Frequency and clinical characteristics of ketoacidosis at onset of childhood type 1 diabetes mellitus in Northwest Saudi Arabia

Hamed S. Habib, CABP, MRCP (UK).

ABSTRACT

Objective: To determine the frequency, and to describe the clinical characteristics of ketoacidosis at initial diagnosis of childhood type 1 diabetes mellitus (T1DM) in Al-Madina region of the Northwest province of Saudi Arabia.

Methods: We retrospectively analyzed the hospital records of 311 (152 males and 159 females) children diagnosed with childhood T1DM in Al-Madina region, Saudi Arabia between January 1992 and December 2004.

Results: At diagnosis 172 (55.3%) children presented with diabetic ketoacidosis at the onset of their illness, 101 (58.7%) were females and 71 (41.3%) males. We found females to have more ketoacidosis at the onset of their illness with 1.4:1 female to male ratio. The mean age at presentation with ketoacidosis was 6.7 years (95% CI=5.6-7.8) ranging from 4 months to 14 years. Most of the ketoacidosis was mild to moderate (84.9%), while only 26 (15.1%) children had the severe type. Sixty-one (35.5%) children were in the younger age group, 54 (31.4%) were in the middle age group, and 57 (33.1%) were in older age group, there was no significant difference (p=0.5) between the 3 age groups in the frequency of ketoacidosis. The duration of symptoms before presentation with ketoacidosis was 15.8 days (95% CI=13.5-18.1). Altered consciousness was present in 21 (12.2%) children; all of them were from the severe type of ketoacidosis. There was a strong correlation between the severity of the central nervous system depression and the degree of acidosis (r=0.826, p<0.0001), but no correlation with age, gender, duration of symptoms, and blood glucose level.

Conclusion: The frequency of ketoacidosis at onset of childhood diabetes mellitus in our region is significant. Prevention of diabetic ketoacidosis and reduction of its frequency should be a goal in managing children with diabetes. Rising standards of medical information and general awareness can contribute to this.

Saudi Med J 2005; Vol. 26 (12): 1936-1939

Diabetic ketoacidosis (DKA) is the most serious presentation of type 1 diabetes mellitus (T1DM). Worldwide, there is a significant variation in the frequency and the severity of DKA at presentation. Whether these variations in the frequency of DKA at the onset of childhood diabetes are due to different clinical subtypes of the disease is a question under thorough investigation worldwide. One example is the higher prevalence of keto-acidosis at the onset of diabetes mellitus in children with celiac disease, also linked to the more frequent occurrence of other autoimmune diseases in the same group of children.[1] The presence of DKA at diagnosis of T1DM was related to the low beta cell residual function, mainly determined by the intensity of immunological destruction.[2] In different European countries, there was significant variation between 11 centers in the frequency of DKA, which ranged from 26-67%.[3] In Saudi Arabia, reports show DKA ranging between 55-77%.[4,5] The aim of this study

From the Department of Pediatrics, King Abdul-Aziz University, Jeddah, *Kingdom of Saudi Arabia.*

Received 22nd May 2005. Accepted for publication in final form 3rd October 2005.

Address correspondence and reprint request to: Dr. Hamed S. Habib, Department of Pediatrics, King Abdul-Aziz University, PO Box 6597, Jeddah, *Kingdom of Saudi Arabia.* Tel. +966 505611935. Fax. +966 (2) 6701621. E-mail: hamedhabib@hotmail.com

was to determine the frequency, and to describe the clinical characteristics of DKA at initial diagnosis of childhood T1DM in Al-Madina region, Saudi Arabia.

Methods. This retrospective study was carried-out in the Maternity and Childrens Hospital, Al-Madina region, Saudi Arabia. Hospital records of 13 years (January 1992 to December 2004) were reviewed. Children diagnosed to have T1DM, according to the World Health Organization (WHO) multi-national project for childhood Diabetes (WHO DIAMOND) criteria,[6] were included in the study. They were included only if insulin treatment had been started before their 15th birthday. Clinical and laboratory data at the time of presentation were collected and analyzed. Ketoacidosis was defined as hyperglycemia > 14 mmol/L together with pH <7.3 or bicarbonate <15 mmol/L in the presence of ketonuria. Acidosis was considered severe if pH is <7.1.[7,8] Clinical and biochemical data were collected from hospital records retrospectively. To ensure a uniform quality of case registration data, collection was carried out by the same person. Subjects were assigned to one of 3 age groups: young (0-4 years), middle (5-9 years), and older (10-14 years) corresponding to the WHO multinational project for childhood diabetes age groups.[6] The age and the duration of symptoms had a normal distribution, and thus calculation of the geometric mean and its 95% confidence interval (CI) was possible. The biochemical values did not produce a normal distribution. Their median and its 95% CI were calculated according to Campbell and Gardner.[9] Our hospital has a DKA management protocol, including the following: conservative adequate fluid replacement; low dose insulin therapy at frequent intervals; adequate potassium replacement from time of first insulin therapy; bicarbonate replacement if pH <7.1; broad-spectrum antibiotics if an infection is suspected and other supportive measures.

Results. During the period of the study, 172 (55.3%) diabetic children <15 years presented with DKA at the onset of their illness, out of 311 children (152 males, 159 females) were diagnosed with childhood T1DM. In the group of children who presented with DKA, 101 (58.7%) were females and 71 (41.3%) males. Females were found to have more DKA at the onset of their illness with 1.4:1 female to male ratio. Saudi nationals comprised 159 (92.4%), while 13 (7.6%) were of different other nationalities. Sixty-one (35.5%) of the DKA children were in the young age group, 54 (31.4%) were in the middle age group, and 57 (33.1%) were in the older age group, there were no significant differences (p=0.5) between the 3 age groups in the frequency of DKA. The mean age at presentation with DKA was 6.7 years (95% CI=5.6-7.8) ranging from 4 months to 14 years. The mean age at diagnosis for males was 6.7 years (95% CI=5.5-8.0) while the mean age for females was 6.9 years (95% CI = 5.9-8.0) with no significant difference. Most of the ketoacidosis were mild to moderate (84.9%), while only 26 (15.1%) children were of the severe type. Nine children (5 females and 4 males) of the severe type were in the younger age group, another 9 (5 males and 4 females) children were in the middle age group, and only 8 (4 males and 4 females) children were in the older age group. There was no preference in the frequency of severe DKA to age groups or gender. All the children who presented with DKA were admitted to the hospital, 131 (76%) children were admitted initially to the intensive care unit. No deaths were recorded, and all the children recovered completely without complications. Polyuria and polydipsia were the most frequent symptoms to be reported at presentation (98%), while weight loss was reported in only 108 (62.8%) of the children. The duration of symptoms before presentation with DKA was 15.8 days (95% CI=13.5-18.1). Altered consciousness was present in 21 (12.2%) children, all of them from severe DKA. There was a strong correlation between central nervous system depression and the degree of acidosis (r = 0.826, p<0.0001), but no correlation with age, gender, duration of symptoms, and blood glucose level. The median blood sugar value was 27.00 mml/L with a maximum of 72 mml/L, the median pH value was 7.16; the lowest value reported was 6.89. The median value of base excess was -19.00, and the lowest value reported was -27.3 (**Figure 1**). Elevated blood urea nitrogen was observed at presentation in (21%) of patients with ketoacidosis with median value within the normal range 4.3 mmol/L, as well as hypokalemia in 31.8% and hyponatremia in 33% of them. A record of the laboratory data at presentation is given in **Table 1**.

Discussion. Diabetic ketoacidosis is a potentially preventable presentation and complication of DM, representing a predominant cause of mortality and morbidity in these children. The frequency of DKA in our region is low within the frequency range of Saudi Arabia which ranges between 55-77%.[4,5] Most of ketoacidotic children in our series (85.1%) were mild to moderate in severity. This agrees with data from another region in Saudi Arabia reported by Kalaylat et al,[5] that although more than three-quarters of his patients with T1DM had ketoacidosis on presentation, none was comatose or developed clinical cerebral edema during treatment.[5] Although the author shares the same definition of DKA with many European studies, the frequency of the severe form was far much less in this series than that reported in Europe, where it was mainly the severe form.[10,11] The fact

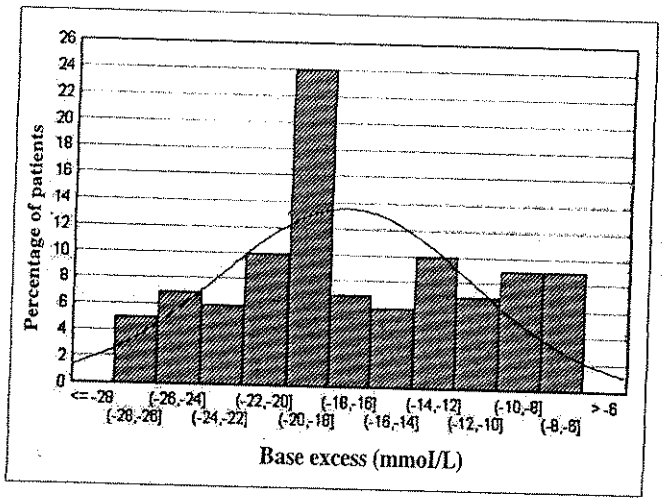

Figure 1 - Distribution of the median value of base excess (mmol/L).

Table 1 - Laboratory data at presentation with ketoacidosis.

Laboratory data	Median	-95% CI	+95% CI
Blood Glucose	27.00	26.87	33.39
Arterial pH	7.16	7.13	7.19
Base excess (mmol/L)	-19.0	-19.33	-15.53
Serum sodium (mmol/L)	133.0	131.24	134.66
Serum potassium (mmol/L)	4.0	3.80	4.28
Blood urea nitrogen (mmol/L)	4.3	4.03	5.25
Serum creatinine (mmol/L)	81.0	67.29	98.74

CI - confidence interval

that there was no single mortality in this study could be explained by the low percentage of the severe form of DKA. The author also found altered consciousness limited to children with the severe form. We can link this to the degree of acidosis, but not with age, gender; duration of symptoms, and blood glucose level. In this study, we found females to have more DKA at the onset of their illness, as reported in another international studies.[10,12] The duration of symptoms before presentation with DKA shows no difference when compared with the duration of symptoms before presentation in all diabetic children as reported in a previous study from the same center.[13] There was no correlation in this series between the clinical severity with age, gender, duration of symptoms, and blood glucose level. There was no difference in the frequency of diabetes or the severity of DKA between the 3 different age groups, while Neu et al,[10,11] reported that younger patients had a shorter duration of symptoms and suffered most frequently from ketoacidosis. This worldwide variation in frequency, severity, and clinical characteristics of DKA at initial diagnosis of childhood T1DM raises the question whether this difference is due to racial and environmental influence, or to different subtypes of childhood diabetes. Recent data suggest that simple community interventions may prevent or reduce the incidence of DKA at the time of diagnosis of diabetes. In a program in Parma, Italy,[14] they provided schools and doctors' offices with colorful posters with practical messages about diabetes, and instructed local pediatricians on the use of glucose meters. In the study area, the incidence of DKA in new-onset cases decreased from 78% in 1987-1991 to 12.5% in 1991–1997; with no cases reported in the last 4 years of the study. In the control region nearby, in which they did not perform the intervention, 83% of new cases presented in DKA. Levy-Marchal et al[3] also showed that rising standards of medical information, and greater awareness concurrent with an overall increase in incidence resulted in changes in the clinical presentation at onset of type 1 childhood diabetes in Europe.

In conclusion, the frequency of DKA at the onset childhood DM in our region is significant. Prevention of DKA and reduction of its frequency should be a goal in managing children with diabetes. Rising standards of medical information and general awareness can contribute to this.

References

1. Valerio G, Maiuri L, Troncone R, Buono P, Lombardi F, Palmieri R, et al. Severe clinical onset of diabetes and increase prevalence of other autoimmune diseases in children with celiac disease diagnosed before diabetes mellitus. ***Diabetologia*** 2002; 45: 1719-1722.
2. Mlynarski W, Zmyslowska A, Kubryn I, Perenc M, Bodalski J. Factors involved in ketoacidosis at the onset of type 1 diabetes in childhood. ***Endokrynol Diabetol Chor Przemiany Materii Wieku Rozw*** 2003; 9: 23-28.
3. Levy-Marchal C, Patterson CC, Green A, EURODIAB ACE Study Group. Geographical variation of presentation of type 1 diabetes in children. ***Diabetologia*** 2001; 44 Suppl 3: B75-B80.
4. Salman H, Abanamy A, Hassan B, Khalil M. Childhood Diabetes in Saudi Arabia. ***Diabet Med*** 1991; 8: 176-178.
5. Kalaylat NA, Narchi H. Clinical picture of childhood type 1 diabetes mellitus in the Eastern province of Saudi Arabia. ***Pediatr Diabetes*** 2001; 2: 43-47.
6. WHO Multinational Project for Childhood Diabetes WHO Diamond Project Group. ***Diabetes Care*** 1990; 13: 1062-1068.
7. Rosenbloom AL, Hanas R. Diabetic ketoacidosis (DKA): treatment guidelines. ***Clin Pediatr*** 1996; 35: 261-266.
8. Kitabchi AE, Fisher JN, Murphy MB, Rumbak MJ. Diabetic ketoacidosis and the hyperglycemic, hyperosmolar nonketotic state. In: Weir CR, Kahn GC, editors. Joslin's Diabetes Mellitus. Philadelphia (PA): Lea & Febiger; 1994. p. 739-747.

9. Campbell MJ, Gardner MJ. Calculating confidence intervals for some non-parametric analysis. In: Gardner MJ, Altman DG, editors. Statistic with confidence, confidence intervals and Statistic Guidelines. London (UK): BMJ Publications; 1990. p. 71-79.
10. Neu A, Willasch A, Ehehalt S, Hub R, Ranke MB, DIARY Group Baden-Wuerttemberg. Ketoacidosis at onset of type 1 diabetes mellitus in children--frequency and clinical presentation. ***Pediatr Diabetes*** 2003; 4: 77-81.
11. Neu A, Ehehalt S, Willasch A, Kehrer M, Hub R, Ranke MB. Varying clinical presentations at onset of type 1 diabetes mellitus in children--epidemiological evidence for different subtypes of the disease? ***Pediatr Diabetes*** 2001; 2; 146-153.
12. Bui TP, Werther GA, Cameron FJ. Trends in diabetic ketoacidosis in childhood and adolescence: a 15-yr experience. ***Pediatr Diabetes*** 2002; 3: 82-88.
13. Al-Magamsi MS, Habib HS. Clinical presentation of childhood type 1 diabetes mellitus in the Al-Madina region of Saudi Arabia. ***Pediatr Diabetes*** 2004: 5: 95-98.
14. Vanelli M, Chiari G, Ghizzoni L, Costi G, Giacalone T, Chiarelli F. Effectiveness of a prevention program for diabetic ketoacidosis in children: an 8-year study in schools and private practices. ***Diabetes Care*** 1999; 22: 7–9.