Original article:

Precipitating factors, clinical features and outcome of diabetic ketoacidosis in children and adolescents admitted in a tertiary care hospital in Dhaka

Islam R^1 , Akhter S^2 , Shelim R^3 , Mohsin F^4 , Begum T^5 , Akhter G^6 .

Abstract:

Background Information: Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes mellitus (DM). It is an acute complication of type 1 DM. Objective: This study was designed to identify the precipitating factors, clinical features and immediate outcomes of DKA in children and adolescents. Method: This was a retrospective study which was done in the department of Pediatrics, BIRDEM, from January 2002 to April 2007. Data were collected from the hospital record for all diabetic children below 18 years admitted with DKA. Result: Fourty nine children and adolescents were admitted with DKA. Sixty one percent were known cases and the remaining (39%) were new DM. Majority were female (63%). Most (49%) of the children were between 11- 15 years. Infection was the commonest (49%) precipitating factor followed by insulin omission (24%). Major clinical features were kussmal breathing (94%) and dehydration (94%).Eighty eight percent patients improved after treatment and mortality was 12%. Conclusion: Infection was the commonest clinical features. Most of the patients improved after treatment.

Key Words: Diabetic ketoacidosis, children and adolescents, tertiary care hospital, Bangladesh

DOI: http://dx.doi.org/10.3329/bjms.v13i1.17429 Bangladesh Journal of Medical Science Vol. 12 No. 05 January '14 Page 53-57

Introduction:

Diabetes mellitus (DM) is one of the main threats to human health in the 21st century. Diabetic ketoacidosis (DKA) is an acute complication and a medical emergency in children and adolescents with type 1 diabetes¹. Approximately 30% of newly -onset diabetic children present with ketoacidosis². In a oneyear review, the proportion of diabetics under 18 years of age was found to be 1.34% among the registered cases of BIRDEM³. Asian children below five years has an eightfold increased risk of diabetic ketoacidosis compared with non-Asian children of the same age^4 . Precipitating events are new onset diabetes, sepsis, insulin omission, delay in diagnosis and previous episodes of DKA⁵.

The clinical features are polyuria, polydipsia, polyphagia, vomiting, abdominal pain, dehydration, acidotic breathing, fever, hypotension, coma and confusion⁶. The mortality rate for DKA in children is $0.15\% - 0.3\%^5$. This study intended to identify the precipitating factors, clinical features and immediate outcomes of diabetic ketoacidosis in all admitted children and adolescents in BIRDEM.

- 1. Dr. Rubaiya Islam, Department of Pediatrics, BIRDEM Hospital, Dhaka
- 2. Dr. Shahida Akhter, Professor of Pediatrics, BIRDEM
- 3. Dr. Rumana Shelim, Asst.Professor, Pediatrics, East West Medical College, Dhaka
- 4. Dr. Fauzia Mohsin, Associate Professor, Pediatrics, BIRDEM
- 5. Prof. Tahmina Begum, Head of the department, Pediatrics, BIRDEM
- 6. Dr. Gulshan Akhter, Asst.Professor, Pediatrics, Greenlife Medical College and Hospital

<u>Corresponds to:</u> Dr. Rubaiya Islam, Senior Medical Officer, Pediatrics and Noenatal ICU, BIRDEM,122 Kazi Nazrul Islam Avenue, Shahbag, Dhaka-1000, Email: ruba114@yahoo.com

Method:

This was a retrospective study which was done in the department of Pediatrics, BIRDEM, from January 2002 to April 2007. All diabetic children below 18 years who presented with DKA were included in the study. Criteria for the diagnosis of DKA was defined as any child with heavy glycosuria, ketonuria, blood glucose ?11.1mmol/L, pH<7.3 and a serum bicarbonate level <15mmol/l and who are 5% or more dehydrated \pm vomiting \pm drowsiness⁶. Children who were treated outside BIRDEM and improved and later referred to BIRDEM were excluded.

The hospital records of the patients were reviewed to ascertain age, sex, documented etiology of DKA, adverse events and outcome. Precipitating factors of DKA were retrieved from case notes. Infection and insulin omission were identified as common precipitating factors. Respiratory tract and urinary tract infection and septicemia were identified. Respiratory tract infection was identified on the basis of the available documents of fever, sore throat, cough, crepitation in lungs, complete blood count (CBC) and chest Xray report. Urinary tract infection (UTI) was identified on the documents of burning sensation during micturition and urine routine and microscopic examination and culture. Septicemia was identified on the basis of available documents of fever and CBC reports. The severity of DKA is defined by the degree of acidosis: mild, venous pH 7.2-7.3; moderate, pH 7.1-7.2; and severe, pH $< 7.1^{7}$.

The clinical features like polyuria, polydipsia, polyphagia, convulsion, vomiting, abdominal pain, level of consciousness (GCS / Grade of consciousness), pupillary reaction, kussmaul breathing, vital signs and dehydration were recorded. Severity of dehydration was noted (5%, 10%, and >10%) according to ISPAD guideline 2000^{6} .

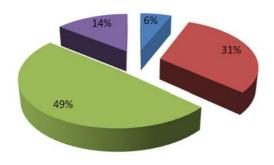
Acute renal failure was identified on the documents of serum creatinine reports and need for peritoneal dialysis. Cerebral edema is suspected when there is an unexpected deterioration in neurological status after initial improvement or persistence of a comatose state without an obvious cause. Warning signs include lethargy, decrease in arousal, headache, vomiting, bradycardia and hypertension. Neurological deterioration may be rapid, with seizures, incontinence, papillary changes and respiratory arrest. Progression may be so rapid that papilledema may not be found⁸. Rapid improvement in neurological status in response to intravenous administration of 3% sodium chloride or hypertonic mannitol further confirms the presumptive diagnosis of early cerebral edema⁸. Immediate outcome regarding improvement and death were recorded. Statistical analyses were done using SPSS program.

Results

Over the five year period, a total of 507 diabetic children were hospitalized in the department of Paediatrics. Fourty nine(9.6%) of these admitted patients presented with diabetic ketoacidosis (DKA). More than half (61%) of the patients were known case of diabetes. Amongst the total patients with DKA with documented etiology, twenty four episodes were precipitated by infection and no cause being documented in 13 of the admissions. (Figure 3) Infections, particularly those of the respiratory tract, were the main precipitating cause for the DKA. UTI and septicemia were other types of infections. The other precipitating factor was omission of insulin (24%). The mean age of patients with DKA was 10.8 ± 4.12 years. Those in the age range 11-15 yrs suffered most frequently from ketoacidosis (n= 22, 45%) compared with those aged less than 5 yrs (6%), 5-10 yrs (35%) and more than 15 years (14%). (Figure 1)The frequency of DKA was higher in girls than in boys (63% vs. 37%).

Female and male ratio was 1.7:1. Dehydration (100%) and kussmaul breathing (94%) were the common clinical features. (Figure 4) Majority had 5% dehydration and 13 patients were in shock. Other symptoms and signs were vomiting (57%), unconsciousness (51%), abdominal pain (27%), fever (27%) and convulsion (10%). (Figure 4) Most of the patients presented with mild DKA (47%) (p=0.00) than moderate (26.5%) and severe (26.5%) DKA. Random blood glucose was high in all patients. Mean HbA1C was 13.08 ± 1.11 . Mean serum creatinine was 2.09 ± 0.44 .

Complications noted were acute renal failure and cerebral edema. Five patients developed acute renal failure which improved after peritoneal dialysis. There were three episodes of cerebral edema with two associated deaths. The outcome of treatment in the whole group was good, 41 (84%) patients recovered without complications. Six patients died, with the causes of death being septicemia (n = 3), cerebral edema (n = 2) and pneumonia (n = 1).



<5 years 5-10 years 11-15 years >15 years

Figure 1: Age Distribution of pts with DKA (n=49)

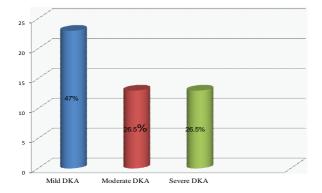


Figure 2: Distribution of pts according to severity (n=49)

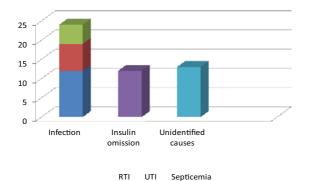


Figure 3: Precipitating factors for DKA

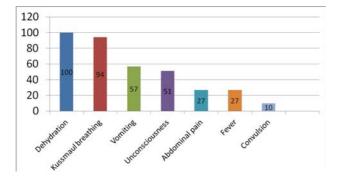


Figure 4: Clinical features of patients with DKA

Discussion:

This study has enriched our knowledge about different aspects of DKA in our population. The frequency of DKA at onset of diabetes varies considerably from country to country. In our study, thirty nine patients presented with ketoacidosis were newly diagnosed DM which is similar to other studies where 25% to 40% of children are newly diagnosed 9-10.More than half of the patients were known cases of DM. Known cases of diabetes patients frequently take irregular insulin in inadequate dose. In addition, they often miss their schedule dose and have poor compliance. They have irregular follow up also.

Children between 11- 15 years numbered the majority in our study which is similar to a different study⁴. Mean age was 10.8 ± 4.12 SD. However another study showed that children <2 years had three times the risk of presenting in diabetic ketoacidosis as children aged 2 years¹¹.

In our study the percentage of DKA cases in girls is more than the boys. It is consistent with other study¹²⁻¹³. One study reported that female sex was significantly associated with increased risk of delayed diagnosis¹¹. In this study the risk factors are deprivation in females, negligence, poverty, delay in diagnosis.

Amongst the precipitating causes, infection was the commonest (49%) which is similar to a study in Sudan where acute infections accounted for 38% of the episodes¹⁴. Mbuqua PK et al reported majority of the DKA children had sepsis followed by insulin omission¹⁵. However this result differs from another study where the commonest precipitating factors was insulin omission followed by infection¹⁶. In our study insulin omission is increased in children with limited access to medical services, low socioeconomic status, ignorance, higher insulin dose, peripubertal and adolescent girls and children with unstable family circumstances. Most of the patients presented with mild DKA which is similar to Habib HS study¹².

Kussmaul breathing and dehydration was the commonest clinical feature of DKA which is similar to a previous study¹⁴. Other study showed altered level of consciousness and dehydration were the common symptoms of DKA¹⁰. Another study showed that impaired consciousness, rapid breathing, vomiting were thecommon symptoms⁹. Altered level of consciousness was present in the severe form of DKA⁹⁻ ¹⁰. The reason for this difference is most of the patients in our study are mild variety DKA.

The poor value of HbA1c was found in other centers^{13,17-19} too. Serum creatinine was high. Elevation of creatinine concentrations could be explained by diminished renal perfusion. Five patients developed acute renal failure that improved after peritoneal dialysis. Acute renal failure (ARF) is a serious condition which still carries a mortality of around 50%.²⁰. There were three episodes of cerebral edema with two associated deaths. Cerebral edema is the most common cause of mortality in children with DKA²¹⁻²². The outcome of treatment was good in 41 (84%) patients who recovered without complications. Six patients died, the causes of death being septicemia (n=3), cerebral oedema (n-2) and pneumonia (n=1). Jayashree M, Sinqhi S showed that among 68 patients 9 patients have died¹⁶. Sepsis and cerebral edema have been reported as cause of death in DKA patients in India¹⁶.

Conclusion

DKA was the first presentation in 39% children with DM and multiple factors affect the risk of developing diabetic ketoacidosis. It can be diagnosed within a few minutes by measuring blood glucose, ketones and venous blood pH. Prompt and effective treatment can reduce the mortality and morbidity. Therefore, awareness about DM and DKA in children and adolescences is important.

Reference:

- 1. Brink SJ. Diabetic Ketoacidosis. *Acta Paediatr Suppl* 1999;**88**(427):14-24 <u>http://dx.doi.org/10.1111/j.1651-</u> 2227.1999.tb14335.x PMid:10195849
- Razavi Z. Frequency of Ketoacidosis in Newly Diagnosed Type 1 Diabetic Children. OMJ 2010;2:114-117 <u>http://dx.doi.org/10.5001/omj.2010.31</u> PMid:22125712 PMCid:PMC3215499
- Abdullah AH, Azad K. Diabetes Mellitus in Children and adolescents. *Bangladesh J Child Health* 1997;**21**(3/4):64-77
- Alvi NS, Davies P, Kirk JM, Shaw NJ. Diabetic ketoacidosis in Asian children. Arch Dis Child 2001;85(1):60-1 <u>http://dx.doi.org/10.1136/adc.85.1.60</u> PMid:11420205 PMCid:PMC1718843
- 5. Arleta R, Peter H C, Todd M et al. Predictors of acute complications in children with type 1 diabetes. *JAMA* 2002;**287**:2511-18 <u>http://dx.doi.org/10.1001/jama.287.19.2511</u>
- 6. Wolfsdorf J, Craig ME, Daneman D, Dunger D, Edge J et al. Diabetic ketoacidosis in children and adolescents with diabetes. ISPAD Clinical Practice Consensus

Guidelines 2009 Compendium. *Pediatric Diabetes* 2009;**10**(12):118–133 http://dx.doi.org/10.1111/j.1399-5448.2009.00569.x PMid:19754623

- 7. Wolfsdorf J, Glaser N, Sperling MA. Diabetic Ketoacidosis in Infants, Children and Adolescents. A consensus statement from the American Diabetes Association
- Shastry R M, Bhatia V. Cerebral edema in diabetic ketoacidosis. *Indian Pediatrics* 2006;43:701-708 PMid:16951433
- Faich G, Fishbein H, Ellis E. The epidemiology of diabetic acidosis: a population-based study. Am J Epidemiol 1983;117: 551 PMid:6405612
- Pinkney J, Bingley P, Sawtell P. Presentation and progress of childhood diabetes mellitus: a prospective population-based study. *Diabetoogia* 1994;**37**:70-74 <u>http://dx.doi.org/10.1007/BF00428780</u>
- Smith JAU, Thompson MJ, Sharp SJ, Walter FM. Factors associated with the presence of diabetic ketoacidosis at diagnosis of diabetes in children and young adults: a systematic review. *BMJ* 2011;343

- Habib HS. Frequency and clinical characteristics of ketoacidosis at onset of childhood type 1 diabetes mellitus in Northwest Saudi Arabia. *Saudi Med J* 2005;**26**(12):1936-9 PMid:16380776
- 13. Bui PB, Werther GA, Cameron FJ. Trends in diabetic ketoacidosis in children and adolescence: a 15-yr experience. *Paediatr Diabetes* 2002;**3**:82-88 <u>http://dx.doi.org/10.1034/j.1399-5448.2002.30204.x</u> PMid:15016161
- Rajasoorya C, Wong SF, Chew LS. Diabetic ketoacidosis--a study of 33 episodes. *Singapore Med J* 1993;**34**(5):381-4 PMid:8153679
- Mbuqua PK, Otieno CF, Kayima JK, Amayo AA, McLigeyo SO. Diabetic ketoacidosis: clinical presentation and precipitating factors at Kenyatta National Hospital, Nairobi. *East Afr Med J* 2005;82(12):S191-6
- Jayashree M, Singhi S. Diabetic ketoacidosis: predictors of outcome in a pediatric intensive care unit of a developing country. *Pediatr Crit Care Med* 2004;5(5):427-33 <u>http://dx.doi.org/10.1097/01.PCC.0000137987.74235.5E</u> PMid:15329157
- 17. Rosilio M, Cottton JB, Wieliczko MC et al. Factors associated with glycaemic control. A cross-sectional nationwide study in 2,579 French children with type 1 diabetes. *Diabetes Care* 1998;21:1146-1153 <u>http://dx.doi.org/10.2337/diacare.21.7.1146</u> PMid:9653610

- Thomsett M, Shield G, Batch J, Cotterill A. How well are we doing? Metabolic control in patients with diabetes. J Pediatr Child Health 1999:35:479-482 <u>http://dx.doi.org/10.1046/j.1440-1754.1999.355424.x</u> PMid:10571763
- 19. Mortensen HB, Robertson KJ, Aanstoot HJ et al. Insulin management and metabolic control of type 1 diabetes mellitus in childhood and adolescence in 18 countries. Hvidore Study Group on Childhood Diabetes. *Diabet Med* 1998:15:752-759 <u>http://dx.doi.org/10.1002/(SICI)1096-</u> 9136(199809)15:9<752::AID-DIA678>3.0.CO;2-W
- 20. Woodrow G, Brownjohn A.M, Turney J.H. Acute renal failure in patients with type 1 diabetes mellitus. *Postgrad Med J* (1994)**70**,192-194 <u>http://dx.doi.org/10.1136/pgmj.70.821.192</u> PMid:8183751 PMCid:PMC2397858
- 21. Glaser N, Barnett P, McCaslin I, et al. Risk factors for cerebral edema in children with diabetic ketoacidosis: the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. N Eng J Med 2001;344:264 –269 http://dx.doi.org/10.1056/NEJM200101253440404 PMid:11172153
- Edge JA, Hawkins MM, Winter DL, Dunger DB. The risk and outcome of cerebral oedema developing during diabetic ketoacidosis. *Arch Dis Child* 2001;85:16–22 <u>http://dx.doi.org/10.1136/adc.85.1.16</u> PMid:11420189 PMCid:PMC1718828