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Original Research Article

Identifying risk factors for development of diabetic ketoacidosis in type 1 diabetes mellitus

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ABSTRACT

Background: DKA [Diabetic keto acidosis] It is the commonest cause of diabetes-related death in children. Children with diabetic ketoacidosis at diagnosis have poorer glycemic control, to identify the risk factors for the development of Diabetic Ketoacidosis in Type1 Diabetes Mellitus in a tertiary care center.
Methods: The study was conducted in Kovai Medical Centre And Hospital Coimbatore in 2018.22 children were included in present study. Each consultant followed different standard DKA treatment protocols. The two protocols used were Milwaukee and BSPED guidelines.
Results: Among the 22 children, 3 children (13%) had recurrent DKA (>1 episode). One child had his third episode and the rest 2 children had their second episode.19 children had their first episode of DKA.
Conclusions: There was no death among the 22 children treated. This was because of the care is given by the team of doctors and adherence to treatment protocol (Milwaukee or BSPED) of DKA.

Keywords: Cerebral edema, Diabetic keto acidosis, Dyslipidaemia, Hyper glycemia

INTRODUCTION

Type 1 diabetes is one of the most common endocrine diseases in children. Worldwide, an estimated 65 000 children under 15 years old develop the disease each year, and among the children, the global incidence increase at a rate of 3% per year.[1] Between 10% and 70% of diagnosed T1DM children present with diabetic ketoacidosis. DKA can lead to life-threatening complications such as cerebral edema. It is the commonest cause of diabetes-related death in children.[2] Children with diabetic ketoacidosis at diagnosis have poorer glycemic control, less residual β cell function up to two years after diagnosis and a lower frequency of remission.[3] It is unclear why some children present in diabetic ketoacidosis whereas others do not and whether the development of diabetic ketoacidosis is due to delayed diagnosis and treatment or whether it reflects a particularly aggressive form of diabetes.[4] Understanding the factors associated with DKA, the impact of delayed diagnosis and treatment is, therefore, important.[5] This potentially informs both our understanding of the disease as well as the development of patient, professional, and population-based interventions to reduce the proportion of children presenting in diabetic ketoacidosis is important.[6] Death in T1DM is predominantly due to DKA. Mortality rates and the cause for mortality in developed countries and developing countries show much variation. Cerebral edema is the predominant cause for mortality in children with DKA from developed countries. But recent data from developing countries have shown a higher incidence of cerebral edema and sepsis,

shock and renal failure as the cause for death in DKA. Prolonged insulin deficiency in patients with newly diagnosed T1DM may lead to diabetic ketoacidosis (DKA).[7] Previous studies have shown worldwide variation in the frequency of DKA at the onset of diabetes ranges from 12.8% to 80% Subtle cerebral changes might occur even when clinically apparent cerebral edema is not observed. Cameron et al, have demonstrated alterations in cerebral white matter particularly in the frontal lobe in children with severe DKA. These changes might affect the memory and attention in children. They also stated that DKA might result in morphologic and functional brain changes. It was found that if T1DM is not diagnosed on the first visit to the physician, the risk of DKA increases significantly. Criteria for diagnosis of DKA: The biochemical criteria for the diagnosis of diabetic ketoacidosis (DKA) are: Hyperglycaemia [blood glucose (BG) >11 mmol/L (>200 mg/dL)], blood pH< 7.3 or bicarbonate<15mmol/L.[8,9]

METHODS

The study was conducted in Kovai Medical Centre and Hospital Coimbatore. 22 children were included in present study. Each consultant followed different standard DKA treatment protocols. The two protocols used were Milwaukee and BSPED guidelines.

Inclusion criteria

- Birth to 18 years of age with features satisfying the criteria for diabetic ketoacidosis.
- Participants willing to sign the informed consent form after thorough understanding.
- Children with new onset of type 1 diabetes mellitus and known children with type 1 diabetes mellitus.

Exclusion criteria

- Those not willing to give consent.

The procedure of the study was Ethical committee clearance was obtained earlier. Performa was prepared to record all data. Children attending emergency department /OPD with features of DKA were focused. Few children were referred to as DKA to Emergency department from an outside hospital. Children who had high glucose value (>200mg/dl) in glucometer were mainly focused. Sampling - Venous blood was collected from a peripheral vein of the child. ABG was taken and urine complete analysis was sent. Based on the report's children were diagnosed to have DKA if they met the diagnostic criteria. Only those children who were diagnosed to have DKA and met the inclusion criteria were included in the study. The child was stabilized in the Emergency Department. The paediatric consultant and the Endocrinologist would decide the further management of the disease. Vitals and anthropometry documentation: Vital signs were documented soon after admission before treatment. Blood pressure was recorded for all the children included under the study using a standard mercury sphygmomanometer with appropriate cuff size. Height and weight were noted, and BMI was calculated. BMI was plot using the standard IAP BMI chart for boys and girls. Further management: Each consultant followed different standard DKA treatment protocols. The two protocols used were Milwaukee and BSPED guidelines. Hence the protocol for management of DKA changed with each endocrinologist and consultant. Sick children were admitted in PICU, especially those with dehydration, tachypnoea, hypotension, and poor GCS. Treatment was continued as per standard DKA protocol. Once the glucose level was controlled and the children were hemodynamically stable, they were shifted to the ward.

Children were followed up until discharge. Any complication addressed was treated and documented. History was obtained from mother preferably. If mother was not available, then the history was obtained from father. Previous HbA1C values were obtained from the previous case sheet /discharge summary/prescription leaflet/lab reports. Criteria for diagnosis of DKA: The biochemical criteria for the diagnosis of diabetic ketoacidosis (DKA) are: Hyperglycaemia [blood glucose (BG) >11 mmol/L (>200mg/dL)], blood pH< 7.3 or bicarbonate<15mmol/L.[20] The severity of DKA is defined by the degree of acidosis: mild, venous pH 7.2-7.3; moderate, pH7.1-7.2; and severe, pH <7.1.[26] BMI was calculated using the revised IAP BMI chart for boys and girls.

Delayed diagnosis was defined as the diagnosis of a disease other than diabetes at first medical consultation. Hypokalaemia was defined as serum potassium <3.5 mEq/L Cerebral Edema: Cerebral Edema was defined as persistence of impaired consciousness despite improvement in pH and random blood glucose <300 mg/dl or deterioration in the level of consciousness accompanied by one or more signs of raised intracranial pressure such as hypertension, bradycardia, abnormal breathing pattern, pupillary abnormalities, strabismus, papilledema, decerebrate/decorticate posturing, or respiratory arrest

Statistical analysis

The data will be entered SPSS spreadsheet and will be double checked. The analysis will be done in SPSS version 16.0 for windows. Descriptive analysis such as mean, standard deviation and percentage is used to exhibit the clinical parameters considered in the research pro-forma. All the statistical tests will be examined with 5% ($P \leq 0.05$) level of significance.

RESULTS

Of the total 22 children enrolled, none of them belonged to 0-5yrs age group, 10 children belonged to 5-12 years age group. Most of the children belonged to >12 years

group. About half of >12years ended up with severe DKA. The mean age at presentation with DKA was 11 years in this study (Table 1).

Table 1: Comparison of age group with severity of DKA.

Age group	The severity of DKA (no. of children)			
	Mild	Moderate	Severe	Total
5-12 years	5	4	1	10
>12 years	6	1	5	12
Total	11	5	6	22

Chi-Square, p-value=0.110

The average BMI (in kg/m^2) of 22 children was 16.86 including boys and girls. The minimum BMI (in kg/m^2) was 12.6 and the maximum BMI (in kg/m^2) was 25.2. The mean BMI for boys was 16.4 kg/m^2 and for girls were 17.4 kg/m^2 (Table 2).

A majority of the children who presented with DKA in this study were already known children with T1DM. 45% of the children were diagnosed to have T1DM while presentation with DKA during this episode. A majority of the children who were known case had T1DM for more than 1year (Table 3).

Table 2: Evaluation of BMI among DKA children.

	No. of children	Min (kg/m^2)	Max (kg/m^2)	Mean (kg/m^2)	SD
BMI	22	12.6	25.2	16.86	3.74

Among the 22 children, 3 children (13%) had recurrent DKA (>1episodes). One child had his third episode and the rest 2 children had their second episode. 19 children had their first episode of DKA (Table 4).

Table 3: Comparison of frequency of known children with T1dm and new children diagnosed with T1dm.

Known case of type 1 DM	No. of children	Percentage
No. (new Case of T1DM)	10	45.50
Yes	12	54.50
Total	22	100.00

Table 4: Comparison of present HBA1C value with severity of DKA.

Parameter	Severity of DKA	No. of children	Mean (%)	SD	P-value
Present HbA1c	Mild	9	17.16	2.94708	0.038
	Moderate	3	11.63	1.60416	
	Severe	7	14.37	3.6165	
	Total	19	15.26	3.57791	

Table 5: Analysis of symptoms at admission with DKA.

	Number of children	Min (in days)	Max (in days)	Mean (in days)	SD
Abdominal pain	3	1	2	1.33	0.58
Vomiting	15	1	2	1.33	0.49
Fever	4	1	2	1.75	0.50
Fast breathing	12	1	2	1.1	2.57
Polyuria	Z8	7	30	19.13	9.31
Polydipsia	9	7	30	17.56	7.88
weight loss	9	21	180	55.67	49.18

The major reason that triggered this episode of DKA was poor supervision with no dietary modification. And in most of the children with New onset T1DM, the exact reason could not be identified. Other causes include infection (Rhino-cerebral Mucor mycosis), improper insulin administration, poor insulin technique, infrequent glucose monitoring, changing the brand of insulin for administration. Most of the children presented with vomiting and fast breathing. Polydipsia, polyuria, and weight loss were the other common presentation (Table 5).

Laboratory investigations revealed a mean pH of 7.13, Hco3 of 8.7 mmol/L, the base deficit of 20.1mmol/L. The average glucose value at admission was 497 mg/dl. The mean serum potassium value was 4.1 mEq/L. The mean HbA1c values done for 19 children were 15.2. For the rest 3 children, HbA1C was not done. The average urea and creatinine values were 22 mg/dl and 0.7 mg/dl respectively. The mean duration of hospital stay was 4.5 days. Only 8 children were treated in ICU. The rest were treated in the ward (Table 6).

Table 6: Evaluations of laboratory values at admission.

Investigation	N	Min	Max	Mean	SD
pH	22	6.88	7.28	7.13	0.14
HCO_3 (mmol/L)	22	2.4	14	8.78	4.07
Base deficit (mmol/L)	22	12.4	30	20.19	5.37
Glucose (mg/dl)	22	335	710	497.41	97.93
Serum potassium (mg/dl)	22	2	6	4.10	0.96
HbA1C value (%)	19	8.3	20	15.26	3.58
Urea (mg/dl)	22	10	35	22.09	5.90
Creatinine (mg/dl)	22	0.5	0.9	0.70	0.10

Among the 22 children who presented with DKA, 11 had mild, 5 had moderate and 6 children had severe DKA. 50% of the admissions were mild DKA. 27 % of the children presented with severe DKA. None of the 22 children admitted had cerebral edema or renal failure. Only one child had prolonged shock in spite of prompt treatment. There were no deaths among the 22 children treated in present hospital (Table 7).

Table 7: Frequency of mild, moderate and severe DKA.

Severity of DKA	No. of children	Percentage
Mild	11	50.00
Moderate	5	22.73
Severe	6	27.27
Total	22	100.00

DISCUSSION

Of the 22 children in the study, 7 children (31.8%) were referred. Remaining 15 children presented to present tertiary care center directly.[5] Among them were known children with T1DM who were on follow up in present hospital.[10] Still, they developed DKA due to poor glucose monitoring, lack of supervision by parents and poor dietary modifications. Their previous medical records suggested that they were on irregular follow up. This fact emphasizes the need for more vigorous diabetic awareness programmed and counseling in present hospital.[11] Among the 7 referred children, 6 of them were referred immediately (<24hrs). Remaining 1 child was treated in outside hospital and as there was no improvement, was referred here. However, 2 European studies found no effect when there were >24 hrs. the delay between first visit and diagnosis.[12] Of the 7 children referred from various hospitals, normal saline bolus was given in 6 hospitals (86%) and insulin was started in 5 hospitals (71%). Only 5 children were referred to as DKA of the total 7 children. Remaining 2 children were referred to as hyperglycemia under evaluation.[13] On contacting these 2 referring physicians, they revealed that they were not aware of the signs and symptoms of DKA and has never witnessed a case of DKA in their practice.[14] The various reasons for referral included poor affordability of the family, lack of facility to treat further and long distance from their hometown.[15] At presentation tachycardia was present in 77% of the children, tachypnea was present in 81% of the children and desaturation (spo2<90%) was noted in 4.5% of the children. At admission, the mean pH was 7.13. The mean bicarbonate was 8.7 mmol/L and the base deficit was 20.1 mmol/L. The minimum blood glucose value at the presentation of DKA was 335 mg/dl and the maximum glucose value recorded was 710 mg/dl. The mean glucose value at presentation was 497 mg/dl. Hypokalemia was present in 27% of the children at admission.[16] Elevated urea or creatinine was not noted in any of the subjects. Mild DKA was the commonest presentation (50%). Moderate and severe DKA constituted 23% and 27% respectively. The average hospital stay was 4.5 days. The average duration of stay in ICU was 2.5 days.[17] Of the 22 children admitted, only 8 were admitted in ICU (36%). None of the admitted children developed cerebral edema or renal failure. One child (4.5%) had prolonged shock in spite of prompt treatment.[18-20]

CONCLUSION

About 45% of the children presented with DKA at first diagnosis. About half of the children presented with mild DKA. Adolescents were more prone to DKA. A multicentre study is needed to evaluate the frequency and causes of DKA in Indian children with T1DM. The low index of suspicion for T1DM, delay in laboratory testing, lack of family awareness leads to DKA. A psychologist should be consulted to identify the psychosocial reasons that might lead to DKA. Increasing general awareness among the public and pediatrician can lead to early diagnosis thus preventing DKA. Children and parents should learn how to recognize and treat impending DKA with additional rapid short-acting insulin and oral fluids.

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