Age-Related Differences in the Frequency of Ketoacidosis at Diagnosis of Type 1 Diabetes in Children and Adolescents

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OBJECTIVE — We studied the prevalence of diabetic ketoacidosis (DKA) at diagnosis of type 1 diabetes in children in Finland.

RESEARCH DESIGN AND METHODS — From 2002 to 2005, data on virtually all children <15 years of age diagnosed with type 1 diabetes (n = 1,656) in Finland were collected.

RESULTS — DKA was present in 19.4% of the case subjects, and 4.3% had severe DKA. In children aged 0–4, 5–9, and 10–14 years, DKA was present in 16.5, 14.8, and 26.4%, respectively ($P < 0.001$). Severe DKA occurred in 3.7, 3.1, and 5.9%, respectively ($P = 0.048$). DKA was present in 30.1% and severe DKA in 7.8% of children aged <2 years.

CONCLUSION — The overall frequency of DKA in children is low in Finland at diagnosis of type 1 diabetes. However, both children <2 years of age and adolescents aged 10–14 years are at increased risk of DKA.

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The incidence of diabetic ketoacidosis (DKA) in children with newly diagnosed type 1 diabetes may be decreasing in developed countries (1,2).

RESEARCH DESIGN AND METHODS

— In Finland, all children presenting with type 1 diabetes are treated in pediatric units, and their parents/guardians are asked whether the child may be recorded in the nationwide Finnish Pediatric Diabetes Register established in 2002 (3). We used data from this register and, in addition, asked the pediatric centers to recheck their hospital records and report the sex, age, and blood pH at diagnosis for all case subjects who were diagnosed with type 1 diabetes between 1 June 2002 and 31 May 2005. The final data encompassed all children <15 years of age diagnosed with type 1 diabetes in Finland during the 3-year study period. Diabetes was diagnosed according to World Health Organization criteria (4). The study was approved by the local ethics committees and the register steering committee.

The study cohort comprised 1,656 children (936 boys, 56.5%), a majority of whom were recorded in the Finnish Pediatric Diabetes Register (1,518 of 1,656, 91.7%). The mean age at diagnosis was 8.0 years (range 0.28–14.99 years), and DKA data were available from 1,616 children (97.6%). The children were treated in 27 centers, 5 of which were university hospitals. In three university hospitals, the prospective type 1 Diabetes Prediction and Prevention (DIPP) project has been running since the mid-1990s to establish strategies for predicting and preventing type 1 diabetes (5). One child, an 8-year-old girl, died soon after diagnosis with a clinical picture of cerebral edema.

The duration of symptoms before diagnosis was recorded. The degree of consciousness at diagnosis, based on evaluation by the attending doctor, was reported to be normal in 94.5% of the case subjects and impaired in 5.2%, and 0.3% were considered unconscious. Body weight and height were measured on admission, and BMI was calculated (kg/m^2).

Standard laboratory methods were used to measure plasma glucose and blood pH. Diabetic ketoacidosis was defined as blood pH <7.30 and considered severe if pH was <7.10.

Data were analyzed using SPSS for Windows (version 15.0; SPSS, Chicago, IL). Two-tailed Student t test, Mann-Whitney U test, cross-tabulation and χ^2 analysis, one-way ANOVA, Kruskal-Wallis test, and Pearson correlation analysis were applied when appropriate.

RESULTS

— At diagnosis of type 1 diabetes, 313 of 1,616 children (19.4%) had DKA, and DKA was severe in 69 case subjects (4.3%). The mean age at diagnosis was higher in boys than in girls (8.2 vs. 7.7 years of age; $P = 0.012$), and the proportion of boys increased by age (Table 1). There was no difference in the frequency of DKA between girls and boys (20.6 vs. 18.4%; $P = 0.274$), but girls more often had severe DKA (5.7 vs. 3.2%; $P = 0.012$). The duration of symptoms was also more often longer than 2 weeks among girls (39.4 vs. 33.2%; $P = 0.021$).

When comparing the three age-groups (0–4.99, 5.0–9.99, and 10.0–14.99 years of age at diagnosis) we observed that the frequency of DKA and severe DKA was highest in the oldest children (Table 1). Furthermore, a significant inverse correlation was observed between pH and age at diagnosis ($r = -0.13$; $P < 0.001$). No differences were observed in the degree of consciousness between the three age-groups. Case subjects with DKA in most age-groups had a lower

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Table 1—*Comparison of children in different age-groups at the time of diagnosis of type 1 diabetes* (N = *1,656*)

	0–4 years	5–9 years	10–14 years	*P*	<2 years	≥2 years	*P*
n (%)	436 (26.3)	629 (38.0)	591 (35.7)		103 (6.2)	1,553 (93.8)	
Boys (%)	53.7	54.2	61.1	0.020	60.2	56.3	0.438
Symptoms of diabetes >2 weeks (%)	29.8	35.8	40.9	0.006	28.2	36.5	0.140
Blood pH†	7.39 (7.34–7.40)	7.38 (7.34–7.41)	7.36 (7.27–7.40)	<0.001	7.36 (7.27–7.39)	7.38 (7.33–7.40)	0.001
Plasma glucose (mmol/l)*	25.8 (24.8–26.9)	24.6 (23.8–25.4)	26.2 (25.3–27.2)	0.173	29.4 (26.8–32.1)	25.3 (24.8–25.9)	<0.001
DKA (%), pH <7.30*	16.5 (14.7–18.3)	14.6 (11.8–17.4)	26.4 (22.8–30.0)	<0.001	30.1 (21.2–38.9)	18.6 (16.6–20.6)	0.004
Severe DKA (%), pH <7.10*	3.7 (1.9–5.5)	3.1 (1.7–4.5)	5.9 (4.0–7.8)	0.048	7.8 (2.6–12.9)	4.0 (3.0–5.0)	0.070
BMI (kg/m^2)							
With DKA†	14.4 (13.4–15.5)‡	14.6 (13.2–16.2)§	15.8 (14.2–17.8)‖		15.1 (13.7–15.6)¶	15.2 (13.7–17.0)#	
Without DKA†	14.8 (13.9–15.9)	15.1 (14.0–16.6)	16.9 (15.2–19.2)		15.0 (14.1–16.0)	15.5 (14.3–17.3)	

Data are means (95% CI)*, medians (interquartile range)†, or proportions (95% CI). ‡$P = 0.026$. §$P = 0.065$. ‖$P < 0.001$. ¶$P = 0.295$. #$P = 0.019$.

BMI at diagnosis than those without DKA (Table 1).

Children <2 years of age more often had DKA and severe DKA at diagnosis when compared with older children (Table 1), and the degree of consciousness was more often impaired in these very young children (14.9 vs. 4.8%; $P < 0.001$). We compared children diagnosed in the university hospitals with those diagnosed in other pediatric centers and observed that the frequency of DKA was higher in subjects admitted to the university hospitals (23.1 vs. 17.1%, $P = 0.003$). Furthermore, severe DKA occurred more frequently in children treated in the university hospitals (6.3 vs. 3.0%; $P = 0.001$). The proportion of children <2 years of age at diagnosis was higher in the university hospitals (7.9 vs. 5.2%; $P = 0.026$).

When comparing children diagnosed in the DIPP centers ($n = 353$) with those treated in other university hospitals ($n = 263$), similar DKA frequencies were observed (21.2 vs. 25.3%, respectively; $P = 0.240$). The frequency of severe DKA was not significantly different in children diagnosed in the DIPP centers (4.7 vs. 8.2%, $P = 0.076$).

CONCLUSIONS — In the current study, the frequency of DKA in children <5 years of age at diagnosis of type 1 diabetes was 16.5% and the lowest reported so far in this age-group (6–10). Earlier studies from Finland have shown that the frequency of DKA has markedly decreased over time in children diagnosed at <5 years of age, at 32.1% from 1982 to 1991 and 17.7% from 1992 to 2001 (6,7). In Germany and Austria, the frequency of DKA at diagnosis was 26.5% in children <5 years of age from 1995 to 2007 (10). In the U.S., DKA was present in 43.7% of children <6 years of age diagnosed with type 1 diabetes during the 1990s in the Boston area (11), and recently a DKA frequency of 37.3% was reported in children <5 years of age (8).

DKA is still common among children <2 years of age, although the present results show that the frequency of DKA in these children was lower (30.1%) than in earlier surveys (6,7). In the Finnish nationwide study from 1986 to 1989, the frequency of DKA in children <2 years was as high as 53.3% (7). In northern Finland the overall frequency of DKA in children <2 years of age at diagnosis was 50.0% from 1982 to 1991 and 39.1% from 1992 to 2001 (6). These very encouraging results indicate that information and awareness have led to earlier diagnosis nowadays with milder metabolic decompensation in these very young children.

It is worrisome that children ≥10 years of age seem to have an increased risk of DKA. It is possible that the emerging independence of teenagers makes them unwilling to admit to their early symptoms of diabetes, and therefore they run a higher risk of developing DKA. In addition, shared time in families has decreased in recent decades, and single-parent families are more frequent. Such factors may play a role in the delayed reporting of symptoms of diabetes in adolescents.

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