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What do we know about the trends in incidence of childhood-onset type 1 diabetes?

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Introduction

Type 1 diabetes requires intensive ongoing management and may lead to complications that affect multiple organ systems. Concern has been raised about the increasing incidence of type 1 diabetes worldwide, given the impact that type 1 diabetes has on quality of life and the long-term cost to healthcare systems and individuals with diabetes and their families.

Trends in incidence of type 1 diabetes

In this issue of *Diabetologia*, Patterson et al [1] report the most recent analysis of data from the EURODIAB study, which is comprised of 26 centres in 22 European countries [1]. A 3.4% annual increase in type 1 diabetes from 1989 to 2013 among children <14 years of age was reported, with the rate of increase tending to be reduced in some high-risk countries with higher incidence rates.

Previously, the same group published a report that focused on the incidence of type 1 diabetes using EURODIAB registry data from 1989 to 2008 [2]. This earlier report demonstrated non-uniformity in rates of increase over time, with periods of less rapid and more rapid increases in incidence identified in many of the registries. As illustrated in Patterson et al [1], incidence rates were reported as 3.2–4.1% per year over the first 15 year period (1989–2003; analysed over three 5 year intervals) with a potential levelling off from 2004 to 2008, when the increase in incidence rate was 1.1% per year. While the earlier report using data from high-risk European countries suggested a plateau, or even a decrease,

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in the incidence of type 1 diabetes over time, that trend appears to have been short lived; the recent analysis [1] shows a persistent, continuous increase in incidence rates, suggesting that there may be a cyclical variation in incidence. Similarly, reports from other parts of the world and in lower-risk populations also show a rising incidence [3,4,5].

In the multicentre SEARCH for Diabetes in Youth Study, which focuses on youth-onset diabetes (0–19 years of age) and is conducted in five centres in the USA, an age-, sex- and race/ethnicity-adjusted annual increase in type 1 diabetes incidence of 1.8% from 2002 to 2012 was recently reported [3]. While type 1 diabetes increased by 1.2% per year in non-Hispanic white youths (the race/ethnic group with the highest incidence of type 1 diabetes incidence in the USA), the incidence of type 1 diabetes increased by 4.2% and 2.2% per year among Hispanic and black youths, respectively. The rate of increase was significantly greater among Hispanic youths than among non-Hispanic white youths [3]. In another study, the annual increase in type 1 diabetes incidence in a sample of Canadian youths (< 20 years) from 2002 to 2003 was reported as 1.3% [4], which is almost identical to the US study [3]. Unfortunately, the Canadian study did not present rates by race and ethnic groups [4].

Relevant to the issue of variability by region, the DIAMOND Project Group demonstrated the dramatic range of type 1 diabetes incidence rates in their 110 centres around the world; the age-adjusted incidence of type 1 diabetes ranged from 0.1 per 100,000/year in China and Venezuela to 40.9 per 100,000/year in Finland. This is more than a 400-fold variation in type 1 diabetes incidence in the period 1990–1999 [5]. More recently, the T1D China Study Group [6] reported a type 1 diabetes incidence rate of 1.01 per 100,000 person-years. Although the China Study Group used somewhat different surveillance methods than the DIAMOND Project, an incidence rate of 1.01 per 100,000 person-years is still much lower than the rates observed in other countries in the DIAMOND Project [5].

Potential influence of genetic and environmental risk factors on trends in type 1 diabetes

The onset of type 1 diabetes results from the interaction of predisposing genetic risk factors and environmental triggers [7,8]. Because environmental triggers drive short-term incidence trends of type 1 diabetes and any condition involving both genetic and non-genetic aetiological determinants, it is not surprising that trends and shapes of these trends vary substantially by geographical region. There is substantial evidence of the genetic contribution to the risk of type 1 diabetes, including the HLA region on chromosome 6p21, the insulin gene and other candidate genes [9,10]; however, it is highly unlikely that the underlying population genetic risk will change in the short term.

Data on incidence trends in type 1 diabetes are important given the slower than hoped for progress in the identification of environmental trigger(s) of the disease and the development of prevention strategies. The Environmental Determinants of Diabetes in the Young (TEDDY) study has evaluated multiple candidate environmental triggers, including infections, probiotics, micronutrients and the microbiome [10], since there are multiple pathways that may lead to the destruction of the beta cells resulting in type 1 diabetes [11]. TEDDY brings tremendous opportunity because of the inclusion of three European centres and three centres in the United States, and the capacity (to the extent feasible based on statistical power) to consider the differential impact of various potential environmental triggers across centres. It appears that there may be a maximum incidence rate determined by the genetic component of the complex aetiology of type 1 diabetes, and that geographical regions with the highest population prevalence of high-risk haplotypes overall and within specific race or ethnic groups may be nearing that maximum. Understanding the population prevalence of type 1 diabetes-related haplotypes would likely be useful to further our understanding of this aspect of the epidemiology of type 1 diabetes. Using this information, it would be possible to map exposure to environmental triggers over time to help advance development of targeted prevention strategies.

Earlier detection may curb high rates of diabetic ketoacidosis at diagnosis

In the meantime, we highlight the importance of early detection of type 1 diabetes, with the goal of reducing risk for diabetic ketoacidosis (DKA) near the time of diagnosis. The prevalence of DKA is unacceptably high around the world. In a recent report from a multinational collaboration with data from 13 countries (New Zealand, Australia, Austria, Czech Republic, Denmark, Germany, Italy, Luxemburg, Norway, Slovenia, Sweden, the USA and the UK [Wales]), DKA was reported to occur in 29.2% of cases at onset of type 1 diabetes (95% CI 28.8, 29.5) [12]. However, Elding Larsson et al found a lower prevalence of DKA at type 1 diabetes diagnosis among children under surveillance as part of the TEDDY study compared with those identified through type 1 diabetes registries from the same regions in Europe and the United States [13].This suggests that the surveillance of individuals at genetic risk (such as TEDDY study participants) and the education of parents about the signs and symptoms of type 1 diabetes may be important strategies to pursue for early detection of type 1 diabetes.

Conclusion

Careful healthcare planning for an ever-increasing population of young adults with type 1 diabetes at risk of lifelong morbidity is becoming crucially important. Advances in technology over the past two decades, including the continuous glucose monitor and the hybrid insulin-only closed-loop system, may assist individuals with type 1 diabetes in the management of their condition, but the prevention of type 1 diabetes requires the unravelling of multiple genetic and environmental risk factors. Researchers around the world must continue to monitor trends in type 1 diabetes incidence while work in the areas of prevention, early detection and improved treatment of type 1 diabetes continues.

Abbreviations

DKA	Diabetic ketoacidosis
TEDDY	The Environmental Determinants of Diabetes in the Young

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