

Original Research Article

Clinical profile and outcome of children presenting with diabetic ketoacidosis at a tertiary care hospital in Dakshina Kannada

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is the most serious metabolic disturbance of type 1 diabetes mellitus (T1DM) and about 25 to 40% of the newly diagnosed T1DM children present with DKA. This research was conducted to study the clinical profile and identify the precipitating factors at time of presentation of DKA and to correlate the type onset of disease with the severity of DKA and the treatment outcome.

Methods: Ambispective record based study of children admitted in the paediatric ward of a tertiary care hospital with DKA between 01 July 2019 and 31 January 2022.

Results: A total of 19 patients were enrolled and the mean age of presentation was 10.79 ± 4.17 years with a female predominance. The family history of type 2 DM was noted in 73.7% and osmotic symptoms in 68.4% of the patients. 52.6% of the patients presented in severe DKA. Mean HbA1C noted was $15.14 \pm 2.74\%$. Acute Kidney Injury was present in 10.5% of the patients. Pneumonia was the major precipitating factor. The average length of hospital stay was 7.42 ± 3.27 days. There was no significant correlation with the type of onset of T1DM and the treatment outcome. There was a significant reduction in HbA1c ($p < 0.05$) on follow-up.

Conclusions: This study highlights the need for creating awareness, early referral and timely management of T1DM presenting not only in DKA but also during the ambulatory management.

Keywords: Diabetic keto acidosis, Metabolic disorder, HbA1C

INTRODUCTION

Diabetic ketoacidosis (DKA) is the end outcome of metabolic issues brought on by a severe insulin deficit or insulin inefficiency. The latter occurs when under stress because the hormones released (counter-regulatory hormones, such as glucagon, growth hormone, adrenaline, and glucagon) inhibit insulin from functioning properly.^{1,2} The major presentation of type 1 diabetes is DKA, a common paediatric endocrine emergency and a situation of absolute or relative insulin insufficiency (T1DM). Whereas children with established T1DM have a 1-8% chance of developing DKA per patient per year, 25-40% of children with newly diagnosed T1DM show DKA.²

DKA is a serious complication of type 1 diabetes in children and is associated with a higher risk of morbidity and mortality.^{3,4} In contrast to children with T1DM, who have already been diagnosed, newly diagnosed diabetics frequently miss insulin doses due to stress and infection.⁵ Although the increasing prevalence of diabetes mellitus in India, DKA and other related consequences continue to represent a neglected public health problem.⁶ There have been relatively few research studies that have investigated the clinical profile and consequences of DKA in children in India, but we need more to evaluate the risk, incidence, and strategies for reducing morbidity and death as well as raising awareness, especially among the rural populations of our state and nation.⁷

It is essential for physicians to comprehend the clinical profile of DKA in children and the current trends in outcomes arising from this condition in order to enhance the management protocols currently employed for DKA in children in India. Hence, it was aimed for the current study to analyse the clinical characteristics and prognosis of children who presented with DKA at a tertiary care centre in the Karnataka district of Dakshina Kannada. To the best of our knowledge, we are reporting this to be first study evaluating the outcomes of DKA in T1DM in children in our district Dakshina Kannada.

METHODS

This was an ambispective record based study of children admitted with DKA between through 2019 July to January 2022 the paediatric ward of a tertiary care level hospital. A total of 19 patients were enrolled in this study. The study subjects included all patients with biochemically confirmed DKA according to ISPAD guidelines admitted to the PICU. DKA is defined as blood glucose concentration greater than 11 mmol/l/200 mg/dl, blood pH less than 7.3 (serum bicarbonate level <18 mmol/l) and ketonemia (beta hydroxy butyrate >3 mmol) or moderate or large ketonuria.⁸

The severity of DKA is classified based on the degree of acidosis into mild, venous pH <7.3 (bi-carbonate <18 mmol/L); moderate, pH <7.2 (bicarbonate <10 mmol/l); and severe, pH <7.1 (bicarbonate <5 mmol/l).⁸ The patient's hourly clinical features (heart rate, respiration rate, blood pressure, urine output, oxygen saturation, sensorium, and presence of headache and vomiting) were documented from the patient's records. Details of 4-6 hourly venous blood gas, serum electrolytes, and hourly blood sugar were recorded. At admission, metabolic, renal and liver parameters were also noted. Urinary and blood ketones were done every 12th hourly. Measured blood sodium levels >150 mmol/l and below 135 mmol/l, respectively, were used to define hyponatremia and hyponatremia. Serum potassium levels over 5.5 mmol/l and below 3.5 mmol/l, respectively, were considered to be hyperkalaemia and hypokalaemia. The treatment regimen was carried out in accordance with the recommended standards.⁸

The treatment for DKA is said to be complete when the ketoacidosis resolved.^{9,10} Replacement potassium was provided as prescribed by the guidelines. When bacterial illness was suspected, antibiotics were initiated as per institution protocol. All treatment information, including information about fluids consumed prior to admission, was gathered with a particular focus on the emergence of cerebral oedema, complications that appeared both before and after therapy were compiled. After recovery, patients were followed up beyond discharge. The four pillars of T1DM management such as medical nutritional therapy, diet advise, regular monitoring of blood glucose, physical activity were reinforced and All patients were sent on newer insulins, education charts/sick days' rules and

emergency contact numbers were given. The repeat hba1c values at a 3-month outpatient department follow-up were recorded to see the effect of our education and training on them.

Data's were analysed using statistical package for the social sciences (SPSS) v.23 software continuous variables and expressed as mean and standard deviation. Categorical data is expressed as number and percentages and continuous variables compared with Mann-Whitney U test. Categorical variables with Chi-square or Fisher's exact test. P value <0.05 was considered statistically significant. Permission was obtained from the Yenepoya Ethical Committee before conducting the study (YEC-1/2022/212).

RESULTS

In our current study, out of the 19 patients, 68.4% cases were between 10-16 years (peripubertal and adolescence) while rest 31.6% cases were between 1 and 10 years of age. The mean age of patients was 10.79±4.17 years. Among these 13 were females (68.4%) and rest males. Mean weight was 28kg and mean height was 134 cm. Mean duration of diagnosis noted was 1.81±2.28 years (Table 1). The family history of type 2 DM was noted in 73.7% of the patients. Osmotic symptoms such as nausea, vomiting, abdominal pain were noted in 68.4% of the patients.

Table 1: Demographic characteristics, clinical manifestations, biochemical alterations of patients (n=19).

| Variable | Mean±SD |
|--|----------------|
| Age (in years) | 10.79±4.17 |
| Glucometric random blood glucose (mg/dl) | 521.21±77.62 |
| HCO ₃ (meq/l) | 11.35±7.35 |
| HbA1c % | 15.14±2.74 |
| S. potassium (meq/l) | 3±1.5 |
| S. sodium (meq/L) | 130±1 |
| Creatinine (mg/dl) | 0.52±0.28 |
| S. phosphate (mg/dl) | 3.54±0.8 |
| Urea (mg/dl) | 23.79±11.09 |
| Blood ketone (IU/l) (n:6/19) | 1.42±0.35 |
| Urine ketone | Most common:3+ |

The degree of ketoacidosis was mild for 26.3% of the patients, moderate for 21.1% of the patients and severe in 52.6% of the patients. The mean glucometric random blood glucose (mg/dl) level was 521.21±77.62. Hyponatremia was the most common dyselectrolytemia (57.9%). Mean HbA1C noted was 15.14±2.74%. Pneumonia was found to be major precipitating factor with 31.6% of incidence followed by UTI (26.3%) and acute gastroenteritis (10.5%) in newly diagnosed cases while among the old cases (known T1DM) the most common precipitating factor was poor adherence to insulin as seen

in 73% of cases. Acute kidney injury was present in 10.5% of the patients (Figure 1).

There is no significant correlation observed between DKA versus age, duration of diagnosis, Glasgow coma scale score in our current study. One patient had clinical hepatic glycogenopathy (Mauriac disease). All known cases of T1DM had lipodystrophy. Early onset diabetic nephropathy was seen in 2 patients. The average length of stay in the hospital was 7.42 ± 3.27 days while the average duration of hospital stay was 7 ± 2.2 days for known T1DM and 7 ± 1.3 days for new onset cases.

Time taken for ketoacidosis correction in known T1DM was 40 ± 8.2 hours while it was 35 ± 6.6 hours in new onset cases. Time taken to shift over to subcutaneous insulin was 41 ± 8.5 hours in known cases while new onset cases had 39 ± 7.1 hours (Table 2). Time taken for ketoacidosis correction and the severity of DKA was correlated where mild cases took 28.40 ± 19.30 hours for correction while moderate and severe cases took 31.00 ± 21.26 and 42.60 ± 18.48 hours respectively. Only 1 case of cerebral oedema was present in our cohort and no mortality was noted.

Table 2: Correlation of treatment outcome and type onset of disease.

| S. no. | Clinical outcome variable | Known case of t1dm (mean \pm SD) | New onset t1dm (mean \pm SD) | P value (<0.05) |
|--------|---|------------------------------------|--------------------------------|-----------------|
| 1 | Duration of hospital stay (days) | 7 ± 2.2 | 7 ± 1.3 | 0.100 |
| 2 | Time taken for ketoacidosis correction (hours) | 40 ± 8.2 | 35 ± 6.6 | 0.391 |
| 3 | Time taken to shift over to s/c insulin (hours) | 41 ± 8.5 | 39 ± 7.1 | 0.679 |

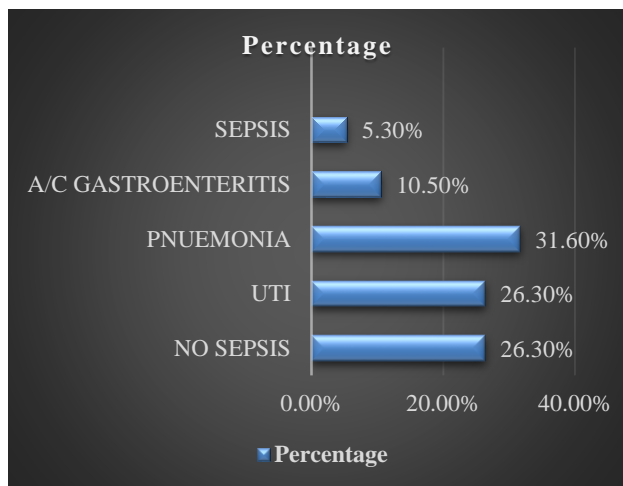


Figure 1: Precipitating factor of DKA (new onset T1DM).

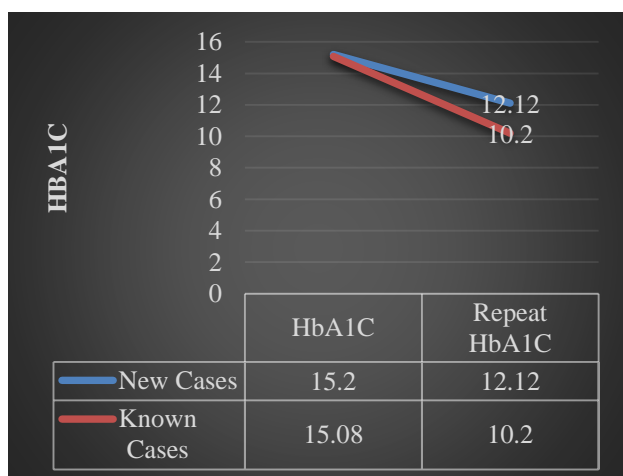


Figure 2: Mean difference of HbA1C and repeat HbA1C with type of onset DM.

All patients were sent on newer insulins, education charts/sick days' rules and emergency contact numbers were given. There was a marked reduction in hba1c with a p value of 0.0001 ($p < 0.05$) seen among 10/19 patients who followed up after 3 months of treatment with medical nutritional therapy and newer insulins (lower mean hba1c seen in known cases compared to new cases) (Figure 2).

DISCUSSION

In this study, we analysed 19 children diagnosed over a period of 2 years and 6 months which fulfilled the criteria of DKA. Nearly 68.4% cases were in age group 10-16 years (peripubertal and adolescence) while rest 31.6% cases were 0-10 years age group, mean age of patients was 10.79 ± 4.17 years. Among these 13 were females (68.4%) and rest males similar to Razavi et al where the mean age at diagnosis was 7.3 ± 5.15 years and 60.4% of patient with DKA were female.¹¹ Nearly half (53.6%) of the total cases were known cases of T1DM cases presenting in DKA similar to Razavi et al.¹¹ The mean age of patients at presentation was 10.79 ± 4.17 . Mean duration of diagnosis noted was 1.81 ± 2.28 years. Family history of type 2 DM was noted in 73.7% of the patients as opposed to Shaltout et al that showed that 17.0% of the children had a history of T1DM in first degree relatives.¹² Analysis for association between family history of diabetes and onset of DKA indicates that family history of T1DM with any of the first degree relatives showed a protective effect on DKA.

The degree of ketoacidosis was mild for 26.3% of the patients, moderate for 21.1% of the patients and severe in 52.6% of the patients. However, there were more patients belonging to the category of known T1DM cases presented with mild DKA, indicating the probable early self-referral in view of pre-existing disease as similar to Basavanthappa et al, where 53.8% presented with severe, 26.9% with moderate and 19.2% with mild DKA.¹³ Osmotic

symptoms was the predominant symptom (68.4%) of the patients as opposed to abdominal pain in Bhardwaj et al.¹⁴ Hyponatremia was the most common electrolyte disturbance (57.9%) similar to Bhardwaj et al (14) while hypokalemia was the most common finding by Basavanthappa et al.¹³

Pneumonia was found to be the major precipitating factor with 31.6% of incidence followed by urinary tract infection (26.3%) and acute gastroenteritis (10.5%) in new cases of T1DM. Poor compliance was the precipitating factor in known cases of T1DM, as opposed to Infection being the commonest (62%) precipitating factor followed by insulin omission (10%). Major clinical features were dehydration (100%), polyuria (98%), Kussmaul's breathing (60%) and abdominal pain (38%) as seen in Yaasmin et al.¹⁵ Acute kidney injury was present in 10.5% of the patients as opposed to various other studies that showed a significant higher percentage of incidence of AKI.¹⁶

In contrast to numerous studies, our cohort only had 1 case of cerebral oedema, and there was no fatality.¹⁷ One patient had hepatic glycogenopathy (Mauriac disease), a rare complication of poorly controlled type 1 DM characterised by hepatomegaly due to glycogen deposition along with growth failure and delayed puberty. All known cases of T1DM had lipodystrophy. Early onset diabetic nephropathy was seen in 2 patients. Mean HbA1c noted was 15.14 ± 2.74 . Average length of stay in the hospital was 7.42 ± 3.27 days. There was no mortality in our study unlike other studies such as Basavanthappa et al that shows 11.6% mortality rate and higher in many other studies.¹⁴ There is no significant correlation observed between DKA vs age, duration of diagnosis, GCS in our current study. There was no significant correlation with the type of onset of T1DM and the treatment outcome. There was a marked reduction in HbA1c ($p < 0.05$) seen among patients (10/19) who were followed up after 3 months of treatment with medical nutritional therapy and newer insulins and lower mean HbA1c was seen in known cases compared to new cases.

DKA is one of the most dangerous side effects of T1DM and can cause significant morbidity if not diagnosed and treated right away. DKA can be the initial presentation of diabetes mellitus or can occur in patients with established diabetes mellitus. Early diagnosis should be based on a high rate of suspicion, which can be determined by being aware of the distinctive symptoms. In many parts of India, insulin is till expensive and rapid acting insulins are not easily accessible due to unawareness or financial issues in various rural areas in India. There is a need for many such studies with a larger cohort to educate not only the clinicians but also the common people at grass root level.

Limitations

The limitation of our study was the small sample size however it was enough to portray the need for educational

programmes for the patients, parents and educators on prevention of recurrent attacks of DKA.

CONCLUSION

This study highlights the need of the hour for creating awareness, early referral and timely management of T1DM presenting not only in DKA but also during the ambulatory management. There was only one case with cerebral oedema and no mortality noted indicating that appropriate care and timely management is the key to avoid such complications.

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