250 units of insulin and 44.4% were given more than 250 units of insulin while 77.8% patients needed insulin therapy for 49 to 72 hours and 22.2% had insulin for more than 72 hours duration. A study by Efstathiou et al reported that higher the dose of insulin required and more the duration of insulin therapy as intensive infusion therapy; worse is the prognosis.[15]

The mean serum electrolytes levels in type 2 DM patients with DKA in the present study were observed to be largely similar to the average levels reported previously. The monitoring of changes in electrolytes levels with ongoing treatment were interesting. The consistent rise in serum Sodium and serum Bicarbonate levels and early fall & subsequent stabilization of serum Potassium levels were on expected lines. We observed the serum Calcium to fluctuate over the duration of hospitalization, but not by much. The mean serum Magnesium concentration had a rapid fall in initial hour of treatment, followed by slow rise over next few days. These changes in electrolyte levels were mostly in agreement with previously similar studies who had studied the trend.[9,10,13,14] The patients were hospitalized for duration of 3 to 6 days with mean duration of hospitalization of 4.31±0.77 days. This was similar to Newton et al who noted an average hospitalization of 4.5±3.3 days, consistent with the CDC's national average length of stay for DKA of 4.5 days.[6,16] In present study one patient died and 59 survived. The mortality was 1.6 %. This is agreement to studies done by Kitabchi et al, Faich et al and Ellemann et al who had reported mortality rates ranging from 2.5% to 9% among patients admitted with DKA.[8,17,18] Comparison of mean findings of crucial parameters according to outcome of DKA revealed statistically significant difference of decreased RBS, lower Sr Osmolality and high pH in alive patients compared to

the one who had died. Although the variables studied varied across studies, these three variables happened to be consistently reported as significantly different in almost all the previously similar studies.

CONCLUSION

In conclusion, we report DKA to be a serious metabolic complication even in cases of type 2 diabetes with features as defined and higher RBS, higher Sr Osmolality and lower pH at the time of presentation correlated directly with poorer outcomes.

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