ORIGINAL ARTICLE

CLINICAL AND INVESTIGATIONAL STUDY OF DIABETIC KETOACIDOSIS

Y. V. L. Narasimham[1], A. Krishna Murthy[2], Y. Satyanarayana[3]

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ABSTRACT: BACKGROUND AND OBJECTIVES: To compare the clinical features and biochemical profile in DKA. To assess the response in the patients with standard treatment of DKA. Clinical descriptions of polyuric states resembling diabetes mellitus have been described in the Ebers papyrus of Egypt in 15th century BC.[1,2] Ayurvedic literature from the times of Charaka and Sushrutha, the ancient Indian physicians identified two forms of "MadhuMeha" (Honeyed Urine) in 400 BC.[3] John Rolo of England in 1797 was one of 1st who coined the term diabetes mellitus. William Prout of England described diabetic coma during 1810–20. In 1886, Dreschfeld8 described DKA and HHNS (Hyper osmolar Hyperglycemic Non-ketotic Syndrome). In 1922 Banting, Best, Collip and Macleod isolated and clinically used insulin and later won Nobel prize for that memorable invention. **SETTING:** Inpatients of king George Hospital attached to Andhra Medical College, Visakhapatnam. **METHODS:** Diagnosis of diabetic ketoacidosis was made according to the inclusion criteria. Hyperglycemia >250 mg/dl, acidosis with blood pH <7.3, serum bicarbonate <15 mEq/l, urine positive for ketones. **RESULTS:** Of the 100 patients admitted for diabetic ketoacidosis; 84 had type 2 diabetes (84%) and 16(16%) were type I diabetes. Average age at the time of presentation was 42.9±12.9 years. The commonest precipitating factor was infection (56%) followed by other factors (28%) and irregular treatment (16%). The most common clinical features at the time of presentation were vomiting, abdominal pain, acidotic breathing and dehydration. The values for RBS, HCO3, and pH were 355.3±69.1, 14.9±3.4 and 7.2±0.1 respectively. **INTERPRETATION AND CONCLUSION:** Most common precipitating factors are infection and omission of insulin or irregular treatment. Most common clinical features at the time of presentation are vomiting, abdominal pain, dehydration, acidotic breathing and tachycardia. Mortality rate in diabetic ketoacidosis is 4% and the most notable predictors of poor prognosis are; severity of altered sensorium.

KEYWORDS: Clinical and biochemical profile; Diabetic ketoacidosis; Mortality predictors; Precipitating factors.

INTRODUCTION: Diabetic ketoacidosis (DKA) is one of the most common medical emergencies in the World. The patient may present with wide range of manifestations like ketosis, ketoacidosis, ketoacidosis pre-coma and coma[1] Even though it is more common in type 1 diabetes mellitus, it occurs in type 2 diabetes also, especially in certain situations like infections and other co-morbid illnesses.[3]

Majority of the patients presenting with diabetic ketoacidosis are known diabetics on treatment and the commonest precipitating factors are infections (Sepsis) and omission of insulin.[4] The commonest presenting complaints include nausea, vomiting, polyuria, polydipsia and

main clinical findings include dehydration, acidotic respiration and confusion or coma.[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.[4]

DEFINITIONS OF DIABETIC KETOACIDOSIS: The syndrome consists of the triad of hyperglycemia, ketosis, and acidemia, The consensus among most workers in this field is that an arterial pH of less than 7.3, a bicarbonate value of less than15 mEq/L, and a blood glucose level of greater than 250 mg/dl, with a moderate degree of ketonemia and ketonuria (as determined by the nitroprusside method) are necessary for the diagnosis.

More than 20% of patients of DKA had previously undiagnoseddiabetes.[6,7,8] Another 15% of admissions were of patients with multiple admissions for DKA.[6] Several studies reported that the average age of patients admitted for DKA was 40 to 50 years.[6]

AIMS OF THE STUDY:

1. To compare the clinical features and biochemical profile in diabetic ketoacidosis:
   a. Before after treatment.
   b. Those who survived & expired.

   Important land marks in the history of diabetes and DKA.

John Rolo of England in 1797 was one of 1st who coined the term diabetes mellitus. William Prout of England described diabetic coma during 1810–20. In 1886, Dreschfeld8 described DKA and HHNS (Hyper osmolar Hyperglycemic Non-ketotic Syndrome). In 1922 Banting, Best, Collip and Macleod isolated[1] and clinically used insulin and later won Nobel prize for that memorable invention.

MATERIALS AND METHODS:

Inclusion Criteria: The following patient's were included in the study: -

1. Those patients who were known diabetics either type 1 or type 2 presenting with diabetic Ketoacidosis.
2. Those patients with accidental detection of diabetic Ketoacidosis but primarily admitted for other diseases.

   For admission to the protocol, patients had to meet all the following criteria:

1. Hyperglycemia >250mg/dl.
2. Acidosis with blood pH <7.3.
3. Serum bicarbonate < 15 mEq/l.
4. Urine positive for ketones.

Exclusion Criteria: Age below 14 years and above 69 years

1. Coma case without diabetes.

Place and Period: 100 patients with diabetic ketoacidosis and meeting the inclusion criteria for diabetic ketoacidosis to the medical wards of king George Hospital, Visakhapatnam, over a period of two years (2012 to 2014).

HISTORY AND EXAMINATION: The syndrome consists of the triad of hyperglycemia, ketosis, and acidemia,[9] The consensus among most workers in this field is that an arterial pH of less than 7.3, a bicarbonate value of less than15 mEq/L, and a blood glucose level of greater than 250 mg/dl, with a moderate degree of ketonemia and ketonuria (As determined by the nitroprusside method) are necessary for the diagnosis. More than 20% of patients of DKA had previously undiagnoseddiabetes.[6,7,8] Another 15% of admissions were of patients with multiple admissions for DKA.[6] Several studies reported that the average age of patients admitted for DKA was 40 to 50 years.[6,9] The major precipitating factors for DKA are infection, inter current illness, and omission or inadequate insulin therapy.[10] In DKA there is severe alterations in the metabolism of carbohydrate, protein, and lipid mainly due to lack or ineffectiveness of insulin with concomitant elevation of counter regulatory hormones such as glucagons, catecholamines and cortisol. So hyperglycemia and lipolysis play central roles in the genesis of DKA.

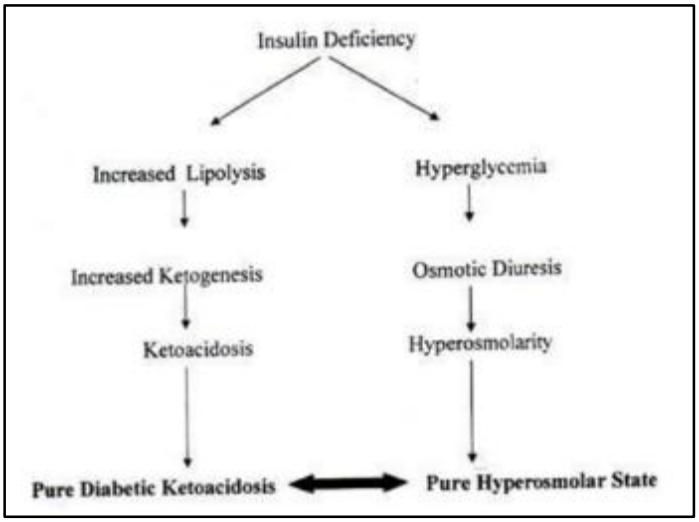


Fig. 1: Proposed biochemical changes that occur during diabetes

Potassium is important for muscle function, and hypokalemia, has been associated with arrhythmias, cardiac arrest, cardiovascular collapse, muscle weakness and respiratory failure. Concentration is restored to >3.3 mEq/ L to avoid arrhythmias or cardiac arrest and respiratory muscle weakness.[11] Potassium should not be given if the patient is uric or serum potassium in more than 5.5 mEq / L.

LABORATORY:

Investigations	Results
Plasma glucose (mg/dl)	> 250
Arterial pH	< 7
Serum bicarbonate (mEq/L)	< 10
Urine ketones by nitroprusside method	Positive
Serum ketones	Positive
Effective serum osmolality (m Osm/kg)	Variable
Anion gap	> 12
Alteration in sensorium or mental obtundation	Stupor / Cons

(potassium less than 3.3 mEq/L) until potassium replacement therapy is given (potassium > 3.5 mEq/kg).

OBSERVATION:

a. **Age:** In this study the minimum age was 14 yrs and the maximum age was 69 years. The mean age was 42.9±12.9 yrs.
b. **Sex:** In our study Male: Female ratio was 1: 1.
c. **Duration of diabetes:** The duration of diabetes in our patients varied from 6 month to 17 years. In the first year of disease there were 9(18%) cases of diabetic ketoacidosis. The maximum number of cases (16) was in the age group 2-5yrs constituting 32%.
d. **Precipitating Factors:** In our study, the commonest precipitating factor was infection (56%). Amongst infections, respiratory tract infection was the commonest cause (12%) followed by urinary tract infection (8%).
e. **Clinical Profile:** In our study the most common symptoms were vomiting and abdominal pain with 74% and 50% respectively. The most commonly found signs were dehydration (82%), and acidotic breathing (80%).
f. **Biochemical Profile:** In our study RBS values ranged from 218-585mg/dl with mean 355.3±69.1. pH ranged from 6.95–7.31 with mean 7.2±0.1.
   Bicarbonate ranged from 5–20 with mean 14.9±3.4.
   There was no significant difference found in the biochemical profile of type 1 and type 2 DM patients.
g. **Insulin Therapy:** In our study, we found that majority of patients required insulin doses between 26-50 units = 21(42%) patients, followed by >100 units i.e. 14 Out of 100 patients, 50 were male (50%) and 50 were female (50%). M: F ratio was 1: 1.

In our study, the minimum age was 14 yrs and the maximum age observed was 69 years Maximum number of cases 40(40%) observed were in the age group 41-50 years. Minimum number of cases 4(4%) were in the age group 21-30 years. Majority of patients are in the age group 31-60, that is 78 patients (78%).

Total No. of cases	Type 1	Type 2
100	16(16%)	84(84%)

Table 1: Distribution of Type 1 and Type 2 diabetes mellitus in diabetic Ketoacidosis

Sex	No. of case	Percentage
Male	50	50
Female	50	50

Table 2: Distribution of Patients according to Sex

Precipitating Factor	No. of Patients (%)
Infection	76(38)
Omission of or inadequate insulin	56(28)
Unknown	4(2)
Newly diagnosed diabetes mellitus*	45(22)
Other+	21(10)
Total	**202(100)**

Table 3: Precipitating factors (incidence)

* No other discernable cause of DKA was determined of the newly diagnosed.

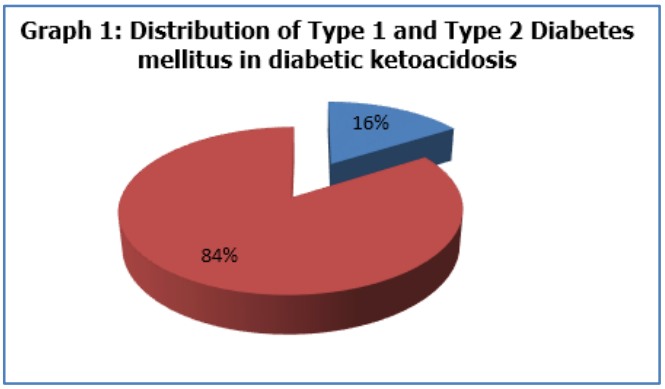
Precipitating Factors	Total(n=100)
I) Irregular treatment	16(16%)
II) Infection:	28(56%)
- UTI	4(8%)
- Acute gastroenteritis	3(6%)
- Diabetic foot	2(4%)
- RTI	6(12%)
- Perianal abscess	2(4%)
- Enteric fever	3(6%)
- CNS infection	2(4%)
- Septic shock	2(4%)
- Acute cholecystitis	2(4%)
-Chronic pancreatitis	2(4%)
III) Others:	14(28%)
- Cerebrovascular accident	4(8%)
- Head injury	2(4)
- Surgery	5(10%)
- IHD	3(6%)

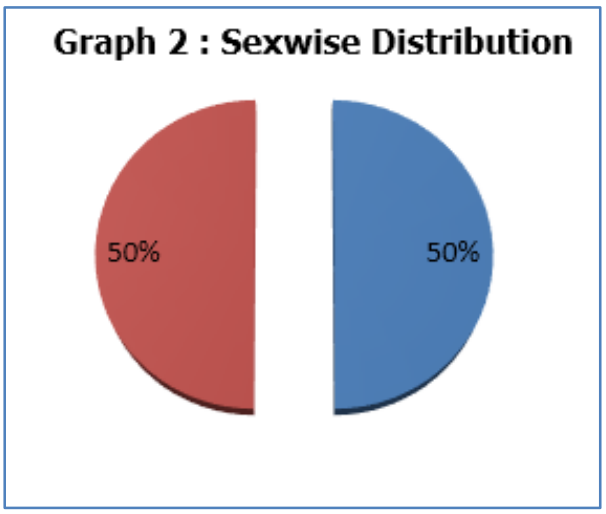
Table 4: Precipitating Factors in Diabetic Ketoacidosis

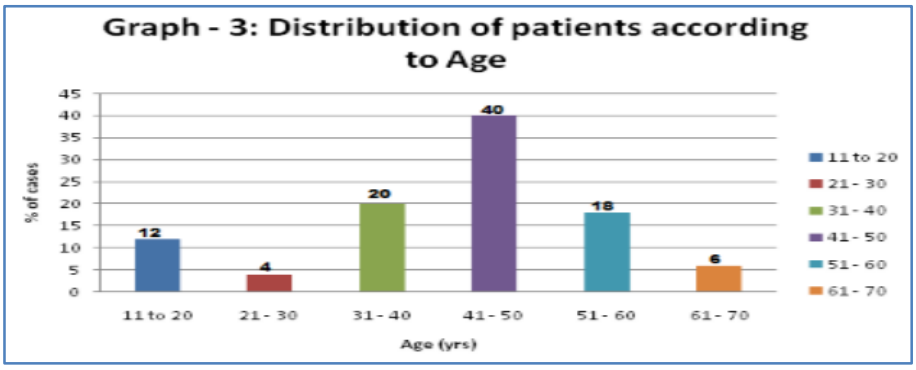
UKB admission	Admission		Post treatment	
	No. of cases	%	No. of cases	%
2+	24	24	-	-
3+	44	44	4*	-
4+	32	32	-	-
Nil	-	-	96	-
Total	**100**	**100**	**100**	**100**

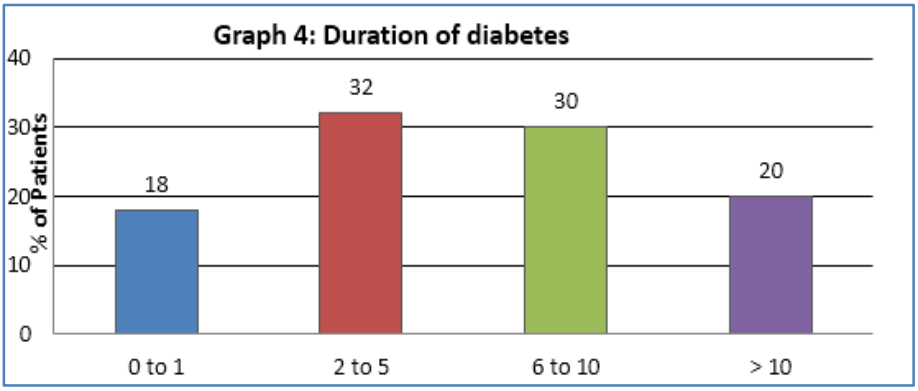
Table 5: Urine ketone bodies before and after treatment

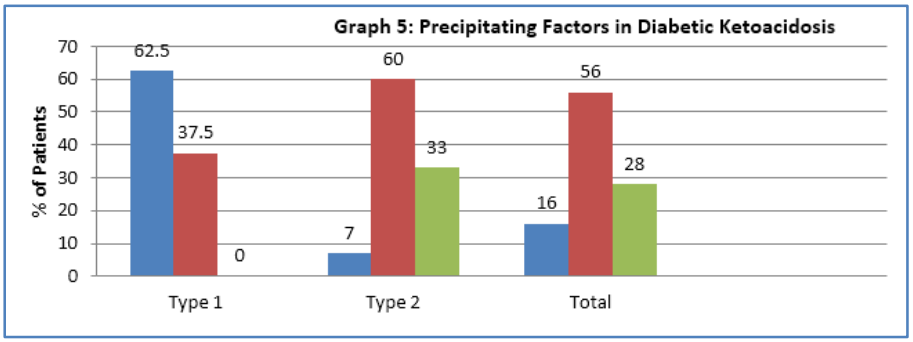
The evolution of the acute DKA episode in both type 1 and type 2 diabetes tends to be much shorter 47. Although the symptoms of poorly controlled diabetes may be present for several days, the metabolic alterations typical of ketoacidosis usually evolve within a short time frame (typically less than 24 hours). Occasionally, the entire symptomatic presentation may evolve or develop acutely and the patient may present in DKA with no prior clues or Follow up care.

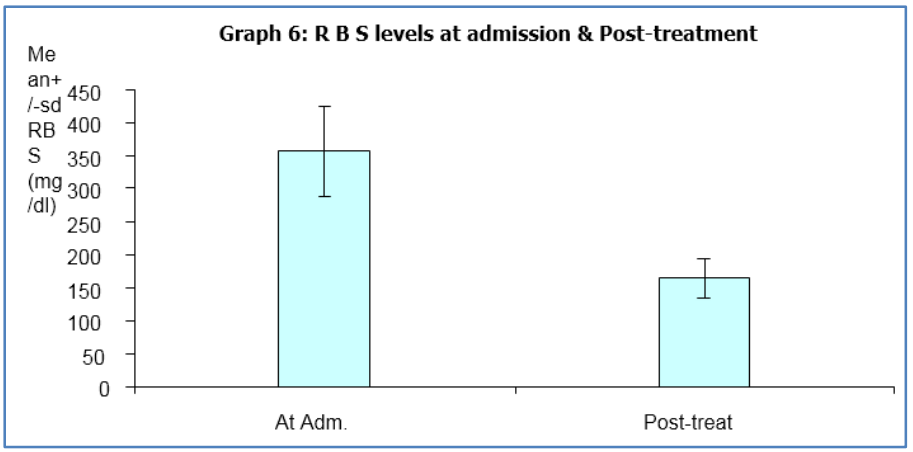





Graph - 3: Distribution of patients according to Age
% of cases
45
40
35
30
25
20
15
10
5
0
12
4
20
40
18
6
11 to 20
21 - 30
31 - 40
41 - 50
51 - 60
61 - 70
Age (yrs)


Graph 4: Duration of diabetes
% of Patients
40
30
20
10
0
18
32
30
20
0 to 1
2 to 5
6 to 10
> 10


Graph 5: Precipitating Factors in Diabetic Ketoacidosis
% of Patients
70
60
50
40
30
20
10
0
62.5
37.5
0
7
60
33
16
56
28
Type 1
Type 2
Total


Graph 6: R B S levels at admission & Post-treatment
Mean+/-sd RBS (mg/dl)
450
400
350
300
250
200
150
100
50
0
At Adm.
Post-treat

CONCLUSION:

- Male to female ratio is 1: 1.
- Diabetes below 20 yrs constituted 12% of patients developing diabetic ketoacidosis. Type 2 diabetics most commonly presents in the age group 40-60 yrs.
- Diabetic ketoacidosis complicates or develops in a significant number of patients with type 2 diabetics.
- Most common cause of diabetic ketoacidosis is infection followed by omission or irregular treatment.
- Most common presenting clinical features are vomiting, abdominal pain, dehydration, acidotic breathing altered sensorium and fever.
- There is no significant difference in the clinical and biochemical profile of patients with type 1 and type 2 DM developing ketoacidosis.
- Mortality rate of diabetic ketoacidosis is 4%.

SUMMARY:

1. The average age of our patients was 42.9±12.9 years. Minimum was 14yrs and maximum was 69yrs. Majority were in the age group of31- 60 yrs.
2. Male: Female ratio was 1: 1.
3. Out of 50 patients, 8 were type 1 diabetes and 42 were type 2diabetics.
4. Infection was the most common precipitating factor or cause followed by irregular treatment. Other factors included head injury, CVA, IHD and surgery.
5. Duration of diabetes was found to be 2-5 years in majority (32%) of patients.
6. Most of the patients had presented with vomiting, abdominal pain, fever dehydration and acidotic breathing.
7. The mean values for RBS, HCO3, and pH were 355.3±69.1, 14.9±3.4, and 7.2±0.1 respectively.
8. By comparing the clinical and biochemical parameter before and after treatment it was found that, factors that predicts the bad prognosis or mortality are severity of acidosis, severity of altered sensorium, amount and duration of insulin therapy required to clear UKB, RB Sat the time of presentation and comorbid conditions.

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AUTHORS:

1. Y. V. L. Narasimham
2. A. Krishna Murthy
3. Y. Satyanarayana

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam.
2. Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam.
3. Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Y. V. L. Narasimham,
10-106, Sri Sai Raghavendra Residency,
Revenue Colony,
Visakhapatnam-43,
Andhra Pradesh.
E-mail: yatirajula_narasimham@yahoo.com

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