A STUDY OF CLINICAL AND LABORATORY PROFILE OF DIABETIC KETOACIDOSIS

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ABSTRACT

BACKGROUND AND OBJECTIVES

To compare the clinical features and biochemical profile in Diabetic Ketoacidosis. To assess the response in the patients with standard treatment of DKA.

MATERIALS AND METHODS

50 patients with diabetic ketoacidosis and meeting the inclusion criteria for diabetic ketoacidosis to the medical wards of SSMC, over a period of 18 months (October 2013 to March 2015). Diagnosis of diabetic ketoacidosis was made according to the inclusion criteria. Hyperglycaemia >250 mg/dl, acidosis with blood pH <7.3, serum bicarbonate <15 mEq/l, urine positive for ketones.

RESULTS

Of the 50 patients admitted for diabetic ketoacidosis; 42 had type 2 diabetes (84%) and 8 (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, acidic breathing and dehydration. The values for RBS, HCO3, and pH was 355.3±69.1, 14.9±3.4 and 7.2±0.1 respectively. There was no significant difference in clinical and biochemical profile of patients with type 1 and type 2 diabetes. Mortality rate was 4% and factors found to be significant predictors were comorbid condition, severity of mental status, severity of dehydration, Random blood sugar at the time of presentation, severe acidosis, and doses and duration of insulin therapy required to clear Urinary Ketone bodies.

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. 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 4% and the most notable predictors of poor prognosis are; severity of altered sensorium, severity of comorbid condition, severe dehydration, severe acidosis and doses and duration of insulin required for clearing UKB.

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 but often these manifestations are submerged in the clinical presentation of precipitating illnesses. 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.2 A lot of improvements have been made in early detection and management of both ketoacidosis and the comorbidities to the extent of making changes in the natural history of this illness.

Therefore, certainly, it will be interesting to look into the present day scenario of clinical presentation of Diabetic Ketoacidosis and the course of illness in the hospitalized patients.

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.3 The commonest presenting complaints include nausea, vomiting, polyuria, polydipsia 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 Parameters related to mortality include mainly:

a. Duration of diabetic ketoacidosis prior to admission.
b. Severity of acidosis.
c. Severity of peripheral vascular insufficiency.
d. Comorbid conditions.3

This study was therefore undertaken to compare the clinical features and biochemical profile in diabetic ketoacidosis patients, and the response in the patients with standard treatment of diabetic ketoacidosis.

METHODOLOGY

This study consists of 50 inpatients admitted SSMC, Tumkur.
The following Patients were included in the Study
1. Those patients who were known diabetics either type 1 or type 2 presenting with diabetic Ketoadisis.
2. Those patients with accidental detection of diabetic Ketoadisis but primarily admitted for other diseases.

For admission to the Protocol, Patients had to meet all the following Criteria:
1. Hyperglycaemia >250 mg/dl.
2. Acidosis with blood pH <7.3.
3. Serum bicarbonate <15 mEq/L.
4. Urine positive for ketones.
5. Plasma positive for Ketones.

On admission, a careful and detailed history was recorded and thorough clinical examination was conducted. All the points mentioned in the proforma were recorded. Additional information if any was recorded and the following investigations were carried out:

Haematological and Biochemical Investigations
a. Hb% WBC count total and differential.
b. Blood sugar estimation was done by Folin Wu method.
c. Serum electrolytes by flame photometry.
   Normal Values
   - Serum sodium 136-145 mEq/L.
   - Serum potassium 3.6 – 5.5 mEq/L.
d. Blood urea estimation
   - Urea Nesselerization method.
   - Normal 25-40 mg/dl.
e. Serum creatinine
   - Normal: 0.5 – 1.9 mg/dl.

Radiological Investigation
- X-ray chest: PA view to see lung pathology.
- E.C.G: To see evidence of ischaemic heart disease and K+ changes in serial.
- ECG’s.
- Urine: For routine and microscopy.
- Urine culture and sensitivity.

URINE SUGAR
Benedict’s Qualitative Test
If the original blue colour of reagent changes to green/yellow-orange/brick red. This is very easy and convenient method for detection and to judge the nature of control of diabetes, but urine sugar estimations are often misleading due to variable renal threshold and do not reflect the sugar. Urine sugar estimation, still today is one of the widely practiced method as it is convenient and can be taught to the patient and easily done at home.

Urine Albumin
By heat and acetic acid test; results are interpreted as 1+ to 4+. This is one of the most basic investigation to judge renal involvement in diabetic patient. The degree of proteinuria parallels renal damage.

URINE FOR KETONE BODIES
Rothera’s Test for Acetone and Acetoacetic Acid
A volume of 10 ml urine is saturated with an excess of ammonium sulphate crystals. 3 drops of a strongly freshly prepared solution of sodium nitroprusside and 2 ml of strong ammonia solution are then added. A deep permanganate colour is produced by acetone and acetoacetic acid. If Rothera’s test is negative, ketones are absent. Presence of ketone bodies in urine is suggestive of diabetic ketoacidosis. In diabetic ketoacidosis serial urine sugar and acetone estimation gives idea regarding the course of the disease and outcome of therapy.

Blood pH
Normal arterial blood pH is 7.35 to 7.45. Arterial pH between 7.25-7.3 is mild DKA, pH between 7.24-7.1 is moderate DKA and pH <7 is severe DKA.5

Serum Bicarbonate
It is measured in mEq/L. Normal value is 22-26 mEq/L.
Mild DKA 15-18 mEq/L, Moderate DKA 10-15 mEq/L, Severe DKA <10 mEq/L 5

RESULTS

Table 1: Precipitating Factors in Diabetic Ketoacidosis

<table>
<thead>
<tr>
<th>Precipitating Factors</th>
<th>Type 1 (n=8)</th>
<th>Type 2 (n=42)</th>
<th>Total (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I) Irregular Treatment</td>
<td>5 (62.5%)</td>
<td>3 (7%)</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>II) Infection:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- UTI</td>
<td>3 (37.5%)</td>
<td>25 (60%)</td>
<td>28 (56%)</td>
</tr>
<tr>
<td>- Acute gastroenteritis</td>
<td>1 (12%)</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>- Diabetic foot</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- RTI</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- Perianal abscess</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- Enteric fever</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- CNS infection</td>
<td></td>
<td>3 (6%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>- Septic shock</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- Acute cholecystitis</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- Chronic pancreatitis</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>II) Others:</td>
<td></td>
<td>14 (28%)</td>
<td>14 (28%)</td>
</tr>
<tr>
<td>- Cerebrovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>accident</td>
<td></td>
<td>4 (8%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>- Head injury</td>
<td></td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>- Surgery</td>
<td></td>
<td>5 (10%)</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>- IHD</td>
<td></td>
<td>3 (6%)</td>
<td>3 (6%)</td>
</tr>
</tbody>
</table>

In this study, the commonest precipitating factor was found to be infection in 28 patients (56%). 8 (16%) patients had either omitted treatment or were on irregular treatment. In 5 (10%) patients, surgery was found to be the precipitating factor and CVA and IHD in 4 (8%) and 3 (6%) patients respectively. Amongst infections, majority i.e. 6(12%)
patients had respiratory tract infection and 4 (8%) had urinary tract infection.

**DISCUSSION**

**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. In one study the age range was 6 to 80 yrs and the mean age was 36 yrs. Several other studies have reported that the average age of patients admitted for diabetic ketoacidosis was 40 to 50 years.

**Sex**
In our study Male: Female ratio was 1:1. One study has shown a higher incidence of diabetic ketoacidosis in women compared to men.

**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) were in the age group 2-5 yrs. constituting 32%. In one study the duration of diabetes varied in the following manner: Up to 1 year incidence of diabetic ketoacidosis was 2.2%, 1-5 years 2.8%, 6-10 yrs 2.9% and >10 yrs 4.3%.

**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%). Other studies have also shown that the most common cause in the development of diabetic ketoacidosis is infection and other factors were CVA, omission or irregular treatment. One study reported infection as the leading precipitating factor in 41%. Another study reported non-compliance with treatment (63.7%), infection (30.5%) and newly diagnosed (5.8%) as the cause.

**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%). Abdominal pain was complained by 50% of patients. Altered sensorium was found in 30% of patients.

**In One Study the Clinical Features were as Follows**
polyuria (75.2%), polydipsia (74.4%), polyphagia (33%), nausea (83.4%), vomiting (78.5%) and abdominal pain (51%). Another study reported polyuria, polydipsia, abdominal pain and vomiting as the predominant clinical features.

**Biochemical Profile**
In our study RBS values ranged from 218-585 mg/dl with mean 355±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. The patients who expired had severe acidosis and most of the parameters fell in to the severe diabetic ketoacidosis criteria. Another study showed the similar findings where there were no significant differences in type 1 and type 2 diabetes developing diabetic ketoacidosis.

**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 (28%) patients and 51-75 units 7 (14%) patients, for clearing UKB. Patients who expired required >140 units of insulin. Insulin was given for 13-24 hrs as infusion in majority of patients i.e., 23 (46%) patients to clear UKB. Patients who expired required >72 hours for the same. A study reported that higher the dose of insulin required and more the duration of insulin therapy, as intensive infusion therapy, to clear UKB; worse is the prognosis.

**Predictors of Bad Prognosis or Mortality**
In our study we found that the factors which were significantly different or altered in patients who expired than those who survived were severity of acidosis, severity of altered sensorium, severity of dehydration, amount and duration of insulin therapy required to clear UKB and RBS at the time of presentation, and comorbid conditions. Both the patients who expired were in septicaemic shock. One study on mortality prediction model in diabetic ketoacidosis reported the following as the predictors of mortality. These were severe coexisting diseases, pH <7.0 at presentation, 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. Another study reported that septic shock was the most frequent cause of death (31%) and poor prognostic indicators were, older age, hypotension, low Na, pH and HCO3, and high urea.

**CONCLUSION**
- Male to female ratio is 1:1.
- Diabetes below 20 yrs. constituted 12% of patients developing diabetic ketoacidosis. Type 2 diabetes most commonly presents in the age group 40-60 yrs.
- Diabetic ketoacidosis complicates or develops in a significant number of patients with type 2 diabetes.
- 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%.
- Some of the clinical and biochemical parameters may indicate bad prognosis; most notably, severity of altered sensorium, severity of comorbid condition, severe dehydration, severe acidosis, doses and duration of insulin required for clearing UKB.

**REFERENCES**