Incidence of Type 1 Diabetes in Lithuanians Aged 0–39 Years Varies by the Urban-Rural Setting, and the Time Change Differs for Men and Women During 1991–2000

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OBJECTIVE — Type 1 diabetes has been associated with factors related to welfare and social class. During the past decade, Lithuania has experienced a transition period, leading to dramatic changes in the socioeconomic structure of the society.

RESEARCH DESIGN AND METHODS — Incidence in the group aged 0–39 years by urban-rural setting (cities >100,000 inhabitants, towns, and rural areas), period (1991–1995 and 1996–2000), age, and sex were studied using Poisson regression.

RESULTS — The age- and sex-standardized incidence per 100,000 inhabitants per year was higher in men aged 0–39 years than in women (9.5 and 6.9, respectively, incidence rate ratio [IRR] = 1.39, P < 0.001). Incidence was lower in rural areas than in towns and cities (7.1, 9.0, and 8.8, respectively, P < 0.001). The urban-rural differences in incidence were most marked among children aged 0–9 years. From 1991–1995 to 1996–2000, the overall incidence increased from 8.7 to 10.5 (IRR = 1.22, P = 0.001) in men and from 6.2 to 7.8 (IRR = 1.25, P = 0.002) in women. For men, the incidence over time occurred predominantly in the cities, from 8.4 to 11.8 (IRR = 1.40, P < 0.001), and in the older age-groups. In contrast, for women, the incidence increased more in small towns and rural areas, from 5.8 to 7.7 (IRR = 1.33, P = 0.003), and in the younger age-groups.

CONCLUSIONS — The incidence of type 1 diabetes in Lithuania differs depending on the urban-rural setting, and the pattern of change over time differs between the sexes, both by urban-rural setting and age-group. The findings support the theory that lifestyle-related factors connected to socioeconomic status are important for the occurrence of type 1 diabetes.

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in Lithuania; 68% lived in urban areas and 41% lived in the five largest cities with >100,000 inhabitants.

In Lithuania, health care is provided on a territorial-administrative basis. At the time of diabetes diagnosis, all children (aged 0–15 years) and most of the adult people with suspected type 1 diabetes are initially treated in hospitals. Regional pediatric endocrinologists situated in the five largest cities provide outpatient diabetes care for children living in the towns and rural areas of the respective region. In the five cities, adult patients with diabetes are followed-up by endocrinologists from district polyclinics or specialized diabetes centers. In the towns and rural areas, endocrinologists (in three regions specialists of internal diseases) from the consulting polyclinics, situated in the administrative centers of the 44 administrative regions, provide outpatient diabetes care. Insulin is free of charge for diabetic patients.

The Lithuanian Childhood Diabetes Register (group aged 0–14 years)

Since 1 January 1983, children diagnosed with type 1 diabetes before their fifteenth birthday and permanently residing in Lithuania have been prospectively registered. Details of the case ascertainment were previously described (15). In short, until August 1989, quarterly reports prepared by five regional pediatric endocrinologists were used as the primary and yearly reports from the Ministry of Health of Lithuania as the secondary data source. The secondary source was, however, not fully independent. In August 1989, a Department of Childhood Endocrinology was established at the Kaunas University of Medicine. Since then, the majority of newly diagnosed cases of childhood diabetes from the entire country are referred to this department for initial treatment and constitute the primary data source of the register. Yearly reports of the regional pediatric endocrinologists are considered as the secondary data source. Due to the strict organization of care for children with diabetes in Lithuania, it is unlikely that cases are missing from the secondary data source; thus, the ascertainment is estimated at 100% (2). During the 10-year period (1991 through 2000), 312 boys and 338 girls aged <15 years at diabetes diagnosis were registered.

The register of type 1 diabetes in adults (group aged 15–39 years)

Since 1 January 1991, patients diagnosed with type 1 diabetes between 15 and 39 years of age and permanently residing in Lithuania have been prospectively registered. All physicians responsible for outpatient care of people with diabetes from territorial health care units throughout the country (n = 106) report new cases with type 1 diabetes to the register center on a special form that is deemed mandatory by the Lithuanian Ministry of Health “Report About Persons with Newly Diagnosed Diabetes Mellitus”. Information, including personal identification code, name, date of birth, sex, address, date of clinical diagnosis, date of first insulin injection, date of reporting, reporting unit and physician, and some clinical characteristics (ketonuria and/or acidosis, blood glucose value at the time of diagnosis), is registered for every patient. Diabetes was diagnosed and classified according to clinical criteria as recommended by the World Health Organization (16) and as was previously described in detail (17). Only those cases where insulin therapy was initiated at or within 2 weeks of diagnosis, and lasted for at least several months, were regarded as having type 1 diabetes and included in the register. For most cases, the delay between the diagnosis of diabetes and initiation of insulin treatment was only a few days. The date of first insulin injection was used as date of diagnosis in the analyses.

In the beginning of the year, every reporting physician is asked to complete three lists and return them to the register center: 1) list of follow-up of all insulin-treated diabetic patients; 2) list of newly insulin-treated diabetic patients (diagnosed during the previous year); and 3) list of insulin-treated diabetic patients removed from the follow-up. New cases reported throughout the year are then checked against the lists to verify that they are still treated with insulin and to find the cases that were missed. These lists are considered the secondary source of ascertainment together with records of the causes of death from the Lithuanian Department of Statistics (including death certificates) and membership lists from the Diabetes Societies. The overall completeness of case ascertainment was estimated at 91.2% during 1991–1997 (17). During the 10-year period (1991 through 2000), 760 male and 410 female patients with newly diagnosed type 1 diabetes were recorded in the group aged 15–39 years in Lithuania.

Statistical methods

Population denominators for calculating incidence rates were obtained from the Lithuanian Department of Statistics. Population of relevant age at the end of the calendar year was used for calculating the incidence rate. For the comparison of incidence rates by the urban-rural setting, we used the classification of the Lithuanian Department of Statistics, which is based on Lithuanian legislation, defining towns as “compactly built-up territories having at least 3,000 inhabitants with more than 2/3 of them employed in non-agricultural occupations.” According to this definition, there were 114 towns in 1991 and 106 in 2000 in Lithuania (the number of towns changed due to administrative reform). Direct age standardization of the incidence rates was performed assuming a standard population with equally sized 5-year age-groups of both sexes. Poisson regression analysis was performed using Egret for Windows (Cytech, Cambridge, MA). Age was categorized according to Poisson regression analysis was performed using Egret for Windows (Cytech, Cambridge, MA). Age was categorized according to World Health Organization (16) and as was previously described in detail (17). Only those cases where insulin therapy was initiated at or within 2 weeks of diagnosis, and lasted for at least several months, were regarded as having type 1 diabetes and included in the register. For most cases, the delay between the diagnosis of diabetes and initiation of insulin treatment was only a few days. The date of first insulin injection was used as date of diagnosis in the analyses.

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RESULTS

Incidence according to age and sex

The average age-standardized incidence during 1991–2000 was higher in 0- to 39-year-old Lithuanian men than in women (9.5 and 6.9/100,000 inhabitants/year, respectively, incidence rate ratio [IRR] = 1.39, P < 0.001). The age distribution of the incidence for men and women during the 10-year period is presented in Fig. 1. The highest incidence was reached at the age of 9–13 years for the girls and at 11–14 years for the boys. After the peak, the incidence decreased to a similar level in men and women aged 16–18 years, but during the third and fourth decade of life, it started increasing again for the men. The incidence did not differ between boys and girls aged 0–4
years, but it was higher for girls aged 5–9 years (male/female IRR = 0.60, \( P < 0.001 \)). There was no difference in incidence between the sexes at the ages of 10–14 and 15–19 years, while at older ages, the incidence in men was increasingly higher than in women (1.50 [\( P = 0.004 \)] and 2.73 [\( P < 0.001 \)] times higher at the ages of 20–24 and 35–39 years, respectively).

Incidence according to age, sex, and period
Compared with 1991–1995, the incidence of type 1 diabetes was higher during 1996–2000 for people aged 0–39 years at diabetes diagnosis. The age-standardized incidence per 100,000 inhabitants per year increased from 8.7 to 10.5 for the men (IRR = 1.22, \( P = 0.001 \)) and from 6.2 to 7.8 for the women (IRR = 1.25, \( P = 0.002 \)). Figure 2 shows the agespecific incidence rates during the two 5-year periods, presented as 3-year moving averages. During the second time period, the incidence tended to be higher for the men aged 10–19, 20–29, and 30–39 years, but only the latter difference was statistically significant (10.7 vs. 13.6, \( P = 0.03 \)). In contrast, for the women, the incidence was higher in the groups aged 0–9 (6.1 and 8.5, \( P = 0.03 \)) and 10–19 years (8.2 and 11.2, \( P = 0.01 \)), but no differences were found at older ages.

Incidence according to age, sex, and urban-rural setting
In Lithuania, the incidence of type 1 diabetes differed depending on the urban-rural setting. The overall age- and sex-standardized incidence in the group aged 0–39 years was lower in the rural areas than in small towns and cities (7.1, 9.0, and 8.8/100,000 inhabitants/year, respectively). Compared with the rural areas, the incidence was 1.22 (\( P < 0.001 \)) times higher in the cities and 1.27 (\( P < 0.001 \)) times higher in small towns.

The age distribution of the incidence according to the urban-rural setting is presented in Table 1. The urban-rural gradient of incidence was most evident in the younger age-groups.

Incidence according to age, sex, urban-rural setting, and period
When comparing the incidence in the group aged 0–39 years during the two 5-year periods, we found a different pattern of change in men and women according to both the urban-rural setting and age. For the men, the incidence per 100,000 inhabitants per year increased predominantly in the cities, from 8.4 to 11.8 (IRR = 1.40, \( P < 0.001 \)), and mainly in the groups aged 10–19 and 20–29 years, from 8.9 to 13.7 (IRR = 1.53, \( P = 0.02 \)) and 7.5 to 11.5 (IRR = 1.53, \( P = 0.02 \)), respectively. On the contrary, for the women, the increase mainly occurred in small towns and rural areas, from 5.8 to 7.7 (IRR = 1.33, \( P = 0.003 \)), and in the groups aged 0–9 and 10–19 years, from 5.0 to 8.4 (IRR = 1.68, \( P = 0.01 \)) and 7.0 to 11.0 (IRR = 1.59, \( P = 0.01 \)), respectively.

CONCLUSIONS — In Lithuania, the incidence of type 1 diabetes in the group aged 0–39 years differed by the urban-rural setting: the incidence was lower in the rural areas than in small towns and cities. The urban-rural gradient of incidence was most evident in the younger children. During the 10-year period, the incidence increased for both men and women but the pattern of change over time differed between the sexes both by the urban-rural setting and age-group.

If type 1 diabetes is a wealth-related disease, as suggested by associations with indicators of wealth (10,11), the urban-rural differences of diabetes incidence might at least partly be a reflection of differential distribution of socioeconomic deprivation in urban and rural areas (6,7,9). Interestingly, in Lithuania the observed urban-rural gradient of type 1 diabetes incidence during the 1990s paralleled the urban-rural differences of the poverty distribution. According to a report prepared by a United Nations Development Programme team (18), 26–28% of people in rural areas, 15–14% in small towns, and 10–7% in cities during 1997–1999 were reported to live below the relative poverty line, defined as consumer expenditure per household member below 50% of the countries average. The Human Development Report (19) estimated that >20% of the preschool children and 31% of the children <18 years of age in Lithuania were below the relative poverty line in 2000.

In our study, the urban-rural gradient of diabetes incidence was most evident in the younger children. Similar findings were reported from Montreal (9) and Turin (4), although in Wisconsin (3), the urban-rural differences were slightly more pronounced in the group aged 15–29 years.

It is unclear which lifestyle-associated factors may be responsible for the observed urban-rural differences of type 1 diabetes in Lithuania. Overweight and low rate of physical activity are known risk factors for type 2 diabetes, but increased insulin demand due to insulin
resistance may also accelerate β-cell damage, leading to an increased risk or earlier onset of type 1 diabetes (20–22). Increased linear growth rate, weight gain, and higher BMI throughout childhood, perhaps especially during the first 3 years of life, are risk factors for the development of diabetes (23–26). In children, overnutrition leads to both accelerated growth and overweight associated with higher insulin demand through two mechanisms: growth hormone decreases tissue sensitivity to insulin and fat accumulation adds to insulin resistance. In adults, overnutrition leads to fat accumulation only. One might speculate that a smaller proportion of children in the poorer rural areas in Lithuania are overnourished and rural children probably are more physically active, which also leads to less insulin resistance.

Different patterns of incidence change over time between the sexes indicate either different lifestyle-related risk factors or their different distribution between men and women. In a national sample investigated in 1997, the prevalence of obesity among 20- to 34-year-old Lithuanians was 6% for both sexes but the prevalence of overweight was higher in men than in women, 34 and 19%, respectively, while 8% of women but no men were underweight (27). Thus, these differences in the prevalence of overweight are consistent with our findings of a greater increase of diabetes incidence in men compared with women in the corresponding age-groups.

Figure 2—Incidence of type 1 diabetes per 100,000 inhabitants per year in 0- to 39-year-old Lithuanian men (A) and women (B) during 1991–1995 and 1996–2000, presented as 3-year moving averages.

Contrary to our findings, a rising incidence trend was observed in rural but not urban areas in the group aged 0–29 years in the Białystok region of northeast Poland for 1994–1998 and mainly in the 5- to 14-year-old age-group (28). However, this study used another definition of the urban-rural areas and did not analyze the changes by sex due to the small size of the study (277 cases).

There are some methodological issues important for the interpretation of our results. The level of ascertainment of the two diabetes registers differs; it is estimated to be 100% in the childhood diabetes register (2) and 91% in the adult diabetes register (17). Moreover, during the last 3 years of the study, the number of physicians involved in the care of adult people with diabetes increased due to health care reform in Lithuania. Another issue is the difficulty of correctly distinguishing diabetes types from the clinical impression at the time of diagnosis in the older age-groups, as the proportion of cases with type 2 diabetes increases with age (29,30), and 20–35% of type 2 diabetes cases in the group aged 25–34 years may have latent autoimmune diabetes (31). No antibody testing or C-peptide measurements have been performed in Lithuania. However, a study that used similar clinical classification criteria of diabetes in the group aged 15–34 years found that only 3% of cases treated with insulin since the diagnosis were not on insulin 2.5–3 years later (29). These possible shortcomings might somewhat affect our results of incidence variability by age, as well as the incidence differences by
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References

Table 1 — Number of cases and incidence of type 1 diabetes per 100,000 inhabitants per year in 10-year age-groups according to the urban-rural setting (cities >100,000 inhabitants, small towns, and rural areas) in 0- to 39-year-old Lithuanian males and females during 1991–2000

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Five cities</th>
<th>Towns</th>
<th>Rural areas</th>
<th>IRR (95% CI)</th>
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<tr>
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<td></td>
<td>Case (n)</td>
<td>Incidence</td>
<td>Case (n)</td>
<td>Incidence</td>
</tr>
<tr>
<td>Males</td>
<td>0–9</td>
<td>81</td>
<td>8.5</td>
<td>37</td>
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<td>10–19</td>
<td>121</td>
<td>11.3</td>
<td>82</td>
<td>9.7</td>
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<tr>
<td></td>
<td>20–29</td>
<td>115</td>
<td>9.4</td>
<td>89</td>
<td>11.8</td>
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<tr>
<td></td>
<td>30–39</td>
<td>131</td>
<td>11.0</td>
<td>139</td>
<td>16.8</td>
</tr>
<tr>
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<td>0–39</td>
<td>453</td>
<td>10.1</td>
<td>347</td>
<td>10.8</td>
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<tr>
<td>Females</td>
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<td>58</td>
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<tr>
<td></td>
<td>10–19</td>
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<td>10.8</td>
<td>74</td>
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<td>6.2</td>
<td>48</td>
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<tr>
<td></td>
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<td>4.6</td>
<td>52</td>
<td>5.8</td>
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<tr>
<td></td>
<td>0–39</td>
<td>321</td>
<td>7.5</td>
<td>232</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Incidence in the group aged 0–39 years is age standardized and IRR adjusted for the age distribution. IRRs are calculated using incidence in rural areas as reference.
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26. The EURODIAB Substudy 2 Study Group: Rapid early growth is associated with increased risk of childhood type 1 diabetes in various European populations. Diabetes Care 25:1755–1760, 2002


