Scope of epidemiology and daily practice in children with type 1 diabetes in the Netherlands
Hummelink, Engelina

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The incidence of type 1 diabetes mellitus is still increasing in the Netherlands, but has stabilised in children under five (Young DUDEs-1)
ABSTRACT

Aim: This study described the incidence and prevalence of type 1 diabetes mellitus in children in the Netherlands in 2010-2011 and to compare these results with earlier studies.

Methods: This was a retrospective nationwide cohort study of Dutch children aged 14 years or younger. Patients were identified using health insurance reimbursement registries for hospital care and invoices for insulin. In the Netherlands, all children with diabetes are treated by hospital-based paediatricians and healthcare for all Dutch citizens is covered by law.

Results: The incidence of type 1 diabetes mellitus almost doubled between 1978-1980 and 2010-2011, from 11.1 to 21.4 per 100,000. In the youngest age group, who were under 5 years, the incidence rate doubled between 1996 and 1999 and remained stable after that. There were no relevant incidence differences between the sexes. The overall prevalence of type 1 diabetes mellitus in the Netherlands during 2009-2011 was 143.6 (95% confidence interval 141.1-146.2) per 100,000 children and was similar for boys and girls.

Conclusion: The incidence of type 1 diabetes mellitus in children in the Netherlands almost doubled between 1978-1980 and 2010-2011, but the incidence in children under five years appeared to stabilise between 1996 and 1999. There were no statistical differences between the sexes.
INTRODUCTION

Type 1 diabetes mellitus is one of the most common chronic disorders in childhood. This autoimmune-mediated disease is not only associated with diabetes-related complications, but also with a relevant decrease in quality of life (1,2). Despite many developments in management and insulin treatment, the risks of acute complications like hypoglycaemia and ketoacidosis as well as developing microvascular and macrovascular complications in the future still remain (3-5).

The Worldwide incidence of type 1 diabetes mellitus increased steadily by 2.8% per year during the period 1990-1999, with up to about 79 000 new cases per year in children younger than 15 years of age (6,7). In Europe, the increase in incidence rate appears to be even larger, approximately 3-4% per year (8,9). The prevalence of type 1 in the United States increases annually with almost 3% (2001-2009) (10). The estimated worldwide prevalence of type 1 diabetes mellitus in children younger than 15 years of age was almost 500 000 in 2013 (11,12). The incidence and prevalence rates of type 1 diabetes mellitus vary, showing large differences in different time periods as well as within and between different, even neighbouring, countries (9-14).

The estimated prevalence is highest in Europe and South-East Asia and lowest in the West pacific region including China (12). In the World Health Organization Diamond Project 1990-1999, the incidence rate of type 1 diabetes mellitus in children younger than 15 years of age ranged from 0.1 per 100 000 in China and Venezuela to 60 per 100 000 per year in Finland (6,15). These global differences are related by a multitude of factors, for example differences in genetic predisposition, differences in environmental exposure to potential triggers of the immune system and differences in the ability to ascertain the diagnosis, the organisation of healthcare, the accessibility of facilities and quality of registration (16-18). The purpose of this study was to assess the incidence and prevalence of type 1 diabetes mellitus in children in the Netherlands during the period 2009 to 2011 and to compare these with earlier reports on the rising incidence of type 1 diabetes mellitus between 1978 and 1999 (19-23).

MATERIAL AND METHODS

Study design
This was a retrospective cohort study covering a 3-year period from 2009 to 2011. This study forms part of the Young DUDEs initiative, with DUDEs standing for DUtch Diabetes Estimates. In the Netherlands, all children with type 1 diabetes mellitus are treated by hospital-based paediatricians. During the time period 2009-2011, reimbursement of hospital care was exclusively claimed using the Diagnose-Behandel Combinatie (DBC) code - Dutch for diagnosis treatment combination - that physicians are required to record for reimbursement purposes.
Each DBC code contains information about the specialism of the treating physician, the patient’s diagnosis and the type of treatment provided. All DBC codes are stored in a national database, managed by Vektis (Vektis, Zeist, the Netherlands). Vektis also manages other databases, such as the Basic Health Insurance Information System, containing demographic information, such as date of birth and sex, for all children registered as inhabitants in the Netherlands. The coverage of this system is 98%, as previously described in a study in type 2 diabetes mellitus (24).

Claims records for pharmaceutical care were derived from the Pharmacy Information System, which had 99% coverage in 2010 (24). It contains information on the date the drug was supplied, who prescribed the drug, the specific drug that was supplied, including the Anatomical Therapeutic Chemical (ATC) code and the quantity supplied. Because all healthcare system records, including the Pharmacy Information System, use the same unique identifying number for each patient, the Citizen Service Number, it is possible to link all claims for any individual together and thereby track each individual through all domains of healthcare and over time (25).

Before being made available for research, all claims and personal data were stripped of their identifying characteristics to ensure anonymity: the Citizen Service Number was encrypted, the date of birth was converted into the person’s age and the postcode was recoded to limit its identifying properties to an estate/neighbourhood level. Under Dutch law, retrospective studies using anonymised database are exempt from ethical review.

Patients
Children aged 14 years or younger on the first of July were selected for every single year in the period 2009 to 2011. In this group, individuals with at least one DBC claim for diabetes with a paediatrics code (0316) and diabetes diagnosis code (7104) or an internal medicine code (0313) and a diabetes diagnosis code (221, 222 or 223) were selected. Patients were also classified as having type 1 diabetes mellitus if pharmaceutical claims showed they were issued with prescriptions and picked up insulin in at least 2 years, including 2008. Patients with a diagnosis code of diabetes were excluded from further analysis if there was no records of diabetes medication. To avoid including children treated with insulin for temporary hyperglycaemia, especially neonates, we only included children that had at least 2 years of pharmaceutical claims for insulin.

Children were classified into three age categories under - 5 years, 5-9 years and 10-14 years – and into boys and girls. They were then compared to population statistics obtained from the Central Bureau of Statistics covering the Netherlands.

Statistical analysis
Incidences and prevalences were calculated as percentages or as the number of cases per 100 000 and 95% confidence intervals (CI) were computed using the Byar method (26).
The incidence of type 1 diabetes mellitus is still increasing in the Netherlands

RESULTS

The changes in the prevalence of children with type 1 diabetes mellitus in the Netherlands from 2009 to 2011 are presented in Table 1.

Table 1. The prevalence from 2009 to 2011 in the Netherlands

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of children with T1DM (0-14 years)</th>
<th>Total number of children (0-14 years) in the Netherlands</th>
<th>Prevalence per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
<td>Girls</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>4232</td>
<td>2166</td>
<td>2,923,058</td>
</tr>
<tr>
<td>2010</td>
<td>4101</td>
<td>2116</td>
<td>2,912,911</td>
</tr>
<tr>
<td>2011</td>
<td>4226</td>
<td>2143</td>
<td>2,907,075</td>
</tr>
</tbody>
</table>

There was no consistent trend in overall type 1 diabetes mellitus prevalence during this time period. There were no significant differences in prevalence between boys (143.6, 95% CI 140.1-147.2) and girls (143.7, 95% CI 140.1-147.3). The estimated prevalence in earlier studies were 70 per 100 000 in 1978-1980 (19) and 80 per 100 000 (95%CI 0.77-0.83) in 1996 (HM Reeser, thesis 1998).

The annual incidence of type 1 diabetes mellitus in children of 14 years of age or younger in the Netherlands was calculated for 2010 and 2011 (Table 2).

Table 2. Incidence (95%CI) of T1DM in the Netherlands

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>0-4 years</td>
<td>6.8 (6.6-7.1)</td>
<td>6.4 (6.2-6.7)</td>
<td>12.9 (12.0-13.9)</td>
<td>12.4 (10.9-14.1)</td>
</tr>
<tr>
<td></td>
<td>13.0 (12.0-13.7)</td>
<td>19.3 (18.0-20.7)</td>
<td>23.6 (21.5-25.8)</td>
<td>22.1 (19.3-25.2)</td>
</tr>
<tr>
<td></td>
<td>23.8 (24.0-30.5)</td>
<td>27.6 (25.3-30.0)</td>
<td>27.1 (24.0-30.5)</td>
<td>25.0 (22.0-28.4)</td>
</tr>
<tr>
<td>Total (0-14 years)</td>
<td>11.1 (10.5-11.7)</td>
<td>12.4 (12.0-12.8)</td>
<td>21.4 (20.2-22.6)</td>
<td>20.8 (19.2-22.5)</td>
</tr>
</tbody>
</table>

We identified 1243 newly diagnosed children from birth to 14 years of age with type 1 diabetes mellitus in the Netherlands in 2010 and 2011, comprising 618 boys and 627 girls. In 2010-2011, the incidence of type 1 diabetes mellitus in the youngest age group, under 5 years of age, was comparable to the rate during the period 1996-1999, which was double the rate in 1978-1990. In the other age groups, however, the rising trend of incidence of type 1 diabetes mellitus observed in earlier studies continued through 2010-2011 to a similar degree in 5 to 9 year olds and 10 to 14 year olds. There were no significant incidence differences between the sexes, although the boy girl ratio increased slightly from 1.00 in 1988-1990, to 1.07 in 1996-1999 and 1.09 in 2009-2011.
DISCUSSION

This study shows that the incidence of type 1 diabetes mellitus in children in the Netherlands has increased steadily by an average of 2.1% per year since 1978-1980, particularly in children aged from 5 to 14 years of age. This accumulates to an overall current type 1 diabetes mellitus prevalence of 0.144% or one child with type 1 diabetes mellitus in every 699 children. The increase in incidence in children under the age of 5 years, which was observed in previous national surveys in our country, appears to have halted, although the number of cases might be too small in this age group to allow definitive conclusions. This could also be due to the fact that, as in other European countries, increases of the incidence of type 1 diabetes mellitus is not uniform, showing periods of less rapid and more rapid increases in incidence in some registers (15). This pattern of change suggests that important risk exposures differ over time in different European countries.

Although there is an overall worldwide increase in the incidence of type 1 diabetes mellitus in children, the size of this increase differs considerably between countries and between age groups. In Finland, the country with the highest incidence worldwide, the largest increase in incidence has been found in the youngest age group, of birth to 4 years, with 4.7% more affected children every year (13). Similarly, the increase in incidence was also largest in the youngest children in the EURODIAB and DIAMOND studies (6,8,15). The EURODIAB study found an overall estimated annual incidence increase of 3.9%, with the highest incidence rise in children under 5 years of age (5.4%) (15). In contrast, in New Zealand, the greatest increase of incidence was observed in children aged 10-14 years and the increase was lowest in the children aged under 5 years (27). This is in agreement with the changes in incidence observed in the Netherlands (23).

In the Netherlands, children with type 1 diabetes mellitus are solely treated by paediatricians and in rare cases by internists. Reimbursement to medical specialists for diabetes care in the Netherlands is exclusively linked to the DBC system. As a result, the number of patients with type 1 diabetes mellitus missed in this nationwide study is expected to be very small and the number of children with type 2 diabetes mellitus in this cohort will probably be very small.

However, a limitation of our study remains that some cases of type 2 diabetes mellitus may have been incorrectly classified as type 1 diabetes mellitus, if these patients were only treated with insulin for at least 1 year.

We used both a medication database and a diagnosis registration database, and a previous study has shown almost 100% coverage for both systems (24). The number of patients included in this study solely on the basis of insulin use, and not on the diagnosis registration, database comprised 109 children (2.3%), which confirms good registration by paediatricians and that very few children with type 1 diabetes mellitus in the Netherlands were missed. If a child was not included because of a DBC and received insulin for the first time in 2011, they were not included in 2011, which means that a small number of patients could have been missed.
CONCLUSION

We conclude that the incidence of type 1 diabetes mellitus in children in the Netherlands continues to increase, particularly in 5 to 14 year old children, but the incidence in children under the age of 5 years appears to have stabilised.
REFERENCES


The incidence of type 1 diabetes mellitus is still increasing in the Netherlands


