





Association of Prodromal Type 1 Diabetes With School Absenteeism of Danish Schoolchildren: A Population-Based Case-Control Study of 1,338 Newly Diagnosed Children

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## **OBJECTIVE**

To investigate school absenteeism before the clinical diagnosis of type 1 diabetes in children who develop the disease.

## RESEARCH DESIGN AND METHODS

This population-based, retrospective case-control study involved all Danish children who developed type 1 diabetes and attended public schools (n=1,338) from 2010 to 2017. Those children were matched at a 1-to-5 ratio, on the basis of sex and date of birth, to children without diabetes (n=6,690). Case and control absenteeism were compared monthly, starting with 12 months prior to the type 1 diabetes diagnosis through 12 months after diagnosis.

## **RESULTS**

Before the diabetes diagnosis (7–12 months), the mean number of days absent from school per month was 0.93 (SD 1.78) among children with diabetes and 0.93 (1.82) among control children (difference  $-0.004\,\mathrm{days}$ , P=0.94). From 4 months before the diagnosis, children who developed diabetes had a statistically significant increase in absenteeism compared with control children (difference 0.24 days, P<0.05).

### CONCLUSIONS

Children who were diagnosed with type 1 diabetes had increased school absenteeism 4 months before diagnosis.

Type 1 diabetes (hereafter referred to as "diabetes") often presents as potentially lifethreatening diabetic ketoacidosis (DKA), and delayed diagnosis is thought to be an important factor in the development of DKA (1–4). Knowing the time span from the onset of symptoms to clinical diagnosis is potentially important for interventions aiming at earlier diagnosis. Increased school absenteeism could be an early indication of symptoms. The primary objective of this study was to investigate the association of school absenteeism before and after a diabetes diagnosis.

## RESEARCH DESIGN AND METHODS

The study was approved by the Danish Data Protection Agency. The Danish Registry of Childhood and Adolescent Diabetes (DanDiabKids), a national database containing

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information based on patient records, clinical examinations, and blood samples, was approved by the Danish National Committee on Health Research Ethics (Copenhagen, Denmark) number KA 95139M. These approvals are legally required and waive informed consent.

This study was a population-based, case-control, retrospective registry study of children attending kindergarten (age 6) through 10th grade (age 16) in Danish public schools from 1 August 2010 to 30 June 2017. It is mandatory for public schools to report individual-level absenteeism to the Danish Ministry of Education. Approximately 85% of Danish schoolchildren attend public schools (5).

Students were identified through Statistics Denmark and linked with school absenteeism data provided by the Danish Ministry of Education. From the DanDiab-Kids database, to which data are uploaded from all pediatric clinics in connection to yearly visits, we identified the population of children who had been diagnosed with diabetes. Children with diabetes were included if they had diabetes onset (date of diagnosis from medical records) during the observation period. For each child diagnosed with diabetes (a case), five children who did not develop diabetes during the study period (controls) were matched on the basis of day of birth and sex. The children were followed for 25 calendar months from the date of diagnosis (12 months before and 12 months after plus the month of diagnosis).

## **Outcome Measures**

School absenteeism, measured in days absent per calendar month, was the primary outcome. The month the child was diagnosed was assigned as month 0. Because a child could be diagnosed in the middle of a calendar month, month 0 could include absenteeism from both before and after the time of diagnosis.

Subgroup analyses of the primary outcome were performed in order to assess factors that might affect the association, including DKA at diabetes onset and diabetes control ( $HbA_{1c}$ ).

## Clinical Measures

HbA<sub>1c</sub> levels were measured centrally by using the standardized method described by the International Federation of Clinical Chemistry. DKA at onset was defined

as standard bicarbonate <15 mmol/L or pH <7.3 (6).

The first  $HbA_{1c}$  level recorded more than 180 days after diagnosis was used. The treatment target for Danish children was  $HbA_{1c} \le 7.5\%$  ( $\le 58$  mmol/mol).

#### Statistical Analysis

Means of selected variables were compared between cases and controls. Linear regression models were estimated in order to investigate the relationship between time to diabetes diagnosis and school absenteeism. Outcomes were observed 12 months before the diagnosis, during the month of diagnosis, and 12 months after the diagnosis (25 months total). Children who developed diabetes were coded as 1 and control children were coded as 0. A linear regression model with monthly absenteeism as the outcome included an interaction of diabetes status (indicator) and month relative to diagnosis indicator variables. Mean absenteeism was compared further by 6-month time periods, two before and two after the diagnosis.

## **Subgroup Analyses**

Children who presented with DKA at onset and those without DKA at onset were identified as two subgroups. In order to identify associations of diabetes control and school absenteeism, the subgroups of children with HbA $_{1c} \le 7.5\%$  ( $\le 58$  mmol/mol) versus > 7.5% (> 58 mmol/mol) were considered.

All statistical analyses were performed in Stata 15 software. All statistical testing was two-sided, and results were considered significant when P < 0.05.

## **RESULTS**

A total of 1,338 children with diabetes were identified and matched to 6,690 control subjects (8,028 children in total), totaling 141,422 child-month observations. Among the children with diabetes,  $HbA_{1c}$  after onset—measured a mean of 387 days (SD 154 days) after diagnosis—was available for 1,290 children. Of those children, 21.1% had DKA at diabetes onset.

Mean age of the matched case-control study population was 10.9 years (SD 2.97 years) at diagnosis. Just more than half (52.7%) were male. Supplementary Table 1 shows descriptive characteristics of the two groups.

## **Primary Outcome**

From 1 year to 6 months before diabetes diagnosis (months -12 to -7) there were no statistically significant differences in absenteeism between children with and those without diabetes (0.93 vs. 0.93 days, P = 0.94). Statistically significant differences in absenteeism were detected as early as 4 months before diabetes diagnosis (month -4) (difference 0.24 days, P < 0.05) (Fig. 1). During the month of diagnosis, absenteeism dramatically increased (mean 4.95 days vs. 1.00 day, difference 3.95, *P* < 0.05). After diagnosis (months 7-12), children with diabetes maintained that increased absenteeism (mean 1.50 vs. 1.02 days, difference 0.48, P < 0.05). The analysis presented in Supplementary Fig. 1 shows that the increase in absenteeism before onset was driven by sickness.

# Subgroup Analysis of the Primary Outcome

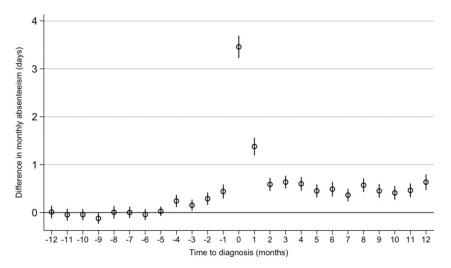
When comparing absenteeism between the subgroups of children with diabetes,  $HbA_{1c} \le 7.5\%$  ( $\le 58$  mmol/mol) was associated with less absenteeism (0.83 days) during the period from 1 year to 6 months before diabetes diagnosis compared with  $HbA_{1c} > 7.5\%$  (> 58 mmol/mol) (1.08 days) (difference -0.24, P < 0.05). In the period after diagnosis (months 7-12), the difference in absenteeism persisted: 1.29 vs. 1.73 days, respectively (difference -0.44, P < 0.05).

Children who presented with DKA did not have statistically significantly different absenteeism before the diagnosis of diabetes but had significantly more absenteeism during the month of diagnosis (mean number of days absent in month of diagnosis, DKA versus no DKA, was 5.76 and 4.73 days, difference 1.03, P < 0.05).

## CONCLUSIONS

In this study, children with diabetes were absent from school significantly more often than children without diabetes. As early as 4 months before the diagnosis, children with diabetes had  $\sim\!25\%$  more absenteeism than the matched control children who did not develop diabetes. The results from the after-diagnosis analysis suggest that children with diabetes were absent roughly 50% more than the controls.

To the degree that this increase in absenteeism preceding the diagnosis is correlated with clinically relevant symptoms, our results suggest a scope for



o Diabetes vs no diabetes

Figure 1—Mean difference (95% CI) in days absent from school during a given month relative to diabetes diagnosis (diabetes vs. no diabetes). Month 0 designates the time of diabetes diagnosis. A total of 1,338 children were diagnosed with type 1 diabetes from 1 August 2010 to 30 June 2017; these children were matched on the basis of age and sex with 6,690 control children. The mean differences were adjusted for specific effects of calendar month and school grade. Because July is the only month of the year with no school days in Denmark, it was left out of the analysis. Nonsignificant differences (with a level of significance at P < 0.05) were found during months -12 to -5.

earlier diagnosis. No evidence was found that children who presented in DKA had different absenteeism before diagnosis than did those who did not present in DKA. Although there is agreement that presentation in DKA is tied to delayed diagnosis (1), this study suggests that this delay is a matter of days, not months.

Other studies have shown diabetes to be associated with increased school absenteeism after onset (7–12). Most recently, a study from Scotland showed that schoolchildren with diabetes had an increased risk of absenteeism and that the risk was higher among children with higher levels of HbA<sub>1c</sub> (8). These findings are consistent with our own.

### Limitations

Not all children who were diagnosed with diabetes during the study period attended public schools. Further, the cause of school absenteeism is multifactorial, and therefore it may be a poor predictor of type 1 diabetes. In that light, the results of this study are informative about symptoms anteceding clinical diagnosis but not about predicting type 1 diabetes by using information on absenteeism. Finally, the results from this study may not generalize to other countries.

Our study suggests a scope for earlier diagnosis, even in a country with high diabetes awareness. Further, attention is warranted on levels of school absenteeism after diabetes onset in children with diabetes.

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Duality of Interest. J.S. serves as an adviser to Medtronic, Janssen, and Novo Nordisk; owns shares in Novo Nordisk; and has received fees for speaking on behalf of Medtronic, Sanofi, Novo Nordisk, and Bayer AG. No other potential conflicts of interest relevant to this article were reported.

Author Contributions, P.R.T. and N.S. wrote the first draft of the manuscript. All authors interpreted the data, critically revised the manuscript, and approved the final version for submission. N.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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