

CLINICAL STUDY

Increasing incidence of type 1 diabetes mellitus in young children in Slovakia

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ABSTRACT

OBJECTIVES: We aimed to study the prevalence of the early onset Type 1 diabetes in Slovakia during the years 1996–2017.

BACKGROUND: Prevalence of Type 1 diabetes in young children is increasing worldwide. However, recent data from Slovakia are missing.

METHODS: All children with newly diagnosed Type 1 diabetes included in the study were diagnosed in the Children Diabetes Centre in Bratislava during the years 1996–2017. The incidence of T1D in children aged below 3 and below 5 years was calculated and compared to the T1D incidence in older children. Incidence trends were calculated with the Poisson regression.

RESULTS: Gender-adjusted incidence of T1D annually increased by 5.4 % (CI: 3.9–6.8; $p < 0.001$) in children <3 years, and by 3.4 % (95 % CI 2.2–4.6; $p < 0.001$) in children <5 years during the last two decades. Moreover, the proportion of young children <3 years of age among all newly diagnosed children and adolescents increased over time (4.2 ± 2.8 % in years 1996–1998; 12.2 ± 5.8 % in years 2004–2008, and 13.7 ± 7.4 % during the years 2013–2017).

CONCLUSION: We found a significant increase in the incidence and proportion of T1D in young children during the last two decades. Similar data were also found in other European countries. This could be explained by changing environmental conditions (Fig. 1, Ref. 32). Text in PDF www.elis.sk.

KEY WORDS: type 1 diabetes mellitus, infants and toddlers, epidemiology.

Introduction

Type 1 diabetes is the most common type of diabetes mellitus (DM) in children and adolescents in majority of countries worldwide. However, the incidence and prevalence of Type 1 diabetes changed significantly over the last several decades. Type 1 diabetes has some specific features in young children such as the absence of classical early symptoms: polyuria, polydipsia, and weight loss could be overlooked leading to high risk of a diabetic ketoacidosis (DKA) (11). In the early twentieth century, Type 1 diabetes in the youngest age group was recognized as a rare disease (1). The increase in incidence of Type 1 diabetes has been observed in recent decades with a variation in between different ethnic groups (2). The highest incidence was reported in Finland (3) and Canada (4) and the lowest in Asia (5, 6). A significant increase in the incidence rate has been reported in the age group of children <5 years with

the shift of diabetes onset to younger age groups (69). The cause of the changing trend in the epidemiology remains unknown (10).

Previous studies on Type 1 diabetes in Slovak children showed an increasing incidence during the years 1985–2000 (11, 12). The overall incidence of type 1 diabetes in children aged below 14 years varied from 5.62/100,000 per year in year 1986 to 14.46/100,000 in year 1998, what represents a 2.57-fold increase. The incidence increased with age and was the highest among children 10–14 years of age.

We aimed to calculate the incidence of T1D in Slovak children in our center, particularly below 5 years of age, clarify the trends in the incidence rate of T1D and compare to the T1D incidence in older children.

Materials and methods*Patients and methods*

Patients diagnosed with newly onset T1D, who had received their first diabetes treatment and who had been regularly followed up were recruited from the Children Diabetes Centre of the Department of Pediatrics, Faculty of Medicine Comenius University and National Institute of Children's Diseases in Bratislava. The Children Diabetes center is the largest center for diabetes in Slovakia with more than 50 % of children and adolescents with DM <19 years. For the diagnosis of Type 1 diabetes, the criteria of the International Society for Pediatric and Adolescent Diabetes (ISPAD)

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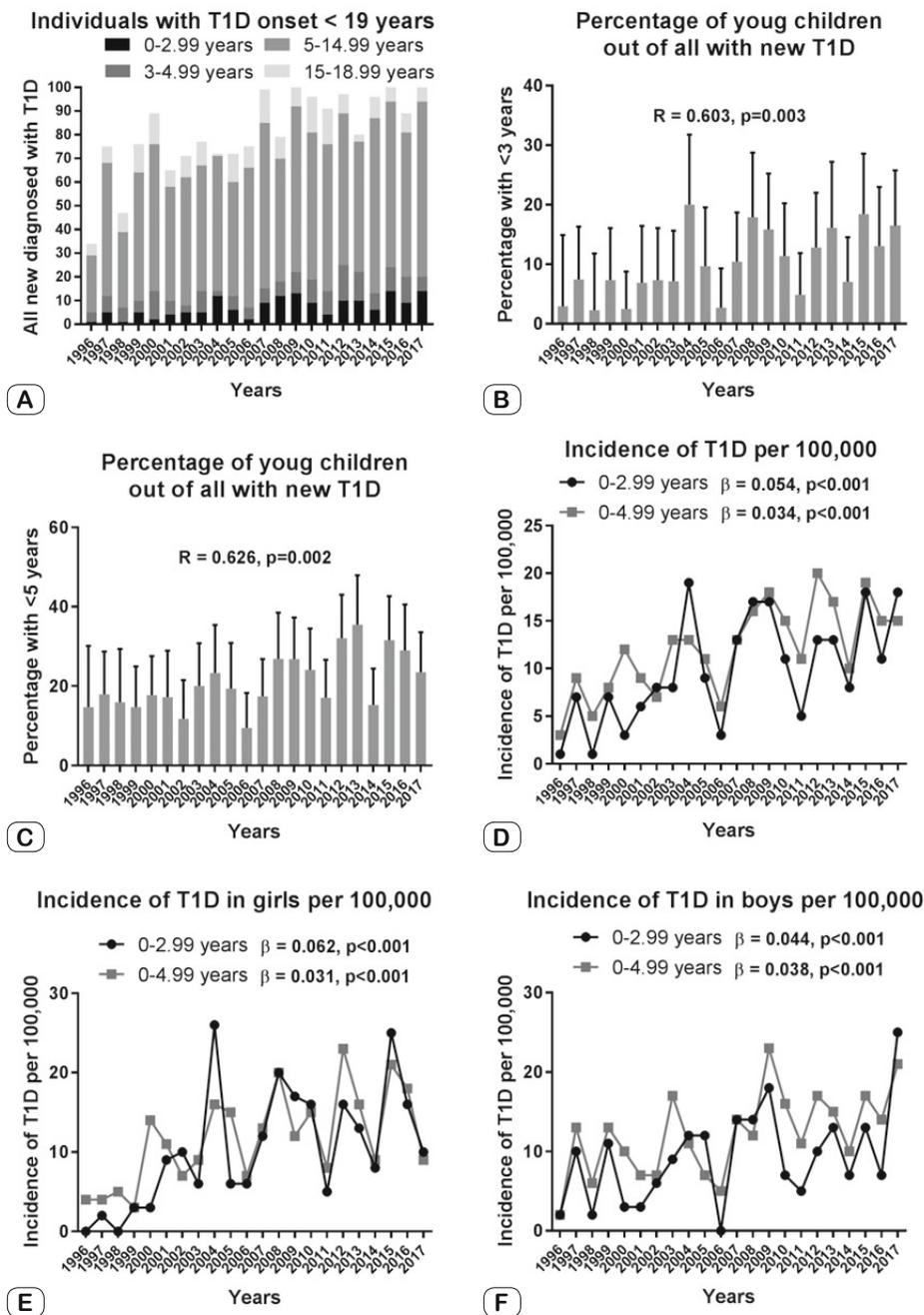


Fig. 1. Frequency data on T1D in children in Slovakia in the years 1996-2017. **A.** Number of newly diagnosed children and adolescents with T1D in various age groups, **B.** Percentage of children < 3 years among all newly diagnosed patients aged < 19 years with confidence intervals. “R” represents Pearson’s correlation coefficient. **C.** Percentage of children < 5 years among all newly diagnosed patients aged < 19 years with confidence intervals. “R” represents Pearson’s correlation coefficient. **D.** Incidence of T1D in all children aged < 3 years and < 5 years, respectively. Regression coefficients were calculated using Poisson regression model. **E.** Incidence of T1D in girls aged < 3 years and < 5 years, respectively. Regression coefficients were calculated using Poisson regression model. **F.** Incidence of T1D in boys aged < 3 years and < 5 years, respectively. Regression coefficients were calculated using Poisson regression model.

were used (9). We excluded patients with other types of diabetes mellitus, including neonatal diabetes with a confirmed monogenic etiology (13, 14), Maturity Onset Diabetes of the Young (15–17), Type 2 diabetes (15), and syndromic forms of diabetes mellitus. All data were collected retrospectively.

The data were used for the calculation of T1D incidence in children and adolescents diagnosed in our center. The incidence of T1D was calculated as follows: number of newly diagnosed children with T1D divided by the number of children of corresponding age using the data from the annual reports of the Slovak

National Health Information Centre (18). The incidence of T1D and the proportion of all newly diagnosed children with T1D was calculated in the 3–5-year periods (8).

Poisson regression models were used to assess the time trends in incidence. P values less than 0.05 were considered statistically significant. Statistical analyses were performed with SPSSv25 software (IBM, NY, USA).

Ethic committee

All steps of the study were approved by the Ethics Committee of the National Institute of Children's Health in Bratislava, Slovakia and adhered to the tenets, outlined in the declaration of Helsinki.

Results

Epidemiology of T1D in infants and toddlers

The incidence of T1D in the age group < 3 years increased over the last two decades ($R=0.626$, $p=0.002$) (Fig. 1A, B, D) in both genders (Fig. 1E, F). During the years 1996–1998, the incidence of T1D was 1.0 ± 1.7 per 100,000 in girls and 5.4 ± 4.7 in boys; during the period 2004–2008, the T1D incidence increased to 14.5 ± 7.9 per 100,000 in girls, and to 10.7 ± 5.1 in boys and peaked in between years 2014–2017 with the incidence of 15.1 ± 10.7 per 100,000 in girls, and 13.4 ± 3.1 in boys, respectively. Moreover, the proportion of young children < 3 years of age among all newly diagnosed children and adolescents in our center increased over time (4.2 ± 2.8 % in years 1996–1998; 12.2 ± 5.8 % in years 2004–2008, and 13.7 ± 7.4 % during the years 2013–2017) (Fig. 1B). A similar trend of an increasing incidence and proportion of T1D in all newly diagnosed children was observed in the age group < 5 years (Fig. 1A–F). Fig 1 also demonstrates the average annual increase of 5.4 % (95 % CI 3.9–6.8; $p<0.001$) after adjustment for sex in children < 3 years, and the average annual increase of 3.4 % (95 % CI 2.2–4.6; $p<0.001$) in children < 5 years calculated with the Poisson regression model. The increase in the incidence of T1D was evident in both genders with higher rates in girls < 3 years (6.2 %; 95 % CI 4.2–8.2; $p<0.001$ in girls and 4.4 %; 95 % CI 2.3–6.6; $p<0.001$ in boys) and in boys < 5 years (3.1 %; 95 % CI 1.6–4.7; $p<0.001$ in age group < 5 years in girls and 3.8 %; 95 % CI 1.9–5.7; $p<0.001$ in boys).

Discussion

Our study was focused on the incidence of T1D and the remission phase in young children. We found a significant increase in the incidence and proportion of T1D in young children during the last two decades.

We found a sustained increase of Type 1 diabetes incidence in children in our center over the last two decades. Similar data were shown also by previous Slovak nation-wide studies on Type 1 epidemiology in years 1985–2000 (11, 12). The incidence of T1D had an increasing trend also worldwide with the most prominent increase occurring in the youngest age group of < 5 years (8). We found a similar trend, when we compared our data to the Central European countries.

The incidence of T1D in Czech pediatric population < 5 years during 1994–1998 was reported to be 6.8 per 100,000 in girls and 7.8 in boys. Similarly, the increasing trend of 12.2 per 100,000 in girls and up to 13.6 per 100,000 in boys was detected in 2004–2008 with a peak of 13.6 per 100,000 in girls and 16.0 per 100,000 in boys in the period of 2009–2013 (19). In Hungarian children < 5 years, the increase in the incidence of T1D from 5.2 per 100,000 (1989–1993) to 14.1 per 100,000 (2004–2009) was present in both genders (20).

In Austria, the incidence of T1D in children < 5 years increased from 5.4 per 100,000 (1989–1993) to 13.2 per 100,000 (2004–2008) (21). Until the year 1994, the incidence rate in children < 5 years was rather stable but increased dramatically by 9.2 % (CI = 5.2–13.4) annually. (21). In addition, a sustained increase in T1D incidence in children < 5 years from 6.3 per 100,000 (1989–2004) to 14.9 per 100,000 (2005–2012) was observed in Poland, with the highest increase in children aged < 5 years (22).

In the large international study by Patterson et al (2019), the annual incidence increase rate in Central Europe was reported to be the highest in Poland (6.6 %), followed by Czech Republic (4.7 %), Austria (4.4 %) and Hungary (4.3 %) (8).

However, there is only a limited number of studies evaluating the incidence of T1D in the youngest age group of children < 3 years. Ehehalt et al (2010) reported that the highest linear increase of T1D incidence in Germany occurred in the age groups of 2- and 3-year old children (12 and 13 % per year, retrospectively) over the years 2000–2006 (23). The mean proportion of T1D diagnosed < 3 years of age in Slovakia over the last decade (9.99 ± 3.85 %) is still lower compared to Finish study in 1992–2001 (8.9 % of children with T1D were diagnosed < 2 years and 31.3 % < 5 years) (24).

The increase in T1D incidence particularly in young children was also found in other European countries. As there is no reason of cumulating high-risk genetic factors for T1D, this phenomenon may be explained by changing environmental conditions. Among considered environmental triggers of T1D were respiratory infections and negative life events suggested (25). Both of them had a high prevalence in the children genetically at risk for T1D (26). Gut microbiome and gut permeability were also linked with T1D development (27). Other considered risk factor for T1D autoimmunity included Cesarean section (28), breastfeeding (29), and vitamin-D deficiency (30). Moreover, childhood obesity could be a factor accelerating the earlier T1D onset in children (31) relevant also to our data, as recently there is an increased prevalence of childhood obesity in Slovakia (32).

Strengths and limitations

The principal strength of our data is represented by the large cohort of children with an early onset of T1D. All patients recruited to this study were diagnosed and treated in one center. The main limitation of this study is the absence of data from nation-wide cohort.

Conclusions

Our findings emphasize the need for further research of the cause, nature and course of diabetes in the young children

with T1D as the incidence of diabetes in this age group is still increasing.

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