

DIABETIC KETOACIDOSIS IN CHILDREN- CLINICAL PROFILE AND OUTCOMEBindu Krishnan Padma¹, Jiji Mary Antony²¹Assistant Professor, Department of Paediatrics, Government Medical College, Kottayam, Kerala.²Associate Professor, Department of Paediatrics, Government Medical College, Kottayam, Kerala.**ABSTRACT****BACKGROUND**

Diabetic ketoacidosis is a potentially life-threatening condition, which accounts for the majority of diabetes-related morbidity and mortality in children with type 1 diabetes mellitus. Early diagnosis and prompt management substantially reduces the mortality.

The aim of the study is to assess the clinical characteristics and early outcome in children with diabetic ketoacidosis.

MATERIALS AND METHODS

This is a descriptive study done in a tertiary care hospital. Fifty two episodes of diabetic ketoacidosis in children of age ≤ 12 years admitted during the period 2011 to 2016 were included in the study. Clinical details, investigations and complications were recorded in a pro forma and data was analysed using statistical tests.

RESULTS

Fifty two episodes of diabetic ketoacidosis were included in the study. Thirty three (63.5%) children presented with DKA at first diagnosis of diabetes, whereas 19 (36.5%) were DKA among children with established diabetes. Mean age at presentation was 9.048 ± 3.24 . Female-to-male ratio was (1.36:1). The mean duration of onset of symptom before hospitalisation was 10.10 ± 9.52 . Most commonly observed presenting symptoms were polyuria (63.46%), polydipsia (65.38%), tiredness (61.54%), vomiting (36.54%) and pain abdomen (32.69%). Mild DKA occurred frequently than moderate and severe forms. Among these children, 40.4% had infection as the predisposing factor. Demographic variables like age, gender, socioeconomic status, family history of diabetes did not have any significant association with the severity of DKA. The clinical parameters like tachypnoea, Kussmaul breathing, shock, altered sensorium at presentation and dehydration had significant association with the severity of DKA. Similarly, hypoglycaemia, hypokalaemia, hyponatraemia, acute kidney injury and cerebral oedema had significant association with the severity of DKA. All the patients recovered with therapy. No mortality was reported.

CONCLUSION

Diabetic ketoacidosis can be the initial presentation of diabetes mellitus or can occur in children with established diabetes mellitus. The mortality can be reduced by timely diagnosis and proper management. Diabetes education programs and follow up care of the patients should be strengthened to reduce the incidence of DKA.

KEYWORDS

Diabetic Ketoacidosis, Clinical Profile, Outcome.

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BACKGROUND

Type 1 diabetes mellitus is the most common endocrine-metabolic disorder of childhood and adolescence.¹ Diabetic ketoacidosis is a life-threatening complication among children with diabetes mellitus. It accounts for a large proportion of hospital admission related to diabetes in children. Diabetic ketoacidosis frequency at the time of diagnosis of paediatric diabetes is 10%-70%. The frequency of new-onset diabetes presenting as DKA varies widely with geographic region and correlates inversely with regional

incidence.² The risk of ketoacidosis in established type 1 diabetes mellitus is 1-10% per year.³ An episode of diabetic ketoacidosis has a mortality risk of 0.15%-0.3%.⁴

Diabetic ketoacidosis is characterised by the biochemical triad of hyperglycaemia, ketonaemia (ketonuria) and acidaemia. It results from absolute or relative deficiency of circulating insulin and the effects of increased concentration of the counter-regulatory hormones.⁵ In addition to the typical symptoms of hyperglycaemia like polyuria, polydipsia, weakness and weight loss, the clinical features specific for diabetic ketoacidosis are dehydration, rapid and deep breathing due to acidosis, abdominal pain, vomiting and drowsiness.⁶ The goals of therapy include, correction of dehydration, restore blood glucose to near normal concentration, correct acidosis and reverse ketosis and avoid complications of treatment. Most of the children recover with treatment, however, complications like cerebral oedema can occur in some. Cerebral oedema accounts for 57-87% of all deaths from diabetic ketoacidosis. Other

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causes of diabetic ketoacidosis related mortality and morbidity include, hypokalaemia, hyperkalaemia, hypoglycaemia, sepsis and other central nervous system complications such as thrombosis.

Diabetic ketoacidosis occur in two contexts in children with type 1 diabetes mellitus, one is newly-diagnosed diabetes mellitus children presenting with ketoacidosis and another is the development of ketoacidosis in children with established diabetes. The factors associated with increased risk of ketoacidosis in new-onset diabetes are younger age, diagnostic error, lower body mass, preceding infection and delayed treatment.⁷ Whereas, the risk factor in patients with known diabetes include, poor metabolic control, insulin omission, previous episodes of ketoacidosis, peripubertal and adolescent girls, children with psychiatric disorders, those with difficult family circumstances including lower socioeconomic status. The number of episode of DKA is a significant outcome measure for diabetic care.⁸ DKA is a preventable disease both in newly-diagnosed diabetes and also among those with known diabetes.⁹ High index of clinical suspicion is essential for early diagnosis and proper intervention. Proper implementation of diabetes education programs, improved follow up care and easy access to healthcare facilities help to reduce the incidence of diabetic ketoacidosis.

Aims and Objectives

To assess the clinical characteristics and early outcome in children admitted with diabetic ketoacidosis.

MATERIALS AND METHODS

This is a descriptive study conducted at the Department of Paediatrics, Government Medical College, Kottayam. Medical records of the children ≤ 12 years admitted with diabetic ketoacidosis from 2011 to 2016 were reviewed. Baseline data including demographics, clinical presentation, predisposing factors, laboratory parameters, management, complications and outcome were recorded in a predesigned pro forma. All of them were managed in the Paediatric Intensive Care Unit. Intravenous fluid and insulin infusion was initially given to them. Blood glucose levels and vital signs were monitored hourly in these patients. Once their ketoacidosis resolved and condition stabilised, the insulin infusion was changed to subcutaneous insulin.

Criteria for diagnosis of diabetic ketoacidosis include- hyperglycaemia (blood glucose ≥ 200 mg/dL), venous pH < 7.3 or bicarbonate < 15 mmol/l with ketonaemia and ketonuria.¹⁰ Diabetic ketoacidosis is categorised as mild, moderate and severe. Mild- venous pH < 7.3 or bicarbonate < 15 mmol/L; Moderate- venous pH < 7.2 or bicarbonate < 10 mmol/L; Severe- venous pH < 7.1 or bicarbonate < 5 mmol/L. New-onset DKA was applied to children diagnosed to have diabetes for the first time and presenting with DKA.¹¹ Hyponatraemia and hypernatraemia was defined as value < 135 mEq/L and > 145 mEq/L, respectively.¹ Similarly, hypokalaemia was defined as value < 3.5 mEq/L and hyperkalaemia as value > 5.5 mEq/L. Hypoglycaemia was defined as value < 70 mg/dL. AKI (acute kidney injury) is an

abrupt reduction in kidney function defined as an absolute increase in serum creatinine of > 0.3 mg/dL, increase in creatinine more than 1.5 fold from baseline or reduction in urine output (documented oliguria < 0.5 mL/kg/hr. for more than 6 hrs.).¹² Shock was defined as tachycardia and signs of poor end-organ perfusion as defined by poor peripheral pulses with normal central pulses, prolonged capillary refill or flash refill, altered sensorium, cool extremities and decreased urine output.¹¹ Normotensive shock was considered when blood pressure was normal. Hypotensive shock was considered when systolic blood pressure was below the fifth percentile for age. Cerebral oedema was diagnosed as per the diagnostic criteria as suggested by Muir et al.¹³ Criteria include- Abnormal motor or verbal response to pain, decorticate or decerebrate posture, cranial nerve palsy (especially 3, 4, 6), abnormal neurogenic respiratory pattern (grunting, tachypnoea, Cheyne-Stokes respiration, apnoeic). Major criteria- altered mentation/fluctuating level of consciousness, sustained heart rate deceleration (decline more than 20 bpm) not attributable to improved intravascular volume or sleep state, age-inappropriate incontinence. Minor criteria- vomiting, headache, lethargy or not easily aroused from sleep, diastolic blood pressure > 90 mm of Hg, age < 5 years. Socioeconomic status was assessed using variables like education, occupation and monthly income. Outcome is defined as either the patient died or recovered with treatment and discharged from hospital with good glycaemic control.

Data collected was entered in Excel format and analysed using SPSS version 22. The qualitative variables were expressed as number or percentage. Descriptive data were analysed with statistical test like mean and standard deviation. Associations were evaluated using Chi-square test, likelihood ratio and Fisher's exact test. A p value of < 0.05 was considered statistically significant.

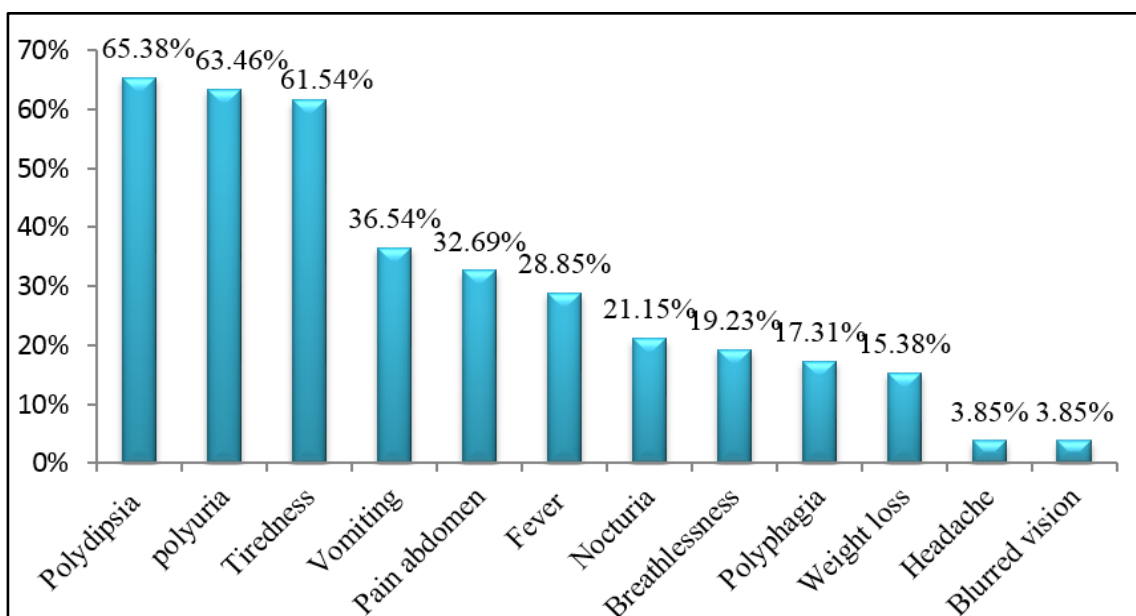
RESULTS

52 episodes of diabetic ketoacidosis were included in the study. Thirty three (63.5%) were new-onset DKA and 19 (36.5%) were DKA among children with established diabetes. There were 22 (42.3%) male and 30 (57.7%) female. Among them, 11 children (21.2%) were in 1-5 years age group, 16 (30.8%) children were in the 5-10 years age group and 25 (48.1%) children were above 10 years. Mean age at presentation was 9.048 ± 3.24 . Majority 38 (73.1%) children belonged to the lower socioeconomic class and 12 (23.1%) were from middle class and 2 (3.8%) belonged to upper class. Family history of diabetes mellitus was present in 32 (61.5%) children. Thirty-one children (59.6%) had mild DKA, 10 (19.2%) had moderate DKA and 11 (21.2%) children presented with severe DKA. Mean blood glucose value at presentation was 475.62 ± 114.05 . The mean duration of symptoms before hospitalisation was 10.10 ± 9.52 . Among these, children 40.4% had infection as the predisposing factor.

The most common presenting symptom observed was polydipsia 34 (65.38%), polyuria 33 (63.46%) and tiredness 32 (61.54%) followed by vomiting 19 (36.54%), pain

abdomen 17 (32.69%) and fever 15 (28.85%). Among the physical signs observed, dehydration was present in 24 (46.15%), altered sensorium in 15 (28.84%), shock at presentation in 10 (19.23%), tachypnoea in 9 (17.31%) and Kussmaul breathing in 7 (13.46%) children. Hypokalaemia

14 (26.92%) and hypoglycaemia 14 (26.92%) were the commonest complication observed. Other complications were AKI (acute kidney injury) in 9 (17.3%), cerebral oedema in 6 (11.53%) and hyponatraemia in 5 (9.61%).



Graph 1. Profile of Symptoms

The following demographic variables did not have any statistically significant association with severity of the diabetic ketoacidosis - age at presentation (p value-0.585), gender (p value-0.530), socioeconomic status (p value-0.765), family history of diabetes mellitus (p value-0.915), new-onset DKA or DKA in established diabetes mellitus (p value-0.385). Other variables like duration of onset symptom till hospitalisation (p value-0.205) and blood glucose at presentation (p value-0.104) too did not have any statistically significant association with the severity of diabetic ketoacidosis.

	Severity			P value
	Mild	Moderate	Severe	
Age Group				
1 to 5	5 (45.5%)	4 (36.4%)	2 (18.2%)	0.585*
5 to 10	10 (62.5%)	2 (12.5%)	4 (25.0%)	
>10	16 (64.0%)	4 (16.0%)	5 (20.0%)	
Gender				
Male	15 (68.2%)	3 (13.6%)	4 (18.2%)	0.530*
Female	16 (53.3%)	7 (23.3%)	7 (23.3%)	
Socioeconomic Status				
Upper	1 (50.0%)	1 (50.0%)	0	0.765*
Middle	8 (66.7%)	2 (16.7%)	2 (16.7%)	
Lower	22 (57.9%)	7 (18.4%)	9 (23.7%)	
Newly-diagnosed cases	21 (63.6%)	7 (21.2%)	5 (15.2%)	0.385*
Old cases	10 (52.6%)	3 (15.8%)	6 (31.6%)	
Family History of Diabetes				
Positive	19 (59.4%)	6 (18.8%)	7 (21.9%)	0.915*
Negative	12 (60.0%)	4 (20.0%)	4 (20.0%)	
Duration of Onset Symptoms in Days				
<2 days	7 (53.8%)	2 (15.4%)	4 (30.8%)	0.205*
3 to 7 days	10 (50.0%)	5 (25.0%)	5 (25.0%)	
8 to 14 days	7 (77.8%)	2 (22.2%)	0 (0.0%)	
>15 days	7 (70.0%)	1 (10.0%)	2 (20.0%)	
Random Blood Sugar at Presentation				
250 to 350	4 (57.1%)	3 (42.9%)	0 (0%)	0.104*
351 to 450	6 (54.5%)	2 (18.2%)	3 (27.3%)	
451 to 550	13 (54.2%)	4 (16.7%)	7 (29.2%)	
>550	8 (80.0%)	1 (10.0%)	1 (10.0%)	

Table 1. Association of Sociodemographic and Baseline Disease Features with the Severity of Diabetic Ketoacidosis

*Not significant.

The following physical signs at admission like tachypnoea (p value-0.000), Kussmaul breathing (p value-0.000), dehydration (p value-0.005), altered sensorium (p value-0.000) and shock at presentation (p value-0.000) have statistically significant association with the severity of diabetic ketoacidosis. Similarly, the complications like hypoglycaemia (p value-0.021), hypokalaemia (p value-0.000), hyponatraemia (p value-0.006), AKI (p value-0.000), cerebral oedema (p value-0.000) also have statistically significant association with the severity of diabetic ketoacidosis. All patients recovered with treatment and there was no mortality.

Physical Signs	Severity			P value
	Mild	Moderate	Severe	
Tachypnoea	0 (0.0%)	0 (10.0%)	9 (90.0%)	0.000
Kussmaul breathing	0 (0.0%)	0 (0.0%)	7 (100.0%)	0.000
Dehydration	9 (37.5%)	6 (25.0%)	9 (37.5%)	0.005
Altered sensorium	1 (6.7%)	5 (33.3%)	9 (60.0%)	0.000
Shock at presentation	0 (0.0%)	2 (20.0%)	8 (80.0%)	0.000

Table 2. Association of Clinical Parameters with Severity of Diabetic Ketoacidosis

Complications	Severity			P value
	Mild	Moderate	Severe	
Hypoglycaemia	4 (28.6%)	5 (35.7%)	5 (35.7%)	0.021
Hypokalaemia	2 (14.3%)	4 (28.6%)	8 (57.1%)	0.000
Hyponatraemia	0 (0.0%)	3 (60.0%)	2 (40.0%)	0.006
AKI	0 (0.0%)	3 (33.3%)	6 (66.7%)	0.000
Cerebral oedema	0 (0.0%)	0 (0.0%)	6 (100.0%)	0.000

Table 3. Association of Clinical Parameters with the Severity of Diabetic Ketoacidosis

DISCUSSION

DKA can be the initial presentation of diabetes or occur in patients with established diabetes. DKA represents a decompensated state of diabetes, which require hospitalisation. The younger the child it becomes more difficult to get the history of polyuria, polydipsia and weight loss. Infants and toddlers who present in DKA maybe misdiagnosed as having respiratory infection and treated accordingly. Lack of awareness of the nonspecific and subtle symptoms of diabetes in infants and young children, among the general population and physicians results in delayed diagnosis and more cases end up in DKA.

In the present study, we had 52 episodes of diabetic ketoacidosis during the study period. Girls comprised 57.7% of our subjects with female-to-male ratio (1.36:1). A female preponderance was also seen in study by Satti Abdulrahim Satti et al¹⁴ (F:M ratio of 1.22:1) and study by Dr. Sudhir Mehta¹⁵ (F:M ratio of 1.3:1). In this study, the frequency of ketoacidosis was more in the early adolescence group (48.1%). Mean age at presentation was 9.048 ± 3.24 . In the study by Adriana Yock-Corrales et al,¹⁶ the mean age at presentation was 8.6 ± 3.78 and it was 10.2 ± 2.9 in the study by Clarice L. S. Lopes et al.¹⁷ Our study shows no association between age and the severity of DKA. As ours is a government teaching hospital, majority of the patients admitted were from lower socioeconomic class (73.1%). Mild DKA dominated our study population (59.6%) followed by severe DKA (21.2%) and moderate DKA (19.2%). In contrast to this, other studies showed a slightly upward trend in the severity of DKA.^{15,18-20}

Data from our study has shown that there is no significant association between the severity of ketoacidosis and the demographic variables like age, gender, socioeconomic status and family history of diabetes. This is supported by report from other studies.^{8,20} The mean RBS at

presentation was 475.62 ± 114.05 . Comparable results were seen in study from Agha Khan University (RBS 480 ± 128)²⁰ and that by Shabir Ahmed et al (RBS 486 ± 128).⁸ There was no significant association between the severity of DKA and factor like RBS at presentation. Similarly, duration of onset of symptom to hospitalisation did not have any significant relation with the severity of ketoacidosis.

In the index study, new-onset diabetes accounted for 63.5% of cases and the remaining were known cases of diabetes. Among them, 40.4% had infection as predisposing factor. Worldwide infection is the most common predisposing factor for DKA occurring in 30-50% of cases.²¹ Whether ketoacidosis occurred in newly-diagnosed cases or in those with established diabetes that does not have a significant association with the severity of DKA (p value - 0.385). Among the 19 cases of established diabetes, the vast majority (84.2%) had past history of DKA, 8 children had infection as the predisposing factor, omission of insulin was seen in 3 children and 2 children had both infection and omission of insulin as the contributing factor. In these children, prompt medical support, knowledge about sick day management would have prevented the recurrence of DKA. This highlights the importance of proper treatment of intercurrent illness and strengthening of follow up care of patients.

As far as the symptom at admission considered, most common symptoms were polyuria (63.46%), polydipsia (65.38%), tiredness (61.54%) followed by vomiting (36.54%) and pain abdomen (32.69%). History of polyuria and polydipsia was seen only in 10% of cases in the study by Dr. Sudhir Mehta, whereas polyuria (93%) and polydipsia (72%) was reported by Shabir Ahmed et al. On physical examination, dehydration was present in 46.15% cases. Shock at presentation, altered sensorium and Kussmaul breathing was mostly seen in patients with severe DKA. The

signs like tachypnoea, Kussmaul breathing, dehydration, altered sensorium and shock at presentation have statistically significant association with the severity of DKA. Hence, the children with these characteristics should be more intensively monitored. Hypoglycaemia as a complication of treatment was observed in 26.92% cases, slightly higher than that observed in other studies.¹⁷ Electrolyte disturbances seen were hypokalaemia and hyponatraemia. Potassium is usually lost as a result of vomiting, osmotic diuresis and secondary hyperaldosteronism due to volume depletion. Hypokalaemia improved after rehydration and electrolyte replacement. AKI was seen in (17.3%) patients, they recovered with prompt therapy. Six of our patients developed cerebral oedema and all of them had severe DKA. Our finding differs from studies carried out by, Shabir Ahmed et al⁸ and that by Madiha Syed et al²⁰ where cerebral oedema was found in 4.5% and 6.8% cases, respectively. Factors associated with increased risk of cerebral oedema are severe acidosis, profound hypocapnia at presentation, increased serum urea nitrogen at presentation and attenuated rise of serum sodium during therapy. An episode of DKA has a mortality risk of 0.15% to 0.3%. In regions where medical services are less well developed, risk of mortality from DKA is high. The study by Poovazhagi found that altered sensorium and higher osmolality at admission, delayed diagnosis, cerebral oedema, shock, renal failure and sepsis were the major risk factors associated with mortality.²² All patients recovered with treatment and no deaths were reported in the present study. Early recognition and proper management during the initial hours lead to a favourable outcome.

CONCLUSION

DKA can be the initial presentation of diabetes mellitus or can occur in patients with established diabetes mellitus. Most common symptoms at admission are osmotic symptoms like polyuria, polydipsia and tiredness followed by vomiting and pain abdomen. Clinical parameters like tachypnoea, Kussmaul breathing, shock at presentation, altered sensorium and dehydration have significant association with the severity of DKA. Infection is the most common predisposing factor for DKA. More efforts should be put into prevent the occurrence of DKA at initial presentation and later.

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