REVIEW


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Abstract

Background: A sudden rise in the incidence of childhood diabetes (DM 1) in Central and Eastern Europe over the last decade has been reported.

Aim: To compare in Slovakia incidence trends in the 80s with those in the 90s.

Subjects and methods: The data from the Slovak Register of Diabetic Children diagnosed in 1985–2000 (n=1818) were divided into 6 groups according to sex and age at diagnosis (0–4, 5–9, 10–14). Trends were computed separately for 1985–1990 and 1990–2000. The 95% confidence estimates of linear regression coefficients and as percentages from the estimated starting values in 1985 and 1990, were calculated by the linear regression based on statistical inferential approach.

Results: Non-significant increasing or decreasing trends were found in 6 gender/age groups 1985–1990. In the 90s, however, significantly increasing trends were present in each of 6 groups. They were significant (p<0.05) in the male groups and in the total of all cases. The overall incidence rise (+0.03 cases per 100 000 children per year) was nonsignificant in the 80s but significant in the 90s (+0.63/100 000/year). As a result, the incidence rate of childhood diabetes in Slovakia rose from 6.01 new cases per 100 000 children per one year in 1985 to 13.53/100 000/year in 2000.

Conclusion: The overall DM 1 incidence increased from the 1980s (80s) to the 1990s (90s), expressed in the number of new cases, is more than a 20-fold absolutely and almost 10-fold in relative terms. This was not due to an improvement in diagnosis in 1990s. Both the gender and age heterogeneity were present. (Tab. 2, Fig. 2, Ref. 25.)

Key words: children, type 1 diabetes mellitus, incidence rate, secular trends, gender/age groups.

Temporal clustering in the incidence rate of childhood diabetes mellitus 1 has attracted scientific interest worldwide (1–6). There is the possibility of understanding deeper the pathogenetic mechanisms of the disease by identification of environmental factors having a time course parallel to that of the observed incidence. Consequently, clues for more effective prevention could be found. A major increase in the childhood diabetes incidence in the USA from an average of 14.4/100 000/year during 1980–1984 to 18.1/100 000/year during 1985–1989 has been reported (11).

The temporal clustering may be as important as the geographic clustering (8). The differences in the incidence rate are most pronounced in Europe, with the highest values (45.00 new cases per 100 000 per one year) in Finland (9) and with the lowest (2.45/100 000/year) in Macedonia (10).

The aim of the present paper is to analyze the trends in the incidence rates of childhood diabetes in Slovak children separately for the years 1985–1990 and 1990–2000. Attention will be paid also to possible differences according to the gender and age of the children.

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Acknowledgements: We thank for the support of Eurodiab (European Union Contract BMHI-CT92-043, associated agreement CIPDCT 93-0136), for the grants KLV 57/97 of the Ministry of Health of the Slovak Republic, 04.92.31.01 of the Institute of Preventive and Clinical Medicine and the Slovak Diabetological Association. Our thanks are due the members of the Slovak Childhood Diabetes Epidemiology Study Group. Also the skilled technical assistance of D. Spacova and D. Vojackova is gratefully acknowledged.
Patients and methods

Subjects

The incidence data, given as the annual number of all newly diagnosed childhood diabetes cases in Slovakia, were taken from the “Slovak National Register of Childhood Diabetes” 1985–2000. (Tab. 1). A prospective registration of newly diagnosed type 1 diabetic patients by the “Slovak Diabetes Registry” was based on a nationwide voluntary reporting in special questionnaires by pediatricians and endocrinologists from outpatient departments. The second source of information were notifications from hospitals, where all children with newly diagnosed diabetes mellitus were sent for initial therapy. Both questionnaires with the given data were stored separately in two auxiliary registers and were regularly brought into conformity and statistically processed for each year for the resulting ascertainment rate. The updated population data were obtained every year from the Slovak National Institute for Statistics. The increasing incidence of DM 1 between 1990–2000 was documented also by the lay organization “The Slovak Diabetes Association”. The patients manifested since 1989 are included in the WHO DiaMond Project files and in the EURODIAB ACE Incidence Study (3, 4). Both studies employed a standard methodology for the incidence registries. To evaluate the DM 1 incidence rate in Slovakia we have proceeded according to the “Methods of Operation” of the World Health Organization’s Multinational Project (7).


<table>
<thead>
<tr>
<th>Years</th>
<th>Annual incidence rates/100 000</th>
<th>95 % confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–4</td>
<td>5–9</td>
</tr>
<tr>
<td>1985</td>
<td>2.89</td>
<td>7.73</td>
</tr>
<tr>
<td>1986</td>
<td>2.47</td>
<td>7.16</td>
</tr>
<tr>
<td>1987</td>
<td>3.88</td>
<td>6.61</td>
</tr>
<tr>
<td>1988</td>
<td>2.32</td>
<td>6.46</td>
</tr>
<tr>
<td>1989</td>
<td>3.09</td>
<td>7.92</td>
</tr>
<tr>
<td>1990</td>
<td>2.91</td>
<td>5.13</td>
</tr>
<tr>
<td>1991</td>
<td>6.54</td>
<td>8.85</td>
</tr>
<tr>
<td>1992</td>
<td>6.54</td>
<td>10.65</td>
</tr>
<tr>
<td>1994</td>
<td>8.86</td>
<td>7.92</td>
</tr>
<tr>
<td>1996</td>
<td>5.57</td>
<td>10.80</td>
</tr>
<tr>
<td>1997</td>
<td>9.54</td>
<td>14.08</td>
</tr>
<tr>
<td>1999</td>
<td>11.45</td>
<td>16.10</td>
</tr>
<tr>
<td>2000</td>
<td>9.77</td>
<td>12.08</td>
</tr>
</tbody>
</table>

Tab. 2. Trend evolution of diabetes type 1 incidence.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (years)</th>
<th>1985–1990</th>
<th>1990–2000</th>
<th>Trend difference (95 %CI) (cases/100 000/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>100b/a</td>
<td>b</td>
<td>100b/a</td>
</tr>
<tr>
<td>Male</td>
<td>0–4</td>
<td>+0.30</td>
<td>+15%</td>
<td>+0.66** +13%*</td>
</tr>
<tr>
<td></td>
<td>5–9</td>
<td>-0.19</td>
<td>-3%</td>
<td>+0.76** +12%**</td>
</tr>
<tr>
<td></td>
<td>10–14</td>
<td>+0.42</td>
<td>+5%</td>
<td>+0.86** +10%**</td>
</tr>
<tr>
<td>Female</td>
<td>0–4</td>
<td>-0.29</td>
<td>-7%</td>
<td>+0.29 +5%</td>
</tr>
<tr>
<td></td>
<td>5–9</td>
<td>-0.43</td>
<td>-5%</td>
<td>+0.60 +7%</td>
</tr>
<tr>
<td></td>
<td>10–14</td>
<td>+0.14</td>
<td>+2%</td>
<td>+0.41 +4%</td>
</tr>
<tr>
<td>Total</td>
<td>0–14</td>
<td>+0.03</td>
<td>+1%</td>
<td>+0.63*** +9%***</td>
</tr>
</tbody>
</table>

Linear regression coefficient = b (cases per 100 000 children per one year), intercept = a (estimated starting value of cases/100 000/year for 1985 and 1990, respectively), estimated % change = 100b/a. * p<0.05; ** p<0.01; *** p<0.001.
Fig. 1. Incidence rates (cases per 100 000 children per year) of diabetes mellitus type 1, in 0–4 (a), 5–9 (b) and 10–14 (c) old Slovak boys (empty bars) and girls (lined bars) during 16 years in Slovakia.

Registrations network
A total of 1818 children were included into the study. The gender–age–specified incidence is reported in 6 groups: 196 boys and 166 girls aged 0–4 years, 307 boys and 327 girls aged 5–9 years, and 421 boys and 401 girls aged 10–14 years (Fig. 1). The number of incident cases diagnosed, their gender and mean age at onset by gender are presented in Table 1. The incidence rates with confidence intervals for each year are presented in Table 1. The overall ascertainment rate was 99–100 %.

Statistical analysis
Linear regression analysis was used for evaluating the trends in the 6 groups as well as in the total of all cases, separately for the 80s (1985–1990) and the 90s (1990–2000). The chosen approximating function is $y = a + b.t$, where $y$ is the estimated incidence rate in cases per 100 000 per year, $t$ the time in years, and $a$ and $b$ are the regression coefficients. The $a$ is an estimate of the starting $y$ value for the time 0, i.e. in 1985 or 1990, and the $b$ is an estimate of the change of the number of cases per 100 000 children per year. Thus, the ratio $100b/a$ (%) shows the increase of the incidence rate per year, related to its starting value. Also the difference $b(90)−b(80)$, i.e. that between the $b$ estimate in the 90s and the 80s, was evaluated. All resulting parameters and graphs of the functions were accompanied by their 95% confidence intervals. The level of statistical significance was set at alpha=0.05.

Results
The outcome of the regression analysis for all 12 gender–age–years’ interval–specified groups, as well as for the total, is in Table 2 together with the trend differences. Figure 2 displays the regression approximation for all children.

The most striking differences were those between the nineties and the eighties. A nonsignificant negligible increase in the 80s is followed by significant, more than 20-times higher absolute increase (in cases per 100 000 per year) and almost 10-fold relative increase (in percentages) in the 90s. The overall incidence rise (+0.03 cases per 100 000 children per year) was nonsignificant in the 80s but significant in the 90s (+0.63 /100 000/ year). This difference (+0.60; with 95% confidence interval between +0.12 and +1.08) is highly significant ($p=0.01$).

The gender differences are remarkable in the 90s. Both the absolute and relative increases are higher and significant only in boys.

The age heterogeneity is less pronounced. The acceleration in the 90s versus the 80s was maximal and significant only in both – male and female – aged (5–9 years) groups.

As the result of the described trend evolution, the overall incidence rate of childhood diabetes in Slovakia rose more than twice – from 6.01 per 100 000 children per year in 1985 up to 13.53/100 000/year in 2000. The incidence increase from 6.01 to 13.53 per 100 000 children – corresponds with a mean annual increment of 6.1% of the 1985 value.
Discussion

Slovak Republic is a country in the Central Europe, with an area of 49 thousand square km, population around 5.5 million inhabitants, including 1.16 million children aged 0–14 years. The resulting population density is approximately 110 inhabitants (24 children) per square km.

The mean level of the standardized Slovak childhood diabetes incidence rate, for the years 89–98, was 9.18 per 100 000 per year, with the 95% confidence interval between 8.66 and 9.12. This compares well with similar values in the surrounding countries: 9.58 in the Czech Republic (12), 9.44 in Hungary (13, 14), 6.96 in Poland (15) and 9.41 in Austria (16, 17). The present incidence is at an intermediate level, compared to other Europe (6).

The male predominance in the youngest (0–4 years aged) groups has been reported in the Oxford region of UK (18) and in Germany (19). According to Karvonen et al (20), the sex ratio in the incidence of childhood diabetes was moved in parallel with the increasing incidence from a female excess towards a male excess. Such an evolution is indicated in our results, too.

In Slovakia, a percentage increase of the incidence rates in children of all ages was recognized as early as 1991–1992 (21). The present confirmation confirms this trend for the time interval extended by years. This acceleration within a relatively short time interval is statistically significant and substantial. The difference in the incidence trends between 1980s and 1990s cannot be explained as an artifact due to an incomplete ascertainment during the 1980s. The total estimated ascertainment was very high each year during the whole period of observation. Attaining high ascertainment is easier in countries with centralized health care system, as is in Slovakia. The present paper is one of a few whole country childhood diabetes studies.

This steep rise could result from an overall rise in more risk factors over time (22, 23). Dramatic socio-economic changes happened in this country in the year 1989. A critical time period appears to be around 1990–1993 when a remarkable peak in the numbers of births of boys, later developing diabetes, was encountered (24). Coincidence changes in the living conditions since 1989 and more than a sixfold incidence increase within a 10-year-period could be regarded as substantial influence of environmental factors in the development of DM 1.

Similar incidence booms have been found in the Czech Republic (10), Poland (13) Slovenia (23), Italy (24) and Switzerland (25). These findings testify indirectly to the important impact of social and natural environment, on the process of development of diabetes type 1 in genetically predisposed children.

Members of the Slovak Childhood Diabetes Epidemiology Study Group: E. Burák (Bratislava), M. Bašťriaková (Košice), A. Čáradská (Topoľčany), M. Debreová (Poprad), K. Hálová (Trnava), E. Hunák (Nitra), E. Jančová (Bratislava), J. Javorcová (Martin), V. Karvaj (Nové Zámky), M. Kecesofová (Dolný Kubín), M. Kúseková (Košice), M. Lukačovič (Čadca), J. Marčok (Trencín), V. Máťková (Rimavská Sobota), D. Michalková (Bratislava), M. Pašková (Košice), G. Nagyová (Spišská Nová Ves), S. Niňajová (Bratislava), M. Rejková (Galanta), D. Reptišová (Prešov), V. Šajdíková (Považská Bystrica), A. Šarišská (Humenné), Z. Šimeková (Žilina), E. Špánitová (Levice), E. Trézová (Košice), B. Milosovičová, J. Strnáová (Bratislava).

References

15. Jarosz-Chobot P, Otto-Buczkowska E, Koehler B, Maklakiewicz E, Green A. The recent trend in the incidence of type 1 diabetes in


Received November 15, 2002.
Accepted December 9, 2002.