Original Article

Frequency, clinical characteristics and outcome of diabetic ketoacidosis in children with type-1 diabetes at a tertiary care hospital

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Abstract

Objective: To observe the frequency, demographic data and outcome of diabetic ketoacidosis (DKA) in children with established type 1 diabetes and newly diagnosed diabetes at a tertiary care hospital.

Methods: The case record review was done of children admitted with the diagnosis of DKA at The National Institute of Child Health, Karachi from 1st June 2008 till 31st May 2009. All records with the diagnosis of DKA were reviewed and those children with only hyperglycaemia, or who did not fulfill the criteria of DKA were excluded. The demographic data and laboratory investigations which included blood sugar monitoring, arterial blood gases, urine analysis especially for ketones, serum electrolytes, complete blood count and blood culture were reviewed. The previous numbers of admissions in children with established DKA were also noted with reasons. The duration of symptoms and fluids required, time of recovery, complications, and outcome were noted and compared between those with established diabetes and children with newly diagnosed diabetes. Data was entered and analyzed on SPSS version 15.

Results: Out of 124 case records, 117 were included which fulfilled the criteria of DKA. A large number, 65 (55.5%) children were in the > 10 years age group with a female predominance. Out of 117 children 50 (42.7%) had established Type 1 diabetes and 67 (57.2 %) children had newly diagnosed diabetes. The commonest presenting complaints in both groups were respiratory distress (87.1%) and vomiting (77.7%). The symptoms of polyuria, polydipsia and nocturia were more among the newly diagnosed children as compared to those with established diabetes with a significant p value <0.001. The comparison of clinical features and laboratory investigations of the two groups showed no difference except that those children with established diabetes improved earlier, required lesser duration of intravenous fluids and their insulin was changed to subcutaneous in less time compared with newly diagnosed children. ($p<0.001$). The commonest complication in both groups was hypoglycaemia followed by hyponatraemia, more in newly diagnosed diabetic children.

Conclusion: These soaring numbers are just from one center, highlighting the issue of this much neglected disease in our country. More studies on a larger scale are needed to assess the prevalence/incidence in our children and also more emphasis with educational programmes on prevention of recurrent attacks of DKA (JPMA 60:725; 2010).

Introduction

Diabetic ketoacidosis (DKA) is an acute life threatening metabolic emergency, frequently requiring hospitalization in children with type 1 diabetes and still remains their major cause of mortality.[1,2] There is a wide variation in the range of children presenting with DKA as the initial manifestation of diabetes depending on the study population. In children with established diabetes the incidence is more homogenous.[3,4] International studies have shown that between 15 and 67% of children, newly diagnosed type 1 diabetes mellitus presents in DKA. The estimated risk of DKA in children /adolescents with established type 1 diabetes is 1-10 per 100 person/year.[5,6]

DKA still remains a significant complication of type 1 diabetes associated with a variety of significant adverse events.[6] Studies indicate that further efforts to reduce the occurrence of DKA must be focused upon early diagnosis and intervention in newly diagnosed children. The physicians[1] aim is to reduce the incidence of DKA through awareness and sensitization of the disorder, and in children with established diabetes through focused management and education. Hence, prevention of DKA, especially after initial diagnosis, is still a primary challenging target for physicians.[7] This desirable goal is achievable through self management programmes and has been amply documented internationally but no data on this aspect is available locally.[8]

DKA is one of the major neglected health issues in Pakistan; although we are managing a large number of children with Type 1 diabetes and believe that its incidence is also on the rise in our country but unfortunately local data about the exact incidence / prevalence is not documented.[9]

National Institute of Child Health, Karachi is a tertiary health care hospital treating children from Sindh, Punjab and even more remote villages all over Pakistan. The institute has been treating diabetic patients since many years and has an average of 8-10 DKA children per month. Majority of these children present with DKA due to late diagnosis and referral, some have been taking oral hypoglycaemic agents or were being managed for acute abdomen. We therefore reviewed our data to observe the various ages, frequency, clinical presentations and outcome of DKA in children with established type 1 diabetes and newly diagnosed diabetes.

Patients and Methods

The case record review was done of children admitted with the diagnosis of DKA at National Institute of Child Health, Karachi from 1st June 2008 till 31st May 2009. All records with the diagnosis of DKA were reviewed and DKA was diagnosed if hyperglycaemia (blood glucose > 200mg/dl), venous pH < 7.3 or bicarbonate < 15 mmol/L and ketonuria were present.[5] Those children with only hyperglycaemia, or who did not fulfill the criteria of DKA were excluded.

The children were divided into two groups, those with newly diagnosed type 1 diabetes (first episode) and those with established diabetes and on treatment with insulin. In children with established diabetes relapse of DKA is common, which occurs due to sudden cessation of subcutaneous insulin or lack of monitoring.[5] In children with established diabetes , those having one episode of DKA/year were non relapsers and those with at least two episodes of DKA per year were relapsers.[6]

In all children the duration of signs and symptoms and in children with established diabetes the duration of diabetes; number of DKA admissions with reasons, dose and type of insulin regime and compliance with treatment were reviewed. The laboratory investigations which included random blood sugar (done 2 hourly), arterial blood gases (4 hourly), detailed urine report especially for ketones, serum electrolytes, complete blood count and blood culture between the two groups were observed. The management in the Paediatric Intensive Care Unit, regarding duration of intravenous fluids and insulin infusion, administered according to the standard DKA protocol of ISPAD (International Society of Pediatric and Adolescent Diabetes) were noted.[10]

Random blood sugar or casual plasma glucose concentration is defined as done at any time of the day without regard to last meal(greater than 200mg/dl with symptoms requires investigation). Hypoglycaemia was defined as blood sugar less than 60 mg/dl, Hypokalaemia: serum potassium less than 3 mEq/L, Hyperkalaemia: serum potassium more than 6 mEq/L, Hyponatraemia: serum sodium less than 135mEq/L after calculating corrected sodium, Hypernatraemia: serum sodium more than 160mEq/L.[6,10,11] Cerebral oedema was defined as having occurred if the child developed irritability, decreased conscious level, rising blood pressure, decreased heart rate and the patient was treated with intravenous mannitol, with or without radiologic (CT) confirmation.[10,12]

Time for resolution of DKA was recorded in all children and the criteria for resolution included a normal sensorium and vitals, no emesis, resolution of acidosis (normal pH, serum bicarbonate of > 18mEq/L and normal anion gap).[10] After resolution of DKA, newly diagnosed children were shifted to ward to counsel about disease, insulin technique and storage and also nutritional advise. Blood sugar was considered to be in normal range if fasting was less than 100mg/dl and 2 hours post meal was < 140mg/dl. Outcome of DKA was defined in terms of death or survival of the child.

Data was entered and analyzed on SPSS version 15.

Statistical Analysis:

The qualitative data (Table-1) of established and newly diagnosed diabetics was analyzed using chi square and fisher exact test where needed. (expressed as percentages). For

quantitative data (Table-2) student un-paired t-test was used and mean and standard deviations were obtained.

In all statistical analysis only p-value <0.05 was considered statistically significant.

Results

The charts of 117 children fulfilled the criteria of DKA; 50 (42.7%) had established Type 1 diabetes and 67 (57.2 %) children were newly diagnosed Type 1 diabetes. A large number 65(55.5%) of children were > 10 years of age with a female predominance in both groups. The commonest presenting complaints in both groups were respiratory distress (87.1%) and vomiting (77.7%) (Table-1).

In children with established diabetes, majority of children 36 (72%) were in > 10 years age group and the main identified cause of DKA was omission of insulin dose. Out of the 50 children with established diabetes, 34(68%) children were non relapsers and 16 (32%) were relapsers. The promoting factors for DKA included insulin omission in 19 (38%) children (9 did it because the child was vomiting, 4 because the child had decreased appetite and 6 due to financial reasons), urinary tract infection in 10 (20%), enteric fever in 6 (12%) and in 15 (30%) children the cause was unknown.

Majority of children having the first episode of DKA as the presentation of type 1 diabetes belonged to the >10 years age group. Sixteen (23.8%) children had urinary tract infection at the time of diagnosis and in the remaining 51 (76.1%) no cause could be identified. Thirty eight (56.7%) children presented with weight loss. The symptoms of polyuria, polydipsia and nocturia were more among the newly diagnosed children as compared to those with established diabetes (p <0.001).

Table-1: Demographic features and presentations of DKA in established and newly diagnosed Type 1 diabetes.

	Total no of children (n=117)	Known diabetic (n=50)	New diabetics (n=67)	P value
Age in years				
< 5	9	2 (4%)	4(5.9%)	
5 - 10	43	11(22%)	23(34.3%)	
>10	65	36(72%)	41(61.1%)	
Gender				
Male	51	24(48%)	27(40.2%)	
Female	66	26 (52%)	40(59.75)	
Presenting complaints				
Respiratory distress	102	41(89%)	61 (90%)	0.565
Vomiting	91	45(97.8%)	46 (85.2%)	0.174
Polyuria	84	24 (51.2%	52 (96.3%)	0.001
Fever	64	22 (47.8%)	42 (77.8%)	0.004
Nocturia	53	7 (15.2%)	46 (85.2%)	0.001
Polydypsia	69	17 (37%)	52 (96.3%)	0.001
Abdominal Pain	79	40 (86.7%)	37 (68.5%)	0.018
Unconscious	59	27(58.7%)	23 (42.6%)	0.115

RBS: Random Blood Sugar. PICU: Paediatric Intensive Care Unit. Na: Sodium.

Table-2: Comparison of clinical features and laboratory investigations of children with DKA.

	Established diabetic (n=50)	New diabetics (n=67)	P value
	Mean ± S.D.	Mean ± S.D.	
Conscious level (G.C.S.)	12.6 ± 2.08	12.84 ± 1.66	0.497
Respiratory Rate(breaths /min)	38.4 ± 7.09	36.7 ± 7.37	0.208
Heart rate(beats/min)	106 ± 14.3	102 ± 14.3	0.123
Systolic blood pressure(mmHg)	108.9 ± 7.9	112 ± 8.06	0.035
Oxygen saturation (%)	90.9 ± 3.03	90.9 ± 3.08	0.710
Haemoglobin (gm/dl)	9.87 ± 1.33	9.59 ± 1.48	0.292
Total leucocyte count/cumm	9716 ± 5952	11305 ± 7202	0.208
PH	7.14 ± 0.13	7.08 ± 0.14	0.041
PO2 mmHg	130.7 ± 46.26	126.1 ± 38.66	0.564
PCO2 mmHg	22.70 ± 11.2	22.6 ± 9.86	0.976
HCO3(mEq/l)	7.2 ± 3.60	6.79 ± 3.31	0.526
S. calcium (mg/dl)	7.97 ±0.68	7.86 ± 1.08	0.524
S. Creatinine (mg/dl)	0.59 ± 0.39	0.62 ± 0.41	0.592
Serum potassium (mEq/l)	3.94 ± 0.88	3.85 ± 0.81	0.567
Serum Na(mEq/l)	133.2 ± 4.7	132 ± 4.8	0.215
RBS normalized (in days)	4.08 ± 1.97	5.87 ± 1.92	0.001
Duration of fluid therapy (hr)	36.4 ± 15.9	44.96 ± 8.9	0.001
I/V insulin switched to subcutaneous (hrs)	27.5 ± 14.1	53 ± 14.7	0.001
Orally allowed (hrs)	26 ± 14.1	39.6 ± 11.74	0.001
Stay in PICU (days)	40.6 ± 12.8	54.1 ± 15.55	0.001
Stay in ward(days)	3.50 ± 2.30	7.18 ± 1.71	0.001

Table-3: Problems encountered during management of DKA.

Complication	Established diabetes (n=50)	Newly diagnosed diabetes (n=67)
Hypokalaemia	2 (4%)	5 (7.4%)
Hyperkalaemia	0	1 (1.4%)
Hyponatraemia	3 (6%)	6 (8.9%)
Hypoglycaemia	7 (14%)	13 (19.4%)

Hypokalaemia: Serum K+ < 3meq/L
Hyperkalaemia: Serum K+ > 6 meq/L
Hyponatraemia: Serum Na < 135 meq/L
Hypoglycaemia: Blood glucose < 60mg/dl.

The comparison of laboratory investigations of the two groups showed no significant differences except that children with established diabetes improved earlier, required less duration of intravenous fluids and their insulin was changed to subcutaneous in less time compared with newly diagnosed children (p<0.001).

All children were acidotic and had urinary ketones 3+ at presentation. There were no significant differences between the two groups regarding acidosis or hyperglycaemia at the time of admission. Out of 117 children 3 (2.5%) received injection sodium bicarbonate, as after rehydration and insulin infusion their acidosis did not improve and their pH was less than 6.7 with cardio respiratory compromise. The stay in PICU and ward of children with established DKA was less as

compared to newly diagnosed children ($p<0.001$) . The children who were newly diagnosed had a longer stay in ward because they had to learn the technique of insulin administration and nutritional counseling.

Table-3 shows the various complications encountered during management of DKA. The commonest complication was hypoglycaemia followed by hyponatraemia in both groups, more in the newly diagnosed children (19% and 4.4%). Fortunately there was no mortality and none of the children developed cerebral oedema or renal failure during the treatment.

Discussion

The incidence of DKA is increasing worldwide, but is still underestimated and unknown in Pakistan due to scarce local data. The frequency of DKA in international studies ranges from 26% to 70% in children with newly diagnosed diabetes. Due to limited data, we do not know about the trend of DKA, whether it is rising or decreasing in children. A local study done showed lower frequency of DKA as compared to ours; 2.2% children with established diabetes and 6.7% with newly diagnosed diabetes presented with DKA.[9]

The age of presentation in our children is similar to that reported in international studies with a female predominance.[4,10] The number of female children was higher in the newly diagnosed group, which differs from other studies as they found a higher number of females in children with established diabetes.[10,12] The reason for this female pre pond evince in newly diagnosed diabetes cannot be explained.

The duration of signs and symptoms of DKA was shorter in children with established diabetes; not being more than 3 days, compared with the newly diagnosed children who had symptoms for an average of 3 weeks. This prolonged stay in newly diagnosed diabetes was because the parents initially were in denial phase requiring repeated counselling. Also due to a low literacy rate and it took long to teach them the technique and storage of insulin and to be certain that the parents would be able to manage the child at home. A local study done by Bhatti et al also showed that children presenting late had more severe derangements of acid base balance.[13]

The complaints in both groups were similar with the main difference in duration.[14,15] Majority of the newly diagnosed children were being treated for abdominal pain or urinary tract infection before they were referred to us; highlighting the need for more programmes for awareness among general practitioners for early diagnosis and referral.

In our study 38% with established diabetes presented in DKA due to insulin omission, Musey et al reported 27 to 60% of children presenting with DKA due to insulin omission.[16] The main reason for insulin omission identified in our patients was non affordability. We cater to the poor people and lack of awareness despite counseling led to the consequences of missing a dose. In western countries the major cause of DKA in children with established diabetes are behavioural problems and in females mostly due to weight reduction.[17] The puberty related factors are also being encountered in our environment, and a multidisciplinary approach will have to be adopted. No cause for DKA could be identified in a large number of children with newly diagnosed diabetes.

The recovery in children with established diabetes was faster compared to those with newly diagnosed diabetes. The former group required less duration of intravenous fluids (36 hr vs 45 hrs), insulin infusion (27 vs 53 hrs) and had a shorter stay in PICU (40 vs 54 hours). Initially all children received insulin infusion and when the DKA was resolved they were changed to subcutaneous insulin. The shift to subcutaneous insulin was early, within 24 hours, in children with established diabetes as compared to newly diagnosed children who needed insulin infusion for 48-72 hours. Those with established diabetes were also discharged earlier from the ward as they only needed treatment for infection or counseling in cases of frequent relapses.

Compared with international studies, complications were less in our study; the commonest was hypoglycaemia (17%), encountered mostly after 24 hours, other studies show a frequency of 12.7%.[18]

The limitations of the presented study are that it is a retrospective review of case records. As NICH is a tertiary care centre for treating children, it is difficult to comment on the incidence of DKA in the country. A central registry along with prospective studies conducted countrywide, would provide the true figures of prevalence of type-1 diabetes and the frequency of DKA.

Conclusion

This study highlights a large number of newly diagnosed children presenting with DKA; these figures are from one center only and definitely more studies at a national level will help us to determine the incidence of DKA in our country. The study also shows the long term need for counseling and educational programmes for children and their families with established diabetes, to prevent complications especially DKA.

References

1. Basu A, Close CF, Jenkins D, Krentz AJ, Nattrass M, Wright AD. Persisting mortality in diabetic ketoacidosis. Diabet Med 1993; 10: 282-4.
2. Alvi NS, Davies P, Kirk JM, Shaw NJ. Diabetic ketoacidosis in Asian children. Arch Dis Child 2001; 85: 60-1.
3. Rewers A, Chase HP, Mackenzie T, Walravens P, Roback M, Rewers M, et al. Predictors of acute complications in children with type 1 diabetes. JAMA 2002; 287: 2511-8.
4. No author listed. Secular trends in incidence of childhood IDDM in 10 countries. Diabetes Epidemiology Research International Group 1990; 39: 858-64.
5. Keeran WJ. Recommendations for management of the child born through

meconium - stained amniotic fluid. Paediatrics 2004; 113: 133-4.

6. Bui TP, Werther GA, Cameron FJ. Trends in diabetic ketoacidosis in childhood and adolescence: a 15-year experience. Paediatr Diabetes 2002; 3: 82-8.
7. DIAMOND Project Group. Incidence and trends of childhood type 1 diabetes worldwide 1990-1999. Diabet Med 2006; 23: 857-66.
8. Sperling MA. No gold at the ends of the glycaemic rainbow. J Pediatr 2002; 141: 754-6.
9. Shera AS, Miyan Z, Basit A, Maqsood A, Ahmadani MY, Fawwad A, et al. Trends of type 1 diabetes in Karachi, Pakistan. Pediat Diabetes 2008; 9: 401-6.
10. Wolfsdorf J, Craig ME, Daneman D, Dunger D, Edge J, Lee, WR; International Society for Paediatric and Adolescent Diabetes, et al. Diabetic ketoacidosis. Paediat Diabetes 2007; 8: 28-43.
11. Clarke W, Jones T, Rewers A, Dunger D, Klingensmith GJ. Assessment and management of hypoglycaemia in children and adolescents with diabetes. Pediat Diabetes 2008; 9: 165-74.
12. Glaser NS, Wootton-Gorges SL, Buonocore MH, Marcin JP, Rewers A, Strain J, et al. Frequency of sub-clinical cerebral edema in children with diabetic ketoacidosis. Paediat Diabetes 2006; 7: 75-80.
13. Bhatti MT, Butt T, Qazi MY. Clinical and Biochemical features of Diabetic Children at initial presentation. Pak Paed J 2002; 26: 195-8.
14. Afzal A, Zaheer H, Jamalvi WA, Nisar K, Mazahir I. Presentation and precipitating factors of Diabetic Ketoacidosis in children. Ann Abbassi Shaheed Hospital Karachi Med Dent Coll 2005; 10: 766-74.
15. Smith CP, Firth D, Bennett S, Howard C, Chisholm P. K. Ketoacidosis occurring in newly diagnosed and established diabetic children. Acta Paediatr 1998; 87: 537-41.
16. Musey VC, Lee JK, Crawford R, Klatka MA, McAdams D, Philips LS. Diabetes in urban African Americans.Cessation of insulin therapy is the major precipitating cause of diabetic ketoacidosis. Diabetes Care 1995; 18: 483-9.
17. Dumont RH, Jacobson AM, Cole C, Hauser ST, Wolfsdorf JI, Willett JB, et al. Psychosocial predictors of acute complications of diabetes in youth. Diabet Med 1995; 12: 612-8.
18. Malone ML, Klos SE, Gennis VM, Goodwin JS. Frequent hypoglycaemic episodes in the treatment of patients with diabetic ketoacidosis. Arch Intern Med 1992; 152: 2472-7.