

Ketoacidosis at Diagnosis of Type 1 Diabetes in Children in Northern Finland

Temporal changes over 20 years

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OBJECTIVE — To study the frequency of diabetic ketoacidosis (DKA) over a 20-year period among children diagnosed with type 1 diabetes in northern Finland.

RESEARCH DESIGN AND METHODS — The study population comprised 585 patients (328 boys) diagnosed with type 1 diabetes aged <15 years in the Department of Pediatrics, Oulu University Hospital, between 1 January 1982 and 31 December 2001. The data for clinical characteristics were collected retrospectively from the patients' case records. The earlier 10-year period (1982–1991) was compared with the later 10-year period (1992–2001). Two definitions for DKA were used: DKA(i) pH <7.30 or DKA(ii) pH <7.30 and/or bicarbonate <15 mmol/L.

RESULTS — During the later 10-year period, children less often had DKA at diagnosis [DKA(i) 15.2 vs. 22.4%, $P = 0.028$, and DKA(ii) 18.9 vs. 29.5%, $P = 0.003$]. The proportion of young children aged <5 years at diagnosis increased over time, but the frequency of DKA also was lower in this age-group during 1992–2001 compared with the earlier 10-year period [DKA(i) 17.7 vs. 32.1%, $P = 0.052$, and DKA(ii) 20.3 vs. 42.6%, $P = 0.005$]. In children aged <2 years at diagnosis, the frequency of DKA remained high during 1992–2001 [DKA(i) 39.1% and DKA(ii) 47.8%].

CONCLUSIONS — The overall frequency of DKA in children with newly diagnosed type 1 diabetes decreased over a 20-year period in northern Finland. However, children aged <2 years are still at high risk for DKA at diagnosis.

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Diabetic ketoacidosis (DKA), a serious consequence of insufficient insulin secretion, is the leading cause of acute morbidity and mortality in children with type 1 diabetes (1). The frequency of DKA at the diagnosis of pediatric type 1 diabetes has been reported to vary from 15 to 67% in Europe and North America (2,3). A valid comparison of studies is, however, difficult because of the variable definitions of DKA used. Furthermore, there is substantial variation in the incidence of type 1 diabetes between different populations (4), and

an inverse correlation between the frequency of DKA and the background incidence of type 1 diabetes has been reported (5,6).

There are some indications that the frequency of DKA may be decreasing at the clinical presentation of type 1 diabetes in children (7,8), but contradictory findings also have been reported (9,10). A series of studies have shown that the incidence of childhood type 1 diabetes has been increasing over the past decades (11,12), and it has been postulated that increasing medical information and

awareness concurrent with an overall increase in incidence might have resulted in changes in the clinical presentation at diagnosis in developed countries (5,13). A recent American study (14) indicated that genetic screening combined with continuous monitoring for signs of β -cell autoimmunity in children at risk results in less severe disease presentation.

The incidence of childhood type 1 diabetes is the highest in the world in Finland. In the mid-1990s, the population-based Type 1 Diabetes Prediction and Prevention Project (DIPP) was initiated in three university hospitals in Finland to assess the strategies for predicting and preventing type 1 diabetes in the general population (15). In the DIPP study, newborn infants carrying HLA-conferred susceptibility to type 1 diabetes are identified and invited to participate in regular follow-up in order to detect possible signs of β -cell autoimmunity.

The purpose of this study was to analyze the clinical and biochemical status of children and adolescents with newly diagnosed type 1 diabetes during a period of 20 years (1982–2001) in the catchment area of Oulu University Hospital in northern Finland. We particularly evaluated the frequency of DKA. We also wanted to assess whether the ongoing DIPP study had any influence on the frequency of DKA at the time of diagnosis.

RESEARCH DESIGN AND METHODS

The study cohort comprised all children aged <15 years who had been diagnosed with type 1 diabetes in the Department of Pediatrics, Oulu University Hospital, between 1 January 1982 and 31 December 2001 and had their permanent address in the catchment area of this hospital at the time of diagnosis. In Finland, all children developing type 1 diabetes under the age of 15 years are treated in pediatric units, each of which is responsible for patients within a certain geographic area. The patients for the current study were identified from the hospital registry as well as from the register kept at the Diabetes Clinic, Department of Pediatrics. The study was approved by the local ethics committee.

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Abbreviations: DKA, diabetic ketoacidosis; DIPP, Type 1 Diabetes Prediction and Prevention Project.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1— Comparison of children aged <2 years or <5 years and older children at the diagnosis of type 1 diabetes

	All children			All children		
	Children aged <2 years	Children aged ≥2 years	P value	Children aged <5 years	Children aged ≥5 years	P value
n	48	537		137	448	
Male/female	23/25	305/232	0.235	70/67	258/190	0.180
Age at onset [years (95% CI)]	1.4 (1.3–1.5)	8.9 (8.6–9.2)		2.8 (2.6–3.0)	9.9 (9.7–10.2)	
Duration of symptoms [days (95% CI)]	10.2 (7.3–13.0)	20.9 (19.1–22.8)	<0.001	13.5 (11.1–15.9)	22.1 (19.9–24.2)	<0.001
Decrease in weight for height [% (95% CI)]	6.9 (5.7–8.1)	6.9 (6.5–7.3)	0.985	5.6 (4.4–6.4)	7.3 (6.8–7.8)	<0.001
Blood glucose [mmol/l (95% CI)]	26.1 (23.1–29.1)	21.3 (20.5–22.1)	0.001	22.6 (20.9–24.3)	21.4 (20.6–22.3)	0.21
pH (95% CI)	7.27 (7.23–7.32)	7.35 (7.34–7.36)	0.001	7.33 (7.30–7.35)	7.35 (7.34–7.36)	0.048
PCO ₂ [kPa (95% CI)]	3.4 (3.0–3.8)	4.6 (4.5–4.7)	<0.001	4.1 (3.8–4.3)	4.6 (4.5–4.7)	<0.001
Bicarbonate [mmol/l (95% CI)]	13.4 (11.3–15.5)	19.9 (19.4–20.5)	<0.001	17.2 (16.0–18.5)	20.1 (19.5–20.7)	<0.001
Plasma β-hydroxybutyrate [mmol/l (IQR)]	4.3 (1.9–7.2)	1.6 (0.1–4.6)	<0.001	1.9 (0.5–4.8)	1.8 (0.4–4.7)	0.58
Serum osmolality [mosm/l (IQR)]	302 (292–310)	294 (287–302)	0.006	296 (289–297)	294 (287–301)	0.082
Serum sodium [mmol/l (95% CI)]	134 (133–135)	136 (135–136)	0.003	134 (134–135)	136 (135–136)	<0.001
Serum potassium [mmol/l (95% CI)]	4.8 (4.7–4.9)	4.3 (4.2–4.3)	<0.001	4.6 (4.5–4.6)	4.3 (4.2–4.3)	<0.001
Serum creatinine [mmol/l (IQR)]	59 (47–73)	64 (53–76)	0.025	54 (46–63)	66 (57–79)	<0.001
DKA(i), pH <7.30 [% (95% CI)]	44.7 (30.5–58.9)	16.1 (13.0–19.2)	<0.001	23.7 (16.5–30.9)	16.9 (13.4–20.4)	0.073
DKA(ii), pH <7.30 and/or HCO ₃ <15 [% (95% CI)]	54.2 (40.1–68.3)	20.7 (16.7–24.7)	<0.001	29.3 (21.6–37.0)	21.7 (17.8–25.7)	0.073
Severe DKA, pH <7.10 [% (95% CI)]	10.4 (1.8–19.0)	2.7 (1.3–4.1)	0.004	5.9 (1.9–9.8)	2.5 (1.0–4.0)	0.054

Data are mean or frequency (95% CI) or median (interquartile range).

Clinical and laboratory data were collected retrospectively from the patients' records. The study cohort included 585 children (328 boys; 56.1%) whose mean age at diagnosis was 8.3 years (range 0.2–14.9). Forty-eight children (8.2%) were aged <2 years, 137 children (23.4%) were aged <5 years, 234 (40.0%) were aged 5–9.99 years, and 214 (36.6%) were aged 10–14.99 years at diagnosis. One child (0.2%) died soon after the diagnosis because of cardiac arrest induced by severe hyperkalemia (6.6 mmol/l).

The mean duration of symptoms before diagnosis was 20 days (range 0–168). At diagnosis, height and weight were measured and relative weight for height (%) determined by referencing the Finnish growth charts (16). In addition, the weight-for-height curve based on previously recorded individual growth data was drawn, and a decrease in relative weight for height was estimated. The mean estimated decrease in relative weight for height was 6.9% at diagnosis (range 0.0–30.0). Insulin treatment was started for all the patients. About one-third (33.7%) of the children initially were treated with intravenous insulin, while the others received insulin subcutaneously. The mean dose of insulin given over the first 24 h was 0.93 IU/kg (range 0.00–3.40). There were five patients with mild presentation, whose insulin treat-

ment started after initial observation for 1–2 days. The duration of hospitalization varied between 0 and 43 days (median 1.0). Two cases presenting with mild symptoms started insulin injections at the outpatient clinic. Five young patients (aged <7 years) required prolonged hospitalization because of a concurrent gastroenteritis or respiratory tract infection. The degree of consciousness at diagnosis, based on the information provided by the patients' records, was estimated to be normal in 96.8% of the cases, slightly decreased in 2.6%, and clearly suppressed in 0.5% of the cases.

Standard laboratory methods in the clinical laboratory, Oulu University Hospital, were used to measure blood glucose, blood gases, serum electrolyte and creatinine concentrations, and serum osmolality before the initiation of treatment. Plasma β-hydroxybutyrate concentration was analyzed with a kinetic enzymatic assay. The mean blood glucose concentration at the time of diagnosis was 21.7 mmol/l (range 3.2–62.5). Blood pH ranged from 6.82 to 7.51 (mean 7.35), serum bicarbonate concentration from 1.7 to 30.0 mmol/l (mean 19.4), pCO₂ from 0.9 to 7.4 kPa (mean 4.5), and β-hydroxybutyrate from 0.0 to 23.6 mmol/l (median 1.9). The median serum osmolality was 295 mosm/l (range 259–540). The mean serum potassium and sodium

concentrations were 4.3 mmol/l (2.4–6.6) and 136 mmol/l (123–153), respectively, and the median serum creatinine concentration was 63 mmol/l (16–270). Sixteen of 554 children (2.9%) had serum potassium <3.5 mmol/l, and 12 children (2.2%) had serum potassium >5.3 mmol/l on admission. A total of 320 subjects (57.7%) had serum sodium <137 mmol/l, whereas only three children (0.5%) had serum sodium >149 mmol/l at diagnosis.

DKA was defined in two ways: DKA(i) as pH <7.30 or DKA(ii), according to the European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society consensus statement, as pH <7.30 and/or a bicarbonate concentration <15 mmol/l (17). DKA was considered severe if pH <7.10. For analysis, the data were divided into four 5-year periods and two 10-year periods. In addition, the patients were divided into three groups based on their age at diagnosis (aged 0–4.99, 5.0–9.99, and 10.0–14.99 years).

Data analysis was performed with the SPSS for Windows statistical software (version 12.0; SPSS, Chicago, IL). Student's two-tailed *t* test for independent samples was used when comparing variables with normal distribution between two groups. Mann-Whitney *U* test was used for unequally distributed variables.

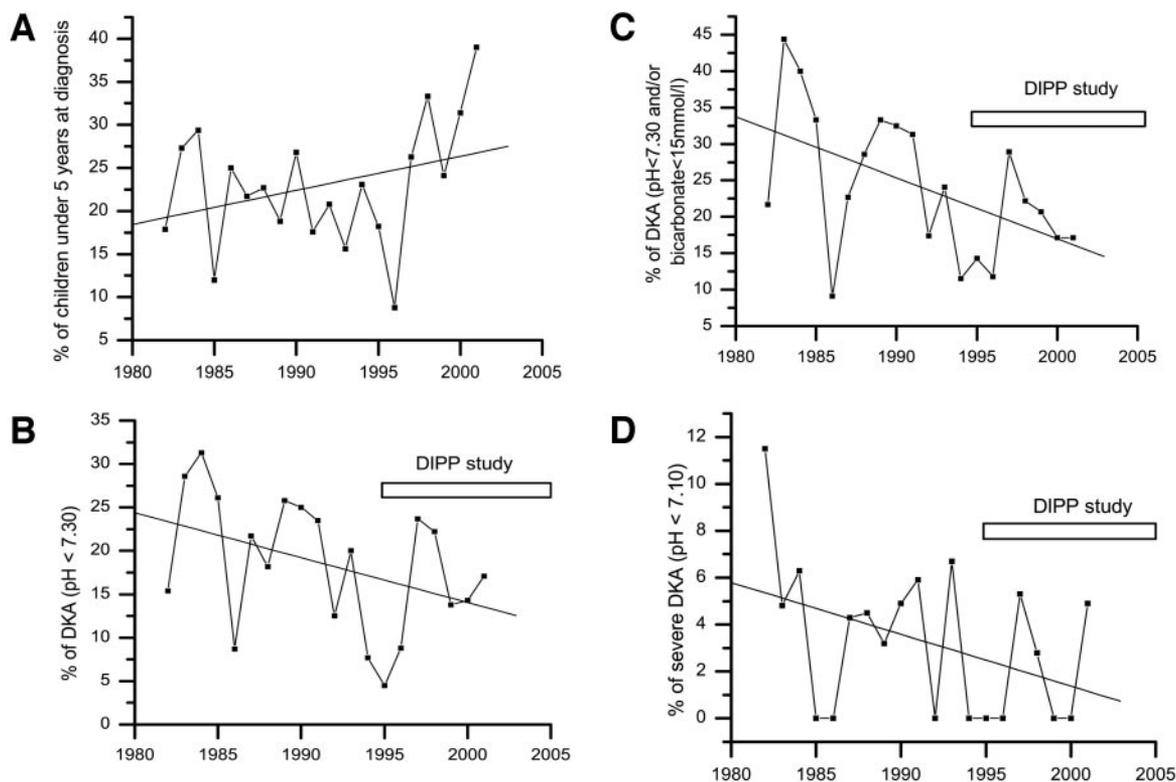


Figure 1—The annual proportion of children aged <5 years at diagnosis (A) and the annual proportion of children with DKA at the diagnosis of type 1 diabetes in Oulu University Hospital in 1982–2001. DKA is defined as pH <7.30 (B) or pH <7.30 and/or bicarbonate <15 (C), whereas severe DKA is defined as pH <7.10 (D). The white bar marks the study period of the DIPP study in Oulu University Hospital. The linear regression lines represent time trends.

Distributions were analyzed by cross-tabulation and χ^2 statistics. Regression lines to illustrate time trends were drawn using Origin (version 7; OriginLab, Northampton, MA).

RESULTS— A total of 106 of 585 patients (18.1%) had ketoacidosis at the diagnosis of type 1 diabetes according to the definition of pH <7.30 [DKA(i)]. Based on the definition of pH <7.30 and/or serum bicarbonate <15 mmol/l [DKA(ii)], the frequency of ketoacidosis was 22.4%. Nineteen children (3.2%) had severe ketoacidosis (pH <7.10) at onset.

The mean age at diagnosis was slightly older in boys (8.5 years [95% CI 8.0–8.9] vs. 7.9 years [7.4–8.4] in girls; $P = 0.08$). An analysis of the different age-groups did not reveal significant differences in the proportions of boys and girls, although the proportion of boys tended to be higher in the older age-groups (51.1% in those aged 0–4.99 years, 57.3% in those aged 5.0–9.99 years, and 57.9% in those aged 10.0–14.99 years; NS). There was no significant difference in the frequency of DKA between boys and girls [DKA(i) 20.6% (95% CI 16.2–25.0) vs. 15.7% (10.5–20.3), re-

spectively, $P = 0.13$, and DKA(ii) 25.0% (20.2–29.8) vs. 21.7% (16.5–26.9), respectively, $P = 0.36$]. Boys tended to be treated initially more often with intravenous insulin than girls (36.6 vs. 29.9%, $P = 0.09$).

The proportion of children aged <5 years at diagnosis increased over time, being 31.3% of all newly diagnosed cases in the most recent 5-year period ($P = 0.017$ in comparison between the four 5-year periods) (Fig. 1A). We compared the children aged <5 years at diagnosis with the older children (Table 1). The children aged <5 years tended to have DKA more often but not significantly. However, when comparing the children aged <4 years at diagnosis ($n = 107$) with the older children, the differences in the frequency of DKA became statistically significant according to both definitions [DKA(i) 28.6% (95% CI 19.9–37.3) vs. 16.2% (12.9–19.5), $P = 0.003$, and DKA(ii) 33.7% (24.6–42.8) vs. 21.2% (17.4–25.0), $P = 0.007$]. Intravenous insulin therapy was initiated more frequently in the subjects aged <5 years (40.7 vs. 31.5%, $P = 0.048$), although there was no significant difference in the mean insulin dose over the first 24 h be-

tween the two groups (0.92 vs. 0.93 IU/kg). Children aged <5 years had reduced consciousness at diagnosis more often (5.8 vs. 2.3%, $P = 0.014$). The duration of the initial hospitalization was longer for the children aged <5 years (15.0 vs. 13.4 days, $P = 0.025$).

We also compared the children aged <2 years at diagnosis with the other children (Table 1). These children had DKA more often according to both definitions. The frequency of severe ketoacidosis also was significantly higher in the subjects aged <2 years at diagnosis. Three-quarters of the children aged <2 years had serum sodium concentrations <137 mmol/l, while the proportion in older children was 56.0% ($P = 0.008$). We found no difference in the frequency of patients having serum potassium >5.3 mmol/l between children aged <2 years and older children. The children aged <2 years were started more often on intravenous insulin therapy (66.7 vs. 30.7%, $P < 0.001$), and the duration of their initial hospitalization was longer (17.5 vs. 12.0 days, $P < 0.001$).

We observed that DKA(i) was most common among the children aged <5 years (23.7%), second most common in

Table 2—Comparison of children diagnosed with type 1 diabetes in 1982–1991 and 1992–2001

	All children			Children aged <5 years			Children aged ≥5 years		
	1982–1991	1992–2001	P value	1982–1991	1992–2001	P value	1982–1991	1992–2001	P value
	n	n		n	n		n	n	
Male/female	268 154/114	317 174/143	0.530	58 32/26	79 38/41	0.413	210 122/88	238 136/102	0.839
Age at onset [years (95% CI)]	8.3 (7.8–8.8)	8.3 (7.8–8.7)	0.92	2.6 (2.2–2.9)	3.0 (2.7–3.2)	0.058	9.9 (9.5–10.2)	10.0 (9.6–10.4)	0.596
Duration of symptoms [days (95% CI)]	21.2 (18.7–23.9)	19.0 (16.6–21.5)	0.028	16.0 (11.7–20.4)	11.7 (9.1–14.3)	0.057	22.7 (19.6–25.8)	21.5 (18.5–24.6)	0.195
Decrease in weight for height [% (95% CI)]	6.9 (6.3–7.5)	6.9 (6.3–7.5)	0.96	5.5 (4.3–6.7)	5.7 (4.7–6.6)	0.852	7.3 (6.6–8.0)	7.3 (6.7–8.0)	0.932
Blood glucose [mmol/l (IQR)]	21.8 (20.7–22.9)	21.6 (20.6–22.7)	0.84	22.6 (19.7–25.6)	22.5 (20.4–24.7)	0.950	21.5 (20.3–22.7)	21.3 (20.1–22.5)	0.801
pH (95% CI)	7.33 (7.32–7.35)	7.36 (7.35–7.37)	0.013	7.30 (7.26–7.34)	7.35 (7.32–7.38)	0.021	7.34 (7.33–7.36)	7.36 (7.35–7.37)	0.123
pCO ₂ [kPa (95% CI)]	4.2 (4.1–4.4)	4.7 (4.6–4.8)	<0.001	3.7 (3.4–4.0)	4.3 (4.0–4.6)	0.009	4.4 (4.2–4.5)	4.9 (4.7–5.0)	<0.001
Bicarbonate [mmol/l (95% CI)]	17.9 (17.0–18.7)	20.6 (19.9–21.3)	<0.001	14.9 (12.9–16.8)	18.8 (17.3–20.4)	0.002	18.7 (17.8–19.6)	21.2 (20.4–22.0)	<0.001
Plasma β-hydroxybutyrate [mmol/l (IQR)]	2.5 (0.7–6.3)	1.3 (0.4–4.3)	<0.001	3.8 (0.8–6.9)	1.4 (0.4–3.8)	0.011	2.3 (0.5–6.2)	1.2 (0.3–4.3)	0.006
Serum osmolality [mmol/l (IQR)]	295 (288–304)	294 (287–302)	0.075	297 (289–307)	295 (289–305)	0.613	295 (288–303)	293 (287–300)	0.068
Serum sodium [mmol/l (95% CI)]	135 (135–136)	136 (135–136)	0.048	134 (133–135)	135 (134–136)	0.253	136 (135–136)	136 (136–137)	0.069
Serum potassium [mmol/l (95% CI)]	4.4 (4.4–4.5)	4.3 (4.2–4.3)	0.001	4.6 (4.5–4.8)	4.5 (4.4–4.6)	0.053	4.3 (4.3–4.4)	4.2 (4.1–4.3)	0.002
Serum creatinine [mmol/l (IQR)]	71 (59–87)	59 (51–70)	<0.001	63 (49–77)	50 (45–59)	<0.001	73 (62–88)	62 (53–72)	<0.001
DKA(i), pH <7.30 [% (95% CI)]	22.4 (17.3–27.5)	15.2 (11.2–19.2)	0.028	32.1 (19.9–44.3)	17.7 (9.3–26.1)	0.052	19.7 (14.2–25.2)	14.4 (9.9–18.9)	0.139
DKA(ii), pH <7.30 and/or HCO ₃ <15 [% (95% CI)]	29.5 (23.8–35.2)	18.9 (14.6–23.2)	0.003	42.6 (29.4–55.8)	20.3 (11.4–29.2)	0.005	25.8 (20.0–32.0)	18.5 (13.5–23.5)	0.069
Severe DKA, pH <7.10 [% (95% CI)]	4.6 (2.1–7.1)	2.2 (0.6–3.9)	0.11	8.8 (1.5–16.2)	3.8 (0.0–8.0)	0.224	3.4 (1.7–5.9)	1.7 (0.0–3.3)	0.241

Children aged < or ≥5 years at diagnosis have been analyzed separately. Data are mean or frequency (95% CI) or median (interquartile range) unless otherwise indicated.

those aged 10–14.99 years (23.1%), and least common among those aged 5.0–9.99 years (11.3%) ($P = 0.001$ when comparing the three age-groups). The outcome was similar when DKA(ii) was applied (aged 0.0–4.99 years, 29.3%; aged 5.0–9.99 years, 15.8%; and aged 10.0–14.99 years, 28.7%; $P = 0.002$).

We analyzed the data during two consecutive 10-year periods (Table 2). In 1992–2001, children had DKA less often at diagnosis (Table 2, Fig. 1B–D). Among the children aged <5 years, the frequency of DKA also was significantly lower in the latter period. Actually, in 1992–2001 the frequency of DKA was nearly similar in the subjects < and ≥5 years of age. During the later 10-year period, the proportion of DKA was higher in the children aged <2 years at diagnosis than among the others [DKA(i) 39.1 vs. 13.4%, $P = 0.001$, and DKA(ii) 47.8 vs. 16.6%, $P = 0.001$], although a tendency toward lower frequency was observed in comparison with the earlier 10-year period [DKA(i) 39.1 vs. 50.0%, $P = 0.454$, and DKA(ii) 47.8 vs. 60.0%, $P = 0.398$]. During the earlier period, the children initially were treated with intravenous insulin more frequently (57.1 vs. 42.9%, $P < 0.001$) and had a longer duration of initial hospitalization (18.0 vs. 10.0 days, $P < 0.001$).

CONCLUSIONS — The incidence of type 1 diabetes among children in Finland is the highest in the world (18). The rate was 45 per 100,000 person-years in 1996, reaching 54 per 100,000 person-years in 2003, the annual increase being ~3.2% (11,19,20). In northern Finland, we also observed increasing incidence rates during the 20-year study period. Particularly, the proportion of young children aged <5 years at diagnosis has increased (Fig. 1A), as also reported in other countries (11).

We used two different definitions of DKA in order to facilitate comparisons with previously published reports. The overall frequency of DKA in our study was lower [DKA(i) 18.1%, DKA(ii) 22.4%] than the corresponding frequencies in many earlier studies (10,21). For example, in the report of the EURODIAB project covering 24 centers in Europe, the overall proportion of DKA (pH <7.30) was 40% in 11 centers that recorded DKA, varying from 26 to 67% (5).

Compared with earlier Finnish studies, the frequency of DKA was found to be lower in the current survey. In 1978–

1981, at Oulu University Hospital, the DKA frequency was 35.5% in children with newly diagnosed type 1 diabetes, when defined as pH ≤ 7.30 and serum ketone bodies positive in serum diluted $\geq 1:2$ (22), whereas the frequency of DKA was 21.6% when defined as pH < 7.30 in the Finnish nationwide Childhood Diabetes in Finland Study conducted in 1986–1989 (3). The latter frequency is similar to the frequency of the first 10-year period (1982–1991) in our study. When the observation period was extended until the year 2001, we noticed that the proportion of newly diagnosed patients with DKA had decreased by $\sim 50\%$ over the 20-year study period (Fig. 1B and C). Similar time trends have been observed in other studies (8,21), although there also has been a report of increasing DKA frequencies in children with newly diagnosed type 1 diabetes (10).

The observation of a declining DKA rate among Finnish children with newly diagnosed type 1 diabetes is in line with the previous findings of an inverse correlation between the frequency of DKA and the background incidence rate of type 1 diabetes (5). Because of the high type 1 diabetes incidence in our country, the symptoms and signs are fairly well known, and the diagnosis is frequently made before DKA occurs. The DIPP study also may have increased the public awareness of the disease. The duration of symptoms before diagnosis was shorter in the latter 10-year period in our study, suggesting that families contacted the health care system earlier during the more recent time period. This could be one reason for the decreasing DKA frequency over time.

DKA was more common among children aged < 2 years. However, a tendency toward lower DKA frequency also was seen in this age-group during the later 10-year period. The overall frequency of DKA in children aged < 2 years at diagnosis was slightly lower than in an earlier Finnish study [DKA(i) 44.7 vs. 53.3%] (23). Several factors may explain the greater frequency of DKA at diagnosis in this group. The symptoms of the disease may go unrecognized in children aged < 2 years. Also, very young children often suffer from acute infections that may mask the symptoms and signs of type 1 diabetes. Consequently, the diagnosis of diabetes may be delayed. In addition, dehydration and acidosis develop quickly in young children, which also may explain the high frequency of DKA at diagnosis in children aged < 2 years. In an

earlier study, serum C-peptide levels have been observed to be the lowest in children aged < 2 years at diagnosis (23), supporting the concept that β -cell destruction may be more aggressive in the very young children.

We found DKA to be more common among children aged < 4 years at diagnosis, and a similar tendency was seen when subjects aged < 5 years were compared with older children. Higher DKA frequencies in children aged < 4 years also have been reported in earlier surveys (3,9). It was encouraging to notice that in children aged < 5 years, the frequency of DKA had decreased markedly at Oulu University Hospital, being 17.7% [DKA(i)] or 20.3% [DKA(ii)] in the later study period (1992–2001). This frequency is the lowest reported so far in this age-group. For example, Quinn et al. (24) recently reported a DKA frequency of 43.7% [DKA(ii)] in children aged < 6 years at diagnosis. In the Finnish nationwide study conducted in 1986–1989, the frequency of DKA was 22.1% [DKA(i)] in subjects aged < 5 years (23). It is remarkable that in the present study in 1992–2001, the frequency of DKA in children aged < 5 years was close to that observed in older children. It seems that in this series the decrease in the overall DKA frequency mainly was attributed to the decrease of DKA in children aged < 5 years (Table 2).

In the age-group analysis covering the whole 20-year period, the lowest frequency of DKA, only 11.3%, was recorded for those aged 5–9.99 years—possibly related to the careful observation of children by their parents at this age. On the contrary, children aged ≥ 10 years had a similar frequency of DKA (23.1%) as subjects aged < 5 years at diagnosis (23.7%). It is possible that teenagers are more secretive of their symptoms and therefore run a higher risk of developing DKA.

Boys tended to have an increased risk of developing DKA, although the difference was not statistically significant. The boys in this study were slightly older than the girls at the time of diagnosis, which may explain the tendency for higher DKA frequency, when keeping in mind that children aged > 10 years had higher DKA frequency than the 5- to 9-year-old children, and the proportion of boys became higher with increasing age. Previous studies have shown the proportions of cases with DKA to be similar in boys and girls

(9) or have shown that girls have an increased risk (10,25).

The decrease in relative weight for height was estimated on the basis of earlier growth information, which is regularly collected for each child in Finland. Children aged ≥ 5 years had a more pronounced decrease in weight for height at diagnosis and a longer duration of symptoms but a lower frequency of DKA, indicating that the disease process is slower in older children and the weight loss is due to a decrease of fat tissue rather than dehydration.

The ongoing DIPP study may have had an impact on the frequency of DKA. The DIPP study was initiated in Oulu University Hospital in 1995, and it was conducted for the last 6 years of the present survey. The effect of the DIPP study might be seen during the last few years of this study, particularly among the younger children. In 1995–2001, the frequency of DKA was low [DKA(i) 16.8%], but the follow-up period is very short. Further observations are needed to assess the long-term influence of the DIPP study on the frequency of DKA.

In conclusion, although the frequency of DKA in children with newly diagnosed type 1 diabetes decreased in northern Finland by $\sim 50\%$ over a 20-year period, it is notable that children aged < 2 years still often have DKA at diagnosis. The possibility of type 1 diabetes should be taken into account at all levels of health care when treating very young, acutely ill children in order to decrease the DKA frequency in this age-group.

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