

Ketoacidosis at Diabetes Onset Is Still Frequent in Children and Adolescents

A multicenter analysis of 14,664 patients from 106 institutions

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OBJECTIVE — We aimed at analyzing the frequency, clinical characteristics, and trends associated with the occurrence of diabetic ketoacidosis (DKA) at the onset of type 1 diabetes on the basis of long-term follow-up data.

RESEARCH DESIGN AND METHODS — A total of 106 pediatric diabetes centers in Germany and Austria participated in this study. Data from 14,664 patients with type 1 diabetes collected between 1995 and 2007 were suitable for evaluation. DKA was defined and classified according to the International Society for Pediatric and Adolescent Diabetes consensus guidelines.

RESULTS — DKA was observed in 21.1% of patients. The frequency of DKA, including the severe form, remained unchanged throughout the 13-year observation period. The frequency of DKA was particularly striking among children <5 years of age (26.5%).

CONCLUSIONS — Ketoacidosis occurring at diabetes onset continues to be a difficult problem. Our data show no significant change in the frequency and magnitude of DKA over the last 13 years.

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Given that the incidence of type 1 diabetes is rising, and awareness of the disease is thus broadening, it is probably reasonable to expect a drop in the occurrence of diabetic ketoacidosis (DKA) at the onset of diabetes.

By means of a computerized follow-up program for diabetic children called the Diabetes Prospective Documentation Initiative or Diabetes Patienten Verlaufsdokumentation (DPV), we analyzed the frequency and clinical characteristics of DKA occurring at the time of diabetes onset in order to ascertain whether a change

in the frequency of DKA at diabetes onset was discernible over the last 13 years.

RESEARCH DESIGN AND METHODS

Data collection

Data was collected from 106 pediatric diabetes centers in Germany and Austria by means of the DPV. In this report we present an analysis of the incidence rate pertaining to the 13-year period beginning in January 1995 and ending in December 2007.

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Patient characteristics

The data from 14,664 type 1 diabetic patients with an average age of 9.0 years (range 0–17.9) were found suitable for analysis. Of these, 53.1% ($n = 7,787$) were male and 46.9% ($n = 6,877$) were female. For the analysis, we extracted the data of all patients at diabetes onset who were treated at a pediatric diabetes center at which pH measurement could have been done and critical care was available.

Definition of DKA

In our study, a pH value of <7.3 was the biochemical criterion we chose for defining DKA. This was based on the International Society for Pediatric and Adolescent Diabetes consensus guidelines, which we also followed for classifying the severity of DKA: mild, $7.2 \leq \text{pH} < 7.3$; moderate, $7.1 \leq \text{pH} < 7.2$; severe, $\text{pH} < 7.1$ (1).

Statistical analysis

We used the software package SAS version 9.1 (SAS Institute; Cary, NC) for the evaluation of data and the statistical analysis. A P value of <0.05 was considered to be significant. The individual values are given as means \pm SEM unless otherwise indicated. The analysis of the frequency of DKA was done without adjusting for age or sex.

RESULTS

Frequency of DKA

Our findings showed that 21.1% of the 14,664 patients had pH values of <7.3 at the onset of type 1 diabetes and that the remaining 78.9% did not have DKA: 1,430 patients (9.8%) showed mild, 788 (5.4%) moderate, and 873 (5.9%) severe DKA.

In analyzing the frequency of DKA over a span of 13 years, we did not find a statistically significant time trend ($P > 0.163$); thus, we concluded that the frequency of DKA remained consistent throughout this period (Fig. 1). Likewise, we found no evidence of a noticeable shift within the individual groups, since the percentage of cases with severe acidosis

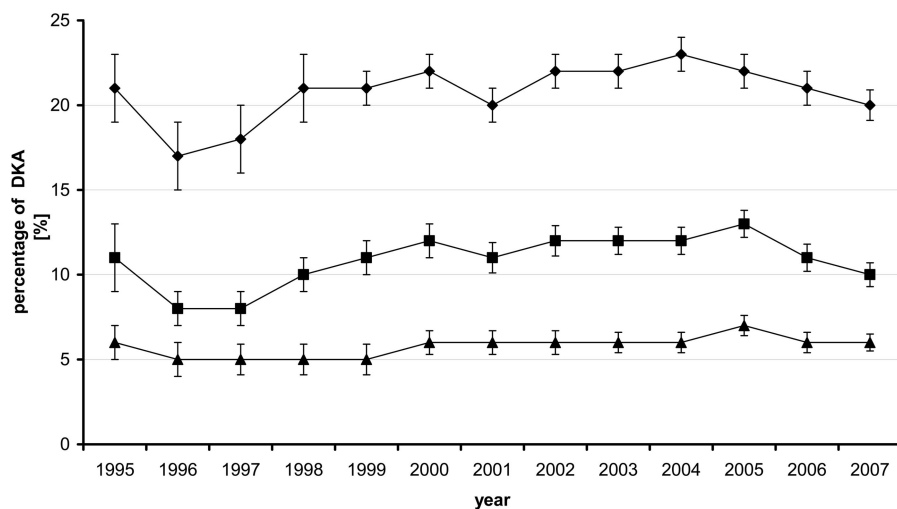


Figure 1—Frequency of DKA according to years. ♦, pH <7.3; ■, pH <7.2; ▲, pH <7.

also remained consistent over time ($P > 0.486$).

Patient characteristics

The average age at the time of diabetes onset was as follows: patients without DKA, 9.2 ± 4.1 years; patients with a mild form of DKA, 8.7 ± 4.5 years; and those with severe DKA, 8.4 ± 4.5 years. Although the age differences are highly significant ($P < 0.001$), they have no clinical relevance. In the total cohort there were more boys (53.1%) than girls (46.9%); however, the proportion of girls was slightly higher in the subgroups with DKA (mild, 50.9% boys vs. 49.1% girls; severe, 49.4% boys vs. 50.6% girls). The highest frequency of DKA (26.5%) was found in children ≤ 5 years of age ($P < 0.001$ vs. other age-groups), followed by the 10- to 15-year-olds (22.0%).

CONCLUSIONS— We present the results of a representative analysis based on the DPV documentation system by means of which broad data were collected. This involved the participation of 106 pediatric diabetes centers, 14,664 documented patients, and a period of observation that exceeded 10 years.

Our findings revealed a high frequency (21.1%) of DKA at diabetes onset, which, however, is comparable with the results of previous analyses of data from the DPV network (1). The comparative frequency between Europe and North America varies between 15 and 70% (2). In a multicenter study in the U.S. that

comprises a large collective of patients ($n = 3,666$), the reported frequency of DKA at diabetes onset was 29.4%, which is somewhat higher than the frequency in Germany (3). For the time span of our study, there was a marked increase in the incidence of diabetes in Germany: whereas in 1995 it was at 14.5 per 100,000 (95% CI 13.1–16.8), by 2006 it had reached 21.1 per 100,000 (18.9–23.3). This corresponds to a mean increase of 4.4% per year (4,5). However, the percentage of patients with DKA at diabetes onset remained relatively consistent during the period of observation. Similar results were found in an analysis of data collected in Germany between 1987 and 1997 (6), which were also corroborated by the Search for Diabetes in Youth (SEARCH) study in the U.S. (3).

Studies in other countries (7) have shown that it is possible to achieve a marked decrease in the frequency of DKA through focused educational campaigns. The results of the present study, however, indicate that the rate of occurrence of DKA has remained consistent over two decades despite the rising incidence of the disease and the broadening awareness. The proportion of severe cases of DKA is high, at 6% of the total group of patients with type 1 diabetes onset. These findings demonstrate that it is imperative for every case of diabetes onset to be regarded as an emergency.

The present study shows that, even in the 21st century, DKA at diabetes onset occurs with regularity in a percentage of

patients that is not at all insignificant. Reinforced efforts aimed at educating both the general public and practicing physicians are imperative if the situation is to improve.

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