Regular peaks and troughs in the Australian incidence of childhood type 1 diabetes mellitus (2000–2011)

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Abstract

Aims/hypothesis The aim of this study was to determine the incidence and incidence rate trends for type 1 diabetes mellitus in children aged 0–14 years, Australia-wide, from 2000 to 2011.

Methods Cases of type 1 diabetes mellitus diagnosed in 0- to 14-year-olds were identified from the National (insulin-treated) Diabetes Register, with a 97% ascertainment rate. Annual age-standardised, sex- and age-specific incidences were calculated and Poisson regression was used to analyse the incidence by calendar year, sex and age at diagnosis. Non-linear temporal trends were analysed using sine and cosine functions applied to Poisson regression models for 3, 4, 5, 6 and 7 year cycles, and the Akaike information criterion was used to assess goodness of fit.

Results A total of 11,575 cases (6,049 boys and 5,526 girls) of childhood type 1 diabetes mellitus were registered between 2000 and 2011, giving a mean incidence of 23.6 per 100,000 person-years (95% CI 23.2, 24.0). The mean incidence was 4.9% (95% CI 1.1%, 8.8%) higher in boys than in girls.

Compared with 0- to 4-year-olds, the mean incidence was 65% higher in 5- to 9-year-olds and 208% higher in 10- to 14-year-olds. A 5 year cyclical variation in incidence was observed overall, in both sexes and in all age groups. An average annual increase in incidence was observed only in the 10- to 14-year-old age group (increase of 1.2% per year [95% CI 0.4%, 2.1%]).

Conclusions/interpretation A sinusoidal pattern was observed in the incidence rate trend of childhood type 1 diabetes mellitus in Australia. The 5-yearly peaks and troughs in incidence rate trends observed Australia-wide corroborate findings previously reported for Western Australia and require further investigation.

Keywords Australia · Childhood · Epidemiology · Incidence · Type 1 diabetes mellitus

Abbreviations

IRR Incidence rate ratio

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Introduction

Type 1 diabetes mellitus is one of the most common chronic diseases of childhood, and those affected require lifelong insulin replacement therapy and monitoring for both acute and chronic multisystem health complications. Type 1 diabetes mellitus is a significant cause of morbidity, with impacts on the physical, psychological, financial and social wellbeing of affected children and their families. Over the past few decades, the incidence of type 1 diabetes mellitus in 0- to 14-year-old children has increased by an average of 3% per year [1]. However, the rates of increase and temporal trends are variable [1],

and a possible plateauing of incidence has been reported in Sweden, Finland [2] and Norway [3], as well as in Australia [4].

In Western Australia, which accounts for one-third of the total land mass of Australia but only 10% of the total population, a cyclical variation in the incidence of childhood type 1 diabetes mellitus has been reported, with peaks and troughs in incidence occurring approximately every 5 years between 1985 and 2010 [5]. This raises questions as to whether the cyclical pattern in the incidence rate trend observed in Western Australia is also evident Australia-wide, and whether the reported lack of increase in the national incidence of childhood type 1 diabetes mellitus is due to a non-linear variation in the national incidence rate trend or to a true plateauing of incidence, as has been observed elsewhere.

Therefore, this study aimed to determine the incidence and incidence rate trends of type 1 diabetes mellitus in children aged 0–14 years Australia-wide, using all available data from 2000 to 2011, and to examine the temporal trends for non-linear, cyclical variation.

Methods

The study population was all children under the age of 15 years with type 1 diabetes mellitus diagnosed in Australia between 2000 and 2011. Cases were identified from the National (insulin-treated) Diabetes Register (NDR), which contains data on patients with diabetes in Australia, including the date of diagnosis and diabetes type. Although the NDR was established in 1999, analyses are usually performed with data from 2000 onwards because of initial data-collection inconsistencies. For 0-

to 14-year-olds, data in the NDR are compiled annually from two sources: the Australasia Paediatric Endocrine Group state and territory diabetes databases and the National Diabetes Services Scheme database maintained by Diabetes Australia. The NDR has an estimated case ascertainment of more than 97% [4].

Data on all eligible cases were extracted from the NDR by managers of the register at the Australian Institute of Health and Welfare, and de-identified data were provided for analysis. Population data published by the Australian Bureau of Statistics were used as the denominator data. Annual age-standardised as well as sex- and age-specific incidences were calculated, and Poisson regression was used to analyse incidence by calendar year, sex and age at diagnosis. To analyse the incidence for non-linear variations, sine and cosine functions were applied to Poisson regression models for 3, 4, 5, 6 and 7 year cycles and the Akaike information criterion was used to assess goodness of fit (see Electronic Supplementary Material [ESM] [Methods](#)) [6].

Patients provide written informed consent for their data to be stored in the Australasia Paediatric Endocrine Group and National Diabetes Subsidy Scheme databases, and the NDR. This study received approval from the Princess Margaret Hospital Ethics Committee and the Human Research Ethics Committee of the Western Australia Department of Health.

Results

Between 2000 and 2011, 11,575 newly diagnosed cases of type 1 diabetes mellitus in children aged 0–14 years (6,049 boys and 5,526 girls) were identified from the NDR (Table 1).

Table 1 Number of newly diagnosed cases, total person-years at risk, mean incidence and average annual increase in IRR of type 1 diabetes mellitus in Australia by sex and age at diagnosis (2000–2011)

Sex and age group at diagnosis	Cases (<i>n</i>)	Total person-years	Mean sex-/age-specific incidence per 100,000 person-years (95% CI)	Average annual increase in IRR (95% CI)
Boys				
0–4 years	1,308	8,222,253	15.9 (15.1, 16.8)	0.987 (0.971, 1.002)
5–9 years	1,971	8,297,880	23.8 (22.7, 24.8)	1.009 (0.996, 1.022)
10–14 years	2,770	8,512,349	32.5 (31.3, 33.8)	1.018 (1.007, 1.029)
0–14 years	6,049	25,032,482	24.2 (23.6, 24.8)	1.007 (0.999, 1.014)
Girls				
0–4 years	1,094	7,878,784	13.9 (13.1, 14.7)	0.991 (0.974, 1.008)
5–9 years	2,036	7,950,824	25.6 (24.5, 26.7)	0.997 (0.984, 1.009)
10–14 years	2,396	8,153,252	29.4 (28.2, 30.6)	1.007 (0.996, 1.019)
0–14 years	5,526	23,982,860	23.0 (22.4, 23.7)	1.000 (0.991, 1.006)
Boys and girls				
0–4 years	2,402	16,101,037	14.9 (14.3, 15.5)	0.988 (0.977, 1.000)
5–9 years	4,007	16,248,704	24.7 (23.9, 25.4)	1.003 (0.994, 1.012)
10–14 years	5,166	16,665,601	31.0 (30.2, 31.9)	1.012 (1.004, 1.021)
0–14 years	11,575	49,015,342	23.6 (23.2, 24.0)	1.004 (0.999, 1.009)

Over the study period, the overall mean incidence was 23.6 (95% CI 23.2, 24.0) per 100,000 person-years, with the mean incidence in boys being 4.9% (incidence rate ratio [IRR] 1.049 [95% CI 1.011, 1.088]) higher than that in girls (Table 1). Compared with 0- to 4-year-olds, the mean incidence was 65% higher in 5- to 9-year-olds (IRR 1.65 [95% CI 1.57, 1.74]) and 208% higher in 10- to 14-year-olds (IRR 2.08 [95% CI 1.98, 2.18]).

From 2000 to 2011, no significant linear increase in the incidence rate trend was observed overall (IRR 1.004 [95% CI 0.999, 1.009]) or by sex. An average linear annual increase in incidence was observed only in 10- to 14-year-old boys (1.8% per year; IRR 1.018 [95% CI 1.007, 1.029]) and 10- to 14-year-olds in both sexes combined (1.2% per year; IRR 1.012 [95% CI 1.004, 1.021]) (Table 1). Analysis of the temporal incidence rate trend for non-linear variation revealed a sinusoidal pattern for the whole group (Fig. 1), and in both boys and girls and in all age groups (ESM Fig. 1). A sinusoidal pattern with a 5-yearly interval between peaks and troughs provided the model of best fit ($p < 0.001$, Akaike information criterion 21.5).

Discussion

This national, population-based study has revealed a sinusoidal cyclical pattern in the temporal trend of childhood type 1 diabetes mellitus in Australia, corroborating similar findings previously observed in the state of Western Australia [5]. Interestingly, the sinusoidal pattern was observed in both boys and girls and in all age groups, suggesting that factors influencing the incidence of childhood type 1 diabetes mellitus in Australia are similar across all these subgroups.

Despite consistency in incidence registry definitions and statistical methods, temporal trends in the incidence of

childhood type 1 diabetes mellitus continue to be highly variable across different populations and studies. For example, an analysis of temporal trends in childhood type 1 diabetes mellitus across Europe between 1989 and 2008 showed an average annual increase in incidence of 3%, with specific countries showing periods of less or more rapid increase over the study period [1].

In addition to the linear temporal trends in the incidence of childhood type 1 diabetes that have been described in many populations, non-linear trends have also been observed in some studies. For example, similar to this study, a cyclical incidence pattern has been reported in north-east England, where peaks and troughs in incidence were observed to occur in 5–6 year intervals [7]. A study from the US Virgin Islands reported an ‘epidemic-like’ spike in incidence in 2006, when the incidence increased threefold compared with the previous year [8]. In Finland, a steeper rise in incidence in the early 1990s contributed a significant non-linear component to the incidence rate trend, resulting in a curvilinear, rather than cyclical, temporal trend between 1980 and 2005 [2]. Other studies have observed a non-linear temporal trend of levelling off, or plateauing, in the incidence of childhood type 1 diabetes mellitus in recent years [2–4].

Differences in the temporal trends of childhood type 1 diabetes mellitus probably reflect changes in environmental factors within the different study populations. Type 1 diabetes mellitus is generally thought to be the result of both genetic and environmental risk factors, although the underlying factors are not yet understood. Transient or rapid changes in incidence are most likely a result of changes in environmental factors, rather than changes in the more stable population gene pool.

Non-linear temporal trends of a cyclical nature, as observed in this study, or those with peaks/epidemics of incidence, may indicate a role for environmental factors such as viral infections or climatic factors, which display similar temporal trends. Viral infections, in particular enteroviruses, have long been implicated in the aetiology of childhood type 1 diabetes mellitus. Climatic factors may influence other factors associated with childhood diabetes mellitus, such as diet, physical activity and exposure to sunlight and vitamin D, as well as to viruses and other infectious agents. Another possible explanation is that peaks in incidence are followed by troughs due to a reduction in the pool of individuals at risk of the disease. However, although this might explain peaks and troughs that occur randomly over time, it would not account for the regular 5-yearly peaks and troughs in incidence observed in this study.

This study reports the interesting observation of a regular cyclical pattern in the incidence of childhood type 1 diabetes mellitus in Australia, similar to that observed over an extended period of time in Western Australia. This suggests that caution should be applied in modelling and predicting future incidences of childhood type 1 diabetes mellitus based on only linear trends.

Fig. 1 Mean age-standardised incidence of childhood type 1 diabetes in Australia (2000–2011). Solid line, observed incidence; dotted line, predicted incidence using a 5 year sinusoidal Poisson regression model; dashed line, linear temporal incidence rate trend

The strengths of this study are its use of population-based data that are more than 97% complete and the application of standard statistical methods, enabling comparison with other studies. A limitation of this study is the relatively short duration of 12 years; however, all available data have been analysed. Furthermore, no national population-level data were available on environmental factors such as viral infections for comparative analyses.

There is much yet to be understood regarding the aetiology, natural history and critical windows in the development of childhood type 1 diabetes mellitus. In the future, determining different phenotypes or subgroups of type 1 diabetes mellitus [9] and understanding more about the timescale and natural history of diabetes will help researchers to identify factors relevant to different phases of the natural history and the likely multiple causal pathways of this complex disease. Meanwhile, worldwide population-based registers will continue to provide invaluable resources for monitoring the incidence of childhood type 1 diabetes mellitus.

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review and writing of the manuscript. MKB contributed to the study design, statistical analyses and interpretation of findings, and reviewed/edited the manuscript. CB reviewed the study design and reviewed/edited the manuscript. TWJ and EAD contributed to the study design, interpretation of findings and discussion, and reviewed the manuscript. All co-authors have provided approval of the final version to be published. EAD is the guarantor of this work.

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