SHORT ARTICLE

Diabetic keto acidosis—among children with established diabetes from a pediatric tertiary care Institute

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Abstract A prospective observational study was undertaken from a pediatric tertiary care Institute at Chennai, among the diabetic keto acidosis (DKA) episodes in children with established diabetes mellitus (DM) and DKA in new onset DM between Jun 2009 and Jan 2012. Clinical and laboratory parameters, predisposing factors, complications and the outcome were compared between the two groups. Among the 97 episodes of DKA treated during the study period 42(43.3 %) were among the known diabetic children. Overall 32 children accounted for 42 episodes of DKA. Female preponderance was encountered among DKA episodes in children with established diabetes. All children with 2 or more episodes of DKA were females. Precipitating factors were infections in 47 % and poor compliance to therapy in 28 % . Difficult or unstable family circumstances were encountered in 40 % of children. Female preponderance (P-0.001), severe DKA (P-0.003), shorter duration of illness(P-0.009), skin infections (P-0.028) and higher insulin requirement (P-0.003) showed a statistically significant difference in DKA among children with established DM in comparison to DKA among new onset DM. The metabolic parameters and complications were almost similar to newly diagnosed diabetic children. Mortality in DKA among established diabetic children is 7.1 % in comparison to 12.7 % in new onset DKA.

Keywords Insulin dose · Precipitating factors · Gender · Diabetic ketoacidosis

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Introduction

The risk of diabetic ketoacidosis (DKA) in children and adolescents with established type 1 diabetes is 1–10 per 100 person-years [1] and is one of the leading causes for mortality in children with diabetes. Among known diabetic children DKA is mostly avoidable. The predis-posing factors among the new onset DKA and DKA among children with established diabetes are different and need to be addressed . Better awareness among the parents and physicians can decrease the onset of diabetes as DKA by earlier diagnosis [2, 3]. Counseling regarding compliance to therapy and improved diabetic care can prevent recurrence of DKA among children with established diabetes. The contri-bution of poor compliance to therapy, social support, or inter-current infections needs to be studied among the children with recurrent DKA.

Aim To study the predisposing factors, complications and outcome of DKA among children with established diabetes and to compare the presentation, laboratory parameters, complications and outcome between the new onset DKA and DKA among established diabetic children. Study setting : The study was conducted at a pediatric tertiary care Institute predominantly treating children from lower socioeconomic strata at Chennai. Study period: Jun 2009 – Jan 2012. Study population: All children admitted with DKA at the Pediatric intensive care unit during the study period. Exclusion criteria: Children diagnosed as DKA, and have received partial treatment elsewhere prior to referral to our Institute were excluded, as the initial parameters of these children will not be available after intervention.

Methodology All the diabetic children admitted with DKA were enrolled in the study. Children with new onset Diabetes were considered as group 1 and DKA among children

established diabetes were considered as group 2. The predisposing factors, laboratory parameters, complications and outcome of DKA among children with established diabetes were studied and were compared with those with new onset DKA. DKAwas diagnosed based on the following lab criteria: hyperglycemia - blood glucose >200 mg/dL, venous pH <7.3 and or bicarbonate <15 mEq/L and ketonemia or ketonuria. The study parameters included age of the child, gender, diabetic duration, diabetic control assessed by HbA1c levels, self monitoring of blood glucose at home, compliance to therapy, missed diagno-sis, severity of DKA, initial osmolality, sensorium at presenta-tion, presence of infections and shock, complications (cerebral edema, renal failure, dyselectrolytemia). Missed diagnosis was defined as any diagnosis other than DKA, entertained by the referral physician or at by the physician at admission for this episode of illness. Severity of DKA was defined as follows. Mild: pH >7.2 and <7.3, bicarbonate <15 mmol/L. Moderate: pH >7.1 and <7.2, bicarbonate <10 mmol/L. Severe: pH <7.1, bicarbonate <5 mmol/L. At the emergency room sensorium was assessed using the AVPU scale. (Alert, verbal, pain respon-sive and unresponsive). Infections were diagnosed as per clin-ical and or laboratory evidence. Shock was defined as per the criteria in pediatric advanced life support. Cerebral edema was defined as per diagnostic criteria,including abnormal motor or verbal responses to pain, decorticate posture, and abnormal neurogenic respiratory pattern. Major, but not diagnostic criteria include altered mentation, sustained heart rate decelerations, and age-inappropriate incontinence. Minor criteria include vomiting, headache, lethargy, diastolic blood pressure more than 90 mm Hg, and age less than 5 years. One diagnostic criterion, two major criteria, or one major and two minor criteria were necessary for diagnosis of cerebral edema [4]. Renal failure was defined according to pediatric RIFLE criteria(Risk, Injury, Failure, Loss, End stage renal disease) by estimated creatinine clearance or urine output . Estimated creatinine clear-ance decrease by 75 % or less than 35 ml/mt/1.73 m^2 or oliguria defined by urine output <0.3 ml/kg/hr over 24 h or anuria for 12 h [5, 6]. Dyselectrolytemia was defined by the following; Hypokalaemia: Serum K^+< 3.5 meq/L, Hyperkalaemia: Serum K^+ > 6 meq/L, Hyponatraemia: Serum Na < 135 meq/ L(calculated sodium), Hypernatremia: Serum Ns>150 meq/L. Poor compliance to therapy was defined as missing one or more doses of insulin or inappropriate reduction of the prescribed insulin dose without indication. Poor social support or difficult/ unstable family circumstances were defined by the following parameters - single parent or lack of both parents, unsupervised self insulin injections, lack of blood glucose monitoring at home, unsupervised blood glucose monitoring at home and child not attending school and lack of regular follow up at the diabetic clinic. HbA1c levels were measured by fully automat-ed HPLC (High pressure liquid chromatography) using TOSOH G8 during the episode of DKA. Infections were cate-gorized as sepsis, bronchopneumonia, urinary tract infection, skin and soft tissue infection, otitis media and acute CNS infections based on clinical and/or radiological or laboratory investigations. Mucosal candidiasis of the external genitalia alone was not considered as an infection predisposing to DKA. Outcome was defined as recovery at discharge or death. All children diagnosed to have DKA were admitted to the pediatric intensive care unit and were treated as per the protocol of the unit. Study was conducted after the Institutional ethical clearance and written informed consent from the primary care givers of these children. Study parameters were analysed using Epi Info statistical software. In the descriptive statistics, mean, standard deviation and percentages were computed. The study parameters were compared between the two groups. P values were calculated by using the chi square test, or fisher exact test wherever applicable and the P value of <0.05 was considered significant.

Results Among the 97 episodes of DKA encountered, 55 episodes were new onset diabetes presenting as DKA and 42 (43.3 %)episodes were among children with established diabetes.

Among the 42 episodes of DKA in known diabetic children, 5 children accounted for 16 episodes of DKA. Overall 32 children accounted for 42 episodes of DKA. All children with two or more episodes of DKA in this study were females. The children with 4 and 5 episodes were all from stressed family environment with single caregiver and one of them had unsupervised injection therapy at home. Among the supervised group voluntary reduction in the dose drawn into the syringe was encountered in 3 children. 36 episodes (85.7 %)were among girls 6(14.28)% were among boys. Female male ratio was 6:1. The age of the children ranged from 8 months to 13 years. Among the boys 3 were less than 5 years and 3 were more than 5 years of age. Among the girls 5 were less than 5 years and 31 were more than 5 years of age. The diabetic age(duration of diabetes) ranged from 1 month to 10 years. Other parameters of Group 2 are summarised in Table 1.

Among the children with new onset Diabetes with Keto acidosis 43.63 % were under 6 years of age in comparison to DKA among children with established DM where it was 23.8 %. The male female ratio was 1:1 unlike in children with established DKA which showed a female preponderance. Mild DKA was encountered in 26 % of the new onset DKA in comparison to 12 % among the DKA in children with established DM. The mean duration of illness was 1.94 days. Among those with dyselectrolytemia hypokalemia was sig-nificantly higher in children with new onset DM, almost 50 % of children with new onset DKA had hypokalemia. Hyperkalemia was more common in DKA among established DM group. Infections were encountered in 41.8 % of the children of which urinary tract infection was the most common. Cerebral edema was the commonest complication encountered in 29 % of the study population. The mean insulin requirement was 1.2 units/kg in children with new onset DKA.

Table 1 Parameters among DKA in children with established DM

	Parameter	N =42
Age at DKA	<5 years	8
	>5 years	34
Gender	Male	6
	Female	36
Diabetic age	<I year	18
	1–3 year	13
	4–5 years	7
	>5 years	4
DKA episodes	1	26
	2	2
	3	1
	4	1
	5	1

The blood glucose at presentation ranged from 273 to 827 mg/dl in new onset and from 200 to 692 mg/dL among known diabetic children. Duration of illness ranged from 1 to 5 days in both groups. Initial osmolality ranged from 274 to 363 mosm/L in new onset DKA and from 271 to 325 mosm/L in DKA among known diabetic children. Initial bicarbonate ranged from 1 to 19 mmol/L in group 1 and 1.6–16 mmol/L in group 2. Hematocrit ranged from 20 to 55 in group1 and 25 to 52 in group 2 . Initial blood pH ranged from 6.7–7.3 in group 1 and 6.72–7.3 in group 2 . Initial $PaCo_2$ ranged from 6.8 to 40 in group 1 and 5.3–46 group 2. Initial Total count ranged from 3,700–35,000/cumm with a mean of 13,678±7,922/cumm in group 1 and from 5,000 to 43,700/cumm with a mean 15,123 ±9,409 in group 2 (P-0.41). With treatment blood glucose declined to 250 mg/dl by 9.3±8.6 h and 6.35±3.50 h in Group 2 with a range of 3–48 h and 2–17 h in respectively. Infusion of insulin ranged from 5.5 to 192 h in new onset DKA and 8– 144 h in children with known diabetes presenting with DKA. Insulin requirement among those with new onset DKA ranged from 0.4 units to 2.73units/kg/day. In group 2 insulin require-ment ranged from 1 to 3.63 units/kg/day. HbA1c ranged from 4.8 to 18.7 in group 1 and from 7.7. to 19.7 in group 2. The mortality among new onset DKA is 12.7 % and among known diabetic children with DKA is 7.1 %. Comparison of the mean values and other parameters among the two groups is shown in Table 2.

Discussion

Among the 42 episodes of DKA in established diabetic children, female predominance was encountered (P-0.001). This is similar to earlier studies. Large multicenter study from Germany and Austria on 28,770 children aged 19 years or younger also reported the greatest risk of DKA in established type 1 diabetes was in the early teenage years, particularly in girls and children from immigrant families [7, 8] New onset presenting with DKA did not show any significant gender difference in our study, similar to earlier reports [7, 8].

Younger the age, more likely were the children to present with DKA. (18 among the 42 were of less than 1 year diabetic duration versus 4 of more than 5 years diabetic duration) . In this study 15 % of the children accounted for 38 % of episodes of DKA. A recent study at Colorado revealed 20 % of the patients accounted for 80 % of the episodes [9]. Among the recurrent DKA (2 or more episodes) children were much older, with poor social support encountered in 13 of the 32(40 %) children with established diabetes. Among the re-current DKA 3 of the 5 children had poor social support. Recurrent episodes (two or more) of DKA during the study period were found in 15.6 % of children in this study . The risk factors for recurrent DKA in literature is almost similar and were poor metabolic control, previous episodes of DKA, female gender (peripubertal or adolescent), psychiatric disor-ders including eating disorders, difficult or unstable family circumstances, limited access to medical services, and insulin pump therapy [9].

Among the DKA in children with established diabetes, 28 % of the episodes were precipitated by poor compliance to therapy and 47 % were precipitated by infections. These results are similar to earlier literature evidence which show it to be 25 % and 40 % respectively [10]. In a study from Pakistan, insulin omission precipitated DKA in upto 38 % pediatric patients with established diabetes [11].

The reasons for poor compliance included intercurrent illness like vomiting and non availability of insulin . Missing of insulin was more common in older children who were not regularly supervised at home by the caregivers. Missing of insulin was less common in children when parents were giving the injections. Responsible adult giving insulin reduced the incidence of recurrent DKA episodes by ten fold . Recur-rent episodes of DKA are much more common in children with problems related to compliance with insulin therapy. Therefore assuring administration of insulin by a responsible adult is critical [12].

Among the infections skin and soft tissue infections like boils, furuncles and abscess were more common followed by UTI, pneumonia and sepsis [13].

Comparison of the study parameters among the DKA in children with established diabetes and those with new onset DKA revealed the following. The mean duration of ketoacidosis symptoms was significantly shorter in children with known diabetes than new onset DKAwhich could be due to increased awareness among the diabetic families for seek-ing appropriate health care. This is similar to the reports from Karachi [11]. Also the DKA episodes among diabetic children

Table 2 Comparison between the New onset DKA and DKA in children with established DM

	Parameter	Newonset (N =55)	Known DM (N =42)	P value
Age	<3 years	16	5	0.18
	3–6 years	8	5	
	6–9 years	10	11	
	9–13 years	21	21	
Gender M:F		27:28(1:1)	6:36 (1:6)	0.001[a]
DKA	Grade1	20	5	
	Grade2	10	19	
	Grade 3	25	18	0.003[a]
Shock		7(12.7 %)	2(4.76 %)	0.16
ER sensorium AVPU		21,15,16,3	20,9,11,2	0.68
Blood glucose		516.2±109	488±108	0.22
Duration of illness		1.94±0.97	1.45±0.80	0.009[a]
Insulin Infusion hrs		39.13±36	27.9±23	0.099
HCO_3(mmol/dl)		6.7±4.9	6.8±4.4	0.96
Hematocrit%		37.9±6.7	38.9±6.23	0.53
PH		7.07±0.19	7.07±0.15	0.92
$PaCo_2$		17.5±8.7	17.16±9.7	0.84
HBA1C %		12.06±3.13	11.14±2.17	0.106
Initial osmolality		301.2±14.98	301.99±11.79	0.22
Hypokalemia		27(49.9 %)	13(30.95 %)	0.07
Hyperkalemia		7(12.7 %)	15(35.7 %)	0.007[a]
Hyponatremia		13(23.6 %)	7(16.6 %)	0.28
Hypernatremia		9(16.36 %)	4(9.52 %)	0.25
Overall Infections		23(41.8 %)	20(47.6 %)	0.358
UTI		7(12.7 %)	5(11.9 %)	0.90
Pneumonia		3(5.45 %)	2(4.76 %)	0.626
Skin soft tissue		3(5.45 %)	9(21.4 %)	0.028[a]
Sepsis		5(9.09 %)	2(4.76 %)	0.51
Mucosal candidiasis		16(29.09 %)	8(19.045)	0.37
ARF		7(12.7 %)	1(2.38 %)	0.067
Cerebral edema		16(29 %)	7(16.66)	0.236
Insulin dose		1.289±0.455	1.58±0.491	0.003[a]
Mortality		7(12.72 %)	3(7.1 %)	0.29

[a] Significant P value

was significantly of greater severity than new onset DKA. This could be due to the early identification of hyperglycemia by home based glucose estimation and appropriate insulin adjustment at home for mild DKA's. Children with moderate and severe DKA were brought for in hospital admission among the established diabetic children. Recurrent DKA was more in female children (P-0.001)

DKA was more common in the first year of diagnosis of diabetes as seen in 42.8 % and the occurrence decreases with increasing diabetic age. Younger the diabetic age more likely were the children to present with DKA (p-0.003). This is likely to be due to the improving ability to manage the diabetic fluctuations at home by the children and the caregivers due to better understanding of the problems and management of diabetes with increasing duration of diabetes. Literature reveals studies which had no such influence of the duration of diabetes with recurrent DKA [7].

The initial parameters (blood glucose, initial bicarbonate, pH, hematocrit, osmolality and paCo2) were not statistically different among the children with diabetes and new onset DKA. However, depressed sensorium at admission at ER was significantly higher in the DKA among diabetic children compared to the new onset DKA. Hypokalemia was common in children with new onset diabetes and this could be possibly due to the unrecognized symptoms in new onset diabetes where the total body potassium would be much lower and for the same reason the occurrence of hyperkalemia is much less in new onset DKA.

Among the complications cerebral edema, acute renal failure and shock were not statistically significant among the

groups. The mean duration of insulin infusion did not differ in contrast to an earlier study from Karachi [11] as our group 2 were predominantly severe DKA's. The insulin requirement after stabilization was much higher in the known diabetic children and this is probably a reflec-tion of inadequate diabetic control in the children with DKA as shown by the higher HbA1C levels. The higher mortality among the new onset DKA may be due to the higher number of sepsis, UTI, renal failure, cerebral ede-ma however there was no statistically significant diffe-rence. Mortality in diabetic children presenting with DKA were related to cerebral edema as in the case of new onset DKA [14].

Conclusions

Intercurrent infections(47 %) and poor compliance to in-sulin(28 %) were found to be the predisposing factors for DKA among children with established diabetes mellitus. Children with 2 or more episodes were all females. Fe-males, shorter diabetic duration(diabetic age) and unstable family circumstances and age more than 5 years among children with established DM were more likely to present with DKA. Female preponderence, severe DKA, shorter duration of illness, skin infections and higher insulin re-quirement showed statistically significant difference in DKA among children with established DM and new onset DM.

Recommendations

Adequate counseling and information about intercurrent ill-ness management and appropriate stable family circumstances including supervision of insulin therapy by a responsible adult at home can reduce the occurrence of DKA among children with established diabetes. Female children with diabetes need to be followed up with frequent counselling to prevent recur-rent DKA .

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Conflict of interest None

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