Clinicodemographic profile of diabetic ketoacidosis and its management in hospitalized children – A prospective study

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ABSTRACT
Background: Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with Type 1 diabetes (T1DM). In developing countries, mortality is between 6 and 24%. Recent studies have documented that DKA in association with cerebral edema (CE) accounted for a mortality of 1–24% with a high rate of permanent neurologic morbidity. Objective: The objective of the study was to study the clinicodemographic profile, clinical presentation at the time of admission, management, and complications of patients diagnosed as T1DM with DKA. Materials and Methods: A prospective observational study was conducted among children admitted in PICU MGM hospital, Warangal, Telangana between December 2016 and November 2018. Children up to the age of 18 years diagnosed as T1DM who presented with DKA were included in the study. Sociodemographic profile, dietary intake, and treatment history of children were collected using a pre-designed pro forma. Clinical features and management were noted. Results: A total of 51 children were included in the study. Among them, 32 (62.74%) cases were newly diagnosed and 19 (37.2%) were previously diagnosed. A majority of the children belonged to lower socioeconomic status with 40% of the children suffering from severe grade of malnutrition. Classical symptoms of polyuria, polydipsia, and polyphagia were observed in 32 patients (62.74%). Vomiting was observed in 59% of cases, tachypnea in 82.35%, and abdominal pain in 29.41% of cases. About 54.90% of cases presented with severe and 33.3% with moderate DKA. Administration of regular insulin was the main modality of management in all cases. The major complication observed was hypoglycemia followed by cerebral edema. Conclusion: Cerebral edema with septic shock is a life-threatening complication of patients suffering with DKA. Active management with regular insulin can avert major complications and can lead to better outcomes.

Key words: Children, Clinicodemographic profile, Complications, Diabetic ketoacidosis, Management

Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with Type 1 diabetes (T1DM), with a case fatality rate ranging from 0.15 to 0.31% in developed countries [1] and 6–24% in developing countries. Recent studies have documented that DKA in association with cerebral edema (CE) accounted for a mortality of 21–24% with a high rate of permanent neurologic morbidity [2-5]. Indian studies have shown that the overall prevalence of T1DM ranges from 3.8 to 10.2 with an urban predominance [6-8].

DKA is considered a common presentation and serious metabolic disturbance, leading to hospitalization of children with T1DM. It is diagnosed in approximately 35–40% of children along with T1DM and is characterized by a biochemical triad of hyperglycemia, ketonemia (ketonuria), and acidemia. The risk of developing DKA in established T1DM cases is 1–8%/patient/year [9-11]. The likelihood of DKA occurring at the onset of T1DM varies between 15 and 67% [12,13]. DKA along with the major complication of CE is the most important cause of mortality and severe morbidity in children with diabetes [14,15]. There is limited literature available on the clinic profile and management of Indian children with DKA.

Thus, the present study was conducted to understand the clinical demographic profile, post-acidotic management, and complications associated with DKA.

MATERIALS AND METHODS
The present study was a prospective observational study, conducted between December 2016 and November 2018 at a tertiary hospital of South India. Children up to the age of 18 year diagnosed as T1DM presenting with DKA, i.e., hyperglycemia (blood glucose >200 mg/dl), acidosis (pH <7.3), and bicarbonate (<15 mmol/L) with associated glycosuria, ketonuria, and ketonemia were included in the study. Children who were >18 years old, with T1DM but without DKA and those whose parents did not give consent were excluded from the study.

Sociodemographic profile, dietary intake, and treatment history of children were collected from the patients or relatives using a pre-designed and pre-tested pro forma. Modified Kuppuswamy classification for socioeconomic status (SES) and IAP classification for nutrition grades were used. A
detailed clinical examination of the child was carried out. The study was approved by the Institutional Ethical Committee. A written informed consent was taken from the parents/guardians.

For all patients (newly diagnosed/known cases), C-peptide and HbA1c samples were collected before starting of IV insulin drip and fluids. Urine examination was done for sugars and ketones every 6 hourly, until ketoacidosis was corrected using glucose and ketone strips. All the patients were managed with Milwaukee protocol. Children presenting with shock were given 10 ml/kg bolus of NS. Children with moderate-to-severe DKA were considered to have severe dehydration (a deficit of 80–100 ml/kg) and corrected by fluid therapy.

Insulin infusion was started at a rate of 0.1 units/kg/h. The infusion was stopped when the children were alert, able to tolerate oral feeds, metabolically stable (blood pH >7.3, bicarbonate >15 mmol/L, and blood sugar around 250 mg/dl). The resolution of DKA was based on resolution of acidosis on ABG (pH >7.3), normalization of blood sugar level, and stabilization of clinical condition. All patients during treatment were monitored for CE and the diagnosis was made by computed tomography scan in cases where the neurological status declined after initial improvement or there was persistently poor neurological status without any obvious cause.

Data were analyzed using SPSS version 17. Qualitative data were expressed in percentages, proportions, and quantitative data in mean and standard deviation. Tests of significance, one-way Chi-square, and unpaired t-test were applied. p<0.05 was considered statistically significant.

RESULTS

A total of 51 children were admitted during the study period and among them, 32 (62.74%) were newly diagnosed and 19 (37.2%) were previously diagnosed. Females constituted 60% of the study population (p=0.33) and male-to-female ratio was 1.2:1. A total of 17 females and 15 males were newly diagnosed. A majority of patients (66%) were in the age group of 10–14 years with 12% in 0–4 year age group. There was increasing proportion of patients with age (Table 1).

Majority of the patients belongs to lower and upper lower SES. Most of the patients (31.37%) belonged to Grade III malnutrition according to the IAP score (Table 2). About 50.98% of study population’s body mass index was below 5th percentile. Clinical features have been presented in Table 3.

While assessing the severity of DKA, 6 cases had mild, 17 cases had moderate, and severe DKA was observed in 28 patients and there was no statistically significant difference in proportions of severity of DKA among known and new cases (p=0.80).

A total of 22 cases (43.13%) recorded blood glucose levels >400 mg/dl, 16 cases (31.3%) had levels of 300–400 mg/dl, and 13 cases (25.49%) were with 200–300 mg/dl levels. A total of 45 children (88.23%) had HbA1c levels above 8%, of these 30 (58.82%) had >10%. None of the patient had HbA1c level <5.6%. The mean HbA1c level for freshly diagnosed and known cases was almost similar which indicated very poor glycemic control (Table 4).

The C-peptide levels were significantly higher in known cases; however, there was no significant difference in management of cases as doses of insulin administered and fluids required to correct were almost similar. DKA was corrected within 24 h in 25 cases (49.01%), within 36 h in 6 cases (11.7%), 48 h in 11 cases (21.56%), 60 h in 3 cases (5.88%), and 72 h in 5 cases (9.80%). A total of 41.17% of cases had hypokalemia during acidotic phase.

Out of 11 patients with complications, 7 (63.66 %) had hypoglycemia and all had HbA1c>10%, which indicated poor glycemic control. There were three patients with cerebral edema, and one patient who died had CE along with septic shock and respiratory failure. The average duration of hospital stay was 11–14 days in 45.09% of cases, 7–10 days in 33.33% , 15–20 days in 11.76%, and >21 days in 9.80% of cases.
DISCUSSION

The findings from the present study suggested that the DKA could present in children at an early age. Studies conducted by Bhardwaj et al. reported mean age of 11.4±4.4 years and Basavanthappa et al. reported the median age of 7.5 years with a minimum age of presentation as 2 years [16,17].

A majority (70.58%) of patients were from lower SES as our hospital is the only tertiary care government hospital within a radius of 55 km. Basavanthappa et al. also reported 88% of the cases belonging to lower SES [17]. Malnutrition was observed in 78.41% of patients, and similar observation was made by Basavanthappa et al., where they reported malnutrition in all admitted patients with DKA.

In the present study, tachypnea was the most common presentation at the time of admission in patients with DKA, followed by polyuria, polydipsia, and polyphagia, whereas Bhardwaj et al. reported abdominal pain as the most common presenting symptom followed by fast breathing [16]. These findings were in accordance with the findings observed by Basavanthappa et al. and Kanwal et al. [17,18]. The non-specific signs and symptoms of DKA may be difficult to diagnose as symptoms of abdominal pain, vomiting, and fast breathing can be misleading toward diagnosis of gastroenteritis, acute abdomen, and pneumonia [19]. Diagnosing DKA in newly diagnosed T1DM poses a greater challenge due to overlapping of signs and symptoms.

In the present study, 88.23% had HbA1c levels >8% which were in accordance with the observations made by Soliman et al. and Syed et al. inferring poor glycemic control in patients suffering with DKA [20,21]. Severe form of DKA was observed in most of the patients and these findings were similar to the studies conducted by Basavanthappa et al. and Bhardwaj et al. stating that patients in PICU suffer with severe forms of DKA compared to mild-to-moderate forms [16,17].

A total of 41.17% of cases had hypokalemia during acidic phase. Basavanthappa et al. reported hypokalemia as the common therapy-related complication in 26.9% of the cases [17]. CE was seen as one of the complications in all the studies related to DKA. In the present study, 1 (1.96%) death was recorded due to CE with septic shock and respiratory failure. In the study conducted by Basavanthappa et al., six cases died during the management of DKA and the cause of death was CE in four of the cases. A study by Glaser et al. showed that CE was the most threatening complication of DKA in children, occurring in 0.3–1% of DKA episodes [5].

Syed et al. in their study reported 3.4% deaths in patients with DKA [21]. Agarwal et al. concluded that CE at admission was common in Indian children with DKA and should be suspected with severe metabolic acidosis and inappropriate prior fluid treatment [22]. Ponjeba and Varadarajan noted that overall mortality among children presenting with DKA as the initial presentation in T1DM was 12.8% [23]. The study had a few limitations. The sample size was small and the study was conducted at a single center. Hence, the results cannot be generalized to larger population.

CONCLUSION

The main stay of treatment is administration of regular insulin which can avert major complications and lead to better outcomes. Further multicentered trials with larger sample size are required.

REFERENCES


Table 4: Laboratory parameters and details of management in PICU

<table>
<thead>
<tr>
<th>Parameter</th>
<th>New cases</th>
<th>Known cases</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean plasma glucose level on the 1st day of admission</td>
<td>484.41±90.21</td>
<td>518.79±66.45</td>
<td>0.158</td>
</tr>
<tr>
<td>HbA1c levels (normal=≤5.60%)</td>
<td>11.50±2.65</td>
<td>11.56±3.10</td>
<td>0.94</td>
</tr>
<tr>
<td>C-peptide levels (normal=0.48–5.05ng/ml)</td>
<td>0.13±0.09</td>
<td>0.32±0.77</td>
<td>0.001*</td>
</tr>
<tr>
<td>Requirement of regular insulin to correct ketoacidosis (units/kg)</td>
<td>78.95±46.14</td>
<td>79.45±46.06</td>
<td>0.11</td>
</tr>
<tr>
<td>Requirement of fluids to correct ketoacidosis (L)</td>
<td>4.65±2.43</td>
<td>4.42±2.20</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean insulin requirement at discharge (intermittent acting insulin u/kg)</td>
<td>1.02±0.16</td>
<td>1.31±0.17</td>
<td>0.12</td>
</tr>
</tbody>
</table>

*Significant

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