The Incidence of Type 1 Diabetes Mellitus among 0-39-year-old Lithuanian Population Varies by Urban and Rural Settings

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Objective of work was to document the differences of incidence of Type 1 diabetes mellitus between Lithuanian 0-39-year-old urban and rural population.

Methods. A specifically developed contact system with all endocrinologists and general practitioners involved in the diabetes care covering 100% of the Lithuanian population aged 0–39 was the initial data source. Annual reports from regional endocrinologists and death certificates served as secondary independent sources for case ascertainment. Direct age-standardisation of the incidence rates was performed assuming a standard population with equally sized five-year age groups of both genders. Incidence in females in 0–4-year-age group, 1991–1995 years calendar period, and rural areas were used as reference. Poisson regression analysis was performed.

Results. The age- and gender-standardised incidence per 100,000 persons was higher in 0–39-yr old males than in females (incidence rate ratio 9.5 and 6.9, RR = 1.39, $p < 0.001$). In the rural areas the incidence was lower than in towns and cities (7.1, 9.0 and 8.8, respectively, $p < 0.001$). The urban–rural differences in the incidence were most pronounced among 0–9 yr-old children. From 1991–1995 to 1996–2000, the overall incidence increased from 8.7 to 10.5 (RR = 1.22, $p = 0.001$) in males and from 6.2 to 7.8 (RR = 1.25, $p = 0.002$) in females. For males, the increase over time occurred predominantly in the cities, 8.4 to 11.8 (RR = 1.40, $p < 0.001$), and in the older age groups. In contrast, for females the incidence was higher in small towns and rural areas, 5.8 to 7.7 (RR = 1.33, $p = 0.003$), and in the younger age groups.

Conclusion. 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 genders by both urban–rural setting and age group.

Key words: Type 1 diabetes mellitus, 0–39-year-age group, incidence by urban–rural setting, period 1991–2000), Poisson regression

INTRODUCTION

The incidence of Type 1 diabetes mellitus among 0–14-year-old children varies in different countries throughout the world (1, 2) and in Europe (3, 4), probably depending on different distribution of both genetic and environmental determinants across the populations.

In some countries the incidence is higher in more densely populated urban areas (5–7), while in others it is higher in more sparsely populated rural areas (8–10). This difference points to other socio-demographic and environmental factors that may vary between urban and rural areas in different countries (11–14). The incidence of childhood Type 1 diabetes mellitus is lower in areas where a larger proportion of the population is socio-economically deprived (9, 15). In Scotland, the incidence rates are particularly low in children living in deprived urban sectors (8). In Sweden, the incidence of childhood diabetes mellitus over time increased in pa-

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rallel with per capita gross domestic product (16). An association between childhood diabetes mellitus incidence and indicators of national prosperity was also reported across European countries (17).

During the nineties of the 20th century, the incidence of childhood Type 1 diabetes mellitus has increased in almost all regions of Europe, particularly rapidly in the former socialist countries of Central Eastern Europe (4). The change of incidence over time seemed to have opposite directions for childhood-onset and adult-onset Type 1 diabetes mellitus in two of three recent reports, including age groups above 14 years of age (18–21).

Lithuania experienced a period of economic transition, leading to dramatic changes in the socio-economic structure and life-style of society in the past decade. We studied the incidence of Type 1 diabetes mellitus among 0–39-year-old Lithuanian population during 1991–2000 according to urban–rural setting and the change of incidence over time by age groups and gender.

METHODS

By the end of the year 2000 there were 3,692,600 inhabitants in Lithuania, of them 68% lived in urban areas and 41% in five largest cities with >100,000 inhabitants. Health care is provided on territorial-administrative basis. At the time of diabetes mellitus diagnosis, all 0–14–year-aged children and most of the 15–39-year-aged adult people with suspected Type 1 diabetes mellitus are initially treated in hospitals. Five regional paediatric endocrinologists situated in the largest cities provide outpatient diabetes care for children. In the cities, adult patients with diabetes are followed-up by endocrinologists from district outpatient centres. In the towns and rural areas, endocrinologists or specialists of internal diseases from the consulting-outpatient centres situated in the administrative centres of the 44 regions provide outpatient care.

All 0–14-year-old children, permanent residents of Lithuania, with a newly diagnosed onset of Type 1 diabetes mellitus are prospectively registered since 1 January 1983. Until 1989, quarterly reports prepared by five regional paediatric endocrinologists were used as the primary and yearly reports from the Ministry of Health of Lithuania as the secondary (although not fully independent) data source. In 1989, Department of Childhood Endocrinology was established at the Hospital of Kaunas University of Medicine, and every newly diagnosed case of childhood diabetes from the whole country was referred to this department for initial treatment. Since 1990, centralised hospital records have been used as the primary and yearly reports of the regional paediatric endocrinologists as the secondary data source. Details of case ascertainment have been described previously (22). In 1989, the Lithuanian Childhood Diabetes Register joined the EURODIAB (Diabetes in Europe) Study Group and the case ascertainment from 1989 to 1998 was estimated to be 100% (3–4). The total of 312 boys and 338 girls below the age of 15 years at Type 1 diabetes mellitus diagnosis were registered during 1991–2000.

Since 1 January 1991 all permanently residing in Lithuania 15–39-year-old patients with newly diagnosed Type 1 diabetes mellitus are prospectively registered. Physicians responsible for outpatient care of people with diabetes from all territorial health care units throughout the country report new cases of Type 1 diabetes mellitus to the register centre on a special form “Report on persons with newly diagnosed diabetes mellitus” prepared in association with the Lithuanian Ministry of Health. Information including the personal identification code, name, date of birth, gender, 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 each patient. The secondary data source consists of the information extracted from special notification forms prepared at the Register centre and distributed to physicians responsible for outpatient care of people with diabetes in territorial health care units throughout the country: 1) list of follow-up of all insulin-treated diabetic patients; 2) list of new insulin-treated diabetic patients at the medical unit; 3) list of insulin-treated diabetic patients removed from the follow-up at the medical unit. At the end of each year these notification forms are filled in by the responsible physicians and returned to the Register centre. In addition, at the end of the year every reporting unit receives for revision a list of cases reported to the Register during that year. Records of the causes of death from the Lithuanian Department of Statistics (including death certificates), and membership lists from the Diabetes Societies were also reviewed for case ascertainment. Diabetes is diagnosed and classified according to clinical criteria as recommended by the WHO (23–25) and as described in detail previously (21, 26). The date of first insulin injection was used as the date of diagnosis in the analyses. The overall completeness of case ascertainment was estimated at about 91% during 1991–1998 (21). The total of 760 male and 410 female patients with newly diagnosed Type 1 diabetes mellitus were recorded during 1991–2000 in the 15–39-year age group in Lithuania.

STATISTICAL METHODS

Population denominators for calculating the 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. To compare the 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 3000 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 the administrative reform). Direct age-standardisation of the incidence rates was performed assuming a standard population with equally sized five-year age groups of both genders. Poisson regression analysis was performed using Egret for Windows (CYTEL, Cambridge, MA, USA). Age was categorised into 5-year and 10-year age groups, calendar time into two 5-year periods (1991–1995, 1996–2000) and the degree of urbanisation into three categories (cities, including 5 largest cities with >100,000 inhabitants; towns, including all other towns except 5 cities; and rural areas). Incidence in females, youngest age group, 1991–1995 calendar period, and rural areas was used as reference.

RESULTS

The average age-standardized incidence during 1991–2000 was higher in 0–39-year-old Lithuanian males than in females, 9.5 and 6.9 per 100,000, respectively, incidence rate ratio (RR) 1.39 ($p < 0.001$). The age distribution of the incidence for males and females during the 10-year period is presented in Fig. 1. The highest incidence was observed at the age of 9–13 years for girls and 11–14 years for boys. After the peak the incidence decreased to a similar level in 16–18-year-old males and females, but during the third and fourth decade of life it started increasing again for males. Table 1 shows a comparison of incidence rates between males and females in 5-year age groups.

Compared to 1996–2000, the incidence of Type 1 diabetes mellitus was lower during 1991–1995 for people aged 0–39 years at diabetes diagnosis. The age-standardized incidence per 100,000 inhabitants increased from 8.7 to 10.5 for males, RR = 1.22 ($p = 0.001$), and from 6.2 to 7.8 for females, RR = = 1.25 ($p = 0.002$). Figure 2 shows the age-specific incidence rates during two 5-year periods, presented as 3-year moving averages. During the second period the incidence tended to be higher for males aged 10–19, 20–29 and 30–39 years, but only the latter difference was statistically significant (10.7 *versus* 13.6, $p = 0.03$). In contrast, for females the incidence was higher in the 0–9 year (6.1 and 8.5,

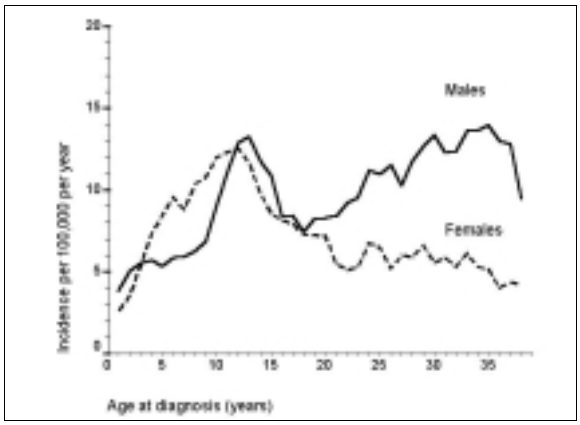

Fig. 1. Incidence of Type 1 diabetes mellitus per 100,000 persons in 0–39-year-old Lithuanian males and females during 1991–2000 presented as a 3-year moving average

Table 1. **Incidence of Type 1 diabetes mellitus per 100,000 persons among 0–39-year-old Lithuanian males and females, 1991–2000**

Age (years)	Males		Females		Male/Female ratio (95% CI)
	Cases (n)	Incidence	Cases (n)	Incidence	
0–4	54	4.6	45	4.0	1.14 (0.77–1.69)
5–9	84	5.9	133	9.8	**0.60 (0.46–0.79)**
10–14	174	12.2	160	11.7	1.05 (0.85–1.30)
15–19	110	8.2	101	7.7	1.06 (0.81–1.39)
20–24	127	9.1	82	6.1	**1.50 (1.13–1.98)**
25–29	173	11.9	82	5.9	**2.02 (1.55–2.63)**
30–34	196	13.2	87	5.9	**2.22 (1.72–2.86)**
35–39	154	11.1	58	4.1	**2.73 (2.02–3.69)**
0–39	1072	9.5	748	6.9	**1.39 (1.27–1.53)**

In the 0–39-year group the incidence is age-standardised and the incidence rate ratio adjusted for the age distribution.

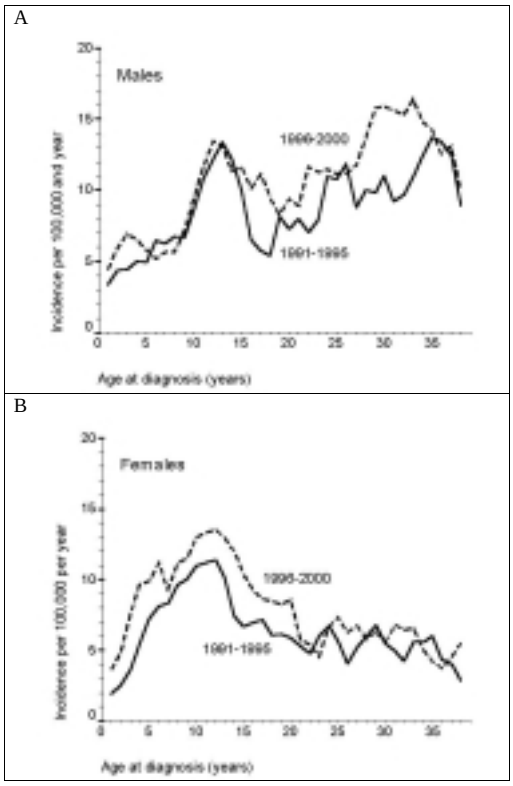

Fig 2. Incidence of Type 1 diabetes mellitus per 100,000 person years and year in 0–39-year-old Lithuanian males (A) and females (B) during 1991–1995 and 1996–2000 presented as a 3-year moving average

p = 0.03) and 10–19 year (8.2 and 11.2, p = 0.01) groups, but no differences were found in older age groups.

The incidence of Type 1 diabetes mellitus differed depending on the urban–rural setting. The overall age and gender-standardised incidence in the 0–39-year age group was lower in rural areas compared to small towns and cities, 7.1, 9.0 and 8.8 per 100,000 inhabitants, respectively. Compared to the rural areas the incidence was 1.22 (p < 0.001) times higher in 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 2. The urban–rural gradient of incidence was most evident in the younger age groups.

When comparing the incidence in the 0–39-year group during two 5-year periods, we found a different pattern of change in males and females both according to the urban–rural setting and age. For males, the incidence per 100,000 and year increased predominantly in cities, from 8.4 to 11.8 (RR = = 1.40, p < 0.001), and mainly in the 10–19- and 20–29-year age groups, from 8.9 to 13.7 (RR = = 1.53, p = 0.02), and 7.5 to 11.5 (RR = 1.53, p = = 0.02), respectively. On the contrary, for females the increase occurred mainly in small towns and rural areas from 5.8 to 7.7 (RR = 1.33, p = 0.003) and in the 0–9 and 10–19-year age groups from 5.0

Table 2. **Incidence of Type 1 diabetes mellitus per 100,000 persons according to the urban–rural setting (cities (>100,000 inhabitants), small towns, and rural areas) among 0–39-year-old Lithuanian males and females in 1991–2000**

Sex	Age (years)	5 cities		Towns		Rural areas		Cities/ rural ratio	Towns/ rural ratio
		Cases (n)	Incidence	Cases (n)	Incidence	Cases (n)	Incidence		
Males	0–9	81	8.5	37	4.8	20	2.3	**3.78 (2.32–6.17)**	**2.15 (1.25–3.70)**
	10–19	121	11.3	82	9.7	81	9.4	1.20 (0.91–1.59)	1.03 (0.76–1.40)
	20–29	115	9.4	89	11.8	96	11.1	0.84 (0.64–1.10)	1.06 (0.79–1.41)
	30–39	136	11.0	139	16.8	73	9.0	1.19 (0.89–1.57)	**1.81 (1.37–2.40)**
	0–39	453	10.1	347	10.8	270	8.0	**1.23 (1.06–1.43)**	**1.35 (1.15–1.58)**
Females	0–9	74	8.2	58	7.9	46	5.4	**1.50 (1.04–2.17)**	**1.46 (0.99–2.15)**
	10–19	114	10.8	74	9.1	73	9.0	1.20 (0.89–1.61)	1.01 (0.73–1.39)
	20–29	74	6.2	48	6.1	42	5.6	1.14 (0.78–1.67)	1.12 (0.74–1.69)
	30–39	59	4.6	52	5.8	34	4.8	0.95 (0.62–1.44)	1.21 (0.78–1.86)
	0–39	321	7.5	232	7.2	195	6.2	**1.20 (1.00–1.43)**	1.18 (0.97–1.42)

Incidence rate ratios are calculated using incidence in rural areas as reference. In the 0–39-year group the incidence is age-standardised and the incidence rate ratio adjusted for the age distribution.

to 8.4 (RR = 1.68, p = 0.01), and 7.0 to 11.0 (RR = 1.59, p = 0.01), respectively.

DISCUSSION

The variation of incidence between urban and rural areas and a different pattern of change over time between the genders by both the urban–rural setting and age groups support the theory that socio-economic wealth, which often results in overnutrition and lower physical activity, is important also for the occurrence of Type 1 diabetes mellitus.

In our study, the urban–rural gradient of diabetes incidence was most evident in younger children – similar findings were reported from Montreal (15) and Turin (6), although in Wisconsin (5) the urban–rural differences were slightly more pronounced in the 15–29-year age group.

If Type 1 diabetes mellitus is a wealth-related disease, as suggested by associations with indicators of wealth (16, 17), the urban–rural differences of diabetes incidence might, at least partly, be a reflection of differential distribution of socio-economic deprivation in urban and rural areas (8, 9, 15). Interestingly, in Lithuania the observed urban–rural gradient of Type 1 diabetes mellitus incidence during the nineties of the 20th century paralleled the urban–rural differences of the poverty distribution. According to a report prepared by a UNDP team (27), 26–28% of people in the rural areas, 15–14% in small towns, and 10–7% in the cities during 1997–1999 were reported to live below the relative poverty line, defined as consumer expenditure per household member below 50 percent of the country's average. The Human Development Report (28) estimated that more than 20% of pre-school children and 31% of children under 18 years were below the poverty line in the year 2000.

Overweight and the low rate of physical activity are the known risk factors for Type 2 diabetes mellitus, but the increased insulin demand due to insulin resistance may also accelerate beta-cell damage leading to an increased risk or earlier onset of Type 1 diabetes mellitus (29–31). An increased linear growth rate, weight gain and a higher body mass index throughout the childhood, perhaps especially during the first three years of life, are the risk factors for developing diabetes (32–33). 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 they also are more physically active, which also leads to a lower insulin resistance. The different pattern of incidence over time between the genders indicates either different life-style-related risk factors or their different distribution between males and females. In a national sample investigated in 1997, the prevalence of obesity among 20–34-year-old Lithuanians was 6% for both genders, but the prevalence of overweight was higher in males than in females, reaching 34% and 19%, respectively, while 8% of females but no males were underweight (34). Differences in the prevalence of overweight are consistent with our findings of a higher increase of diabetes incidence among men compared to women in the corresponding age groups. Contrary to our findings, a rising incidence trend was observed in rural but not urban areas in the 0–29-year age group in Bialystok region of northeast Poland (1994–1998), and mainly in the 5–14-year age group (35).

The methodological issue important for the interpretation of our results is the difficulty to recognize the type of diabetes from the clinical picture at the time of diagnosis in the older age groups, as the proportion of cases with Type 2 diabetes mellitus and LADA (latent autoimmune diabetes mellitus of adults) increases with age (36, 37). No antibody testing or C-peptide measurements have been performed in Lithuania. These possible shortcomings might somewhat affect our results of incidence variability by age. It is, however, not likely that this possible misclassification would differ to a large extent between males and females or between urban and rural areas to explain the differences found.

CONCLUSIONS

1. The incidence of Type 1 diabetes mellitus among 0–39-year-old Lithuanian inhabitants was different by the urban–rural setting: the incidence was lower in the rural areas compared to small towns and cities.

2. The urban–rural gradient of incidence was most evident in the younger children.

3. The incidence was increased for both males and females during 1991–2000, but the pattern of change over time differed between the genders by both the urban–rural setting and age groups.

ACKNOWLEDGEMENTS

This study represents a collaborative effort between all professionals working with Type 1 (insulin-dependent) diabetes mellitus in Lithuania.

Received 10 February 2003
Accepted 24 March 2003

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SKIRTINGAS LIETUVOS 0–39 METŲ MIESTO IR KAIMO GYVENTOJŲ SERGAMUMAS I TIPO CUKRINIU DIABETU

S a n t r a u k a

Darbo tikslas – nustatyti 0–39 metų Lietuvos miesto ir kaimo gyventojų sergamumą I tipo cukriniu diabetu.

Darbo metodas. Žinios apie 0–39 metų naujai susirgusius Lietuvos gyventojus I tipo cukriniu diabetu renkamos iš visų šalies endokrinologų ir kitų už diabetologinę pagalbą atsakingų medicinos darbuotojų. Tai pirminis gaunamos informacijos šaltinis. Antrinis informacijos šaltinis – metinės endokrinologų ataskaitos bei medicininiai mirties liudijimai. Atsižvelgdami į galimus gyventojų struktūros skirtumus didžiuosiuose miestuose, kituose miestuose ir kaimuose naudojome tiesioginę sergamumo rodiklių standartizaciją pagal standartinę populiaciją, kurioje gyventojų skaičius penkerių metų amžiaus grupėse vienodas. Atskaitinėmis kategorijomis, su kuriomis buvo lyginami sergamumo rodikliai kitose to paties kintamojo kategorijose, pasirinkome 1991–1995 metų 0–4 m. mergaičių sergamumą kaimo vietovėse. Sergamumo rodiklių santykis rodo, kiek kartų sergamumo rodiklis atitinkamoje kategorijoje skiriasi nuo rodiklio atskaitinėje kategorijoje. Naudotas Poisson regresinės analizės metodas.

Rezultatai. Pagal Lietuvos gyventojų lytį ir amžiaus grupes standartizuotas 0–39 metų vyrų sergamumas I tipo cukriniu diabetu (9,5/100 000) buvo didesnis nei moterų (6,9/100 000), RR =1,39; $p < 0,001$. Kaimo gyventojai I tipo cukriniu diabetu sirgo mažiau (7,1) nei mažų ir vidutinio dydžio miestų (9,0) bei didelių miestų (8,8) gyventojai; $p < 0,001$. Didžiausi I tipo cukrinio diabeto skirtumai, lyginant miestą ir kaimą, pastebėti tarp 0–9 metų vaikų. Vidutinis vyrų sergamumas I tipo cukriniu diabetu 1991–1995 m., palyginus su 1996–2000 m., išaugo nuo 8,7 iki 10,5 (RR = 1,22; $p = 0,001$), o moterų – nuo 6,2 iki 7,8 (RR = 1,25; $p = 0,002$). Vyrų sergamumas I tipo cukriniu diabetu labiau augo dideliuose miestuose, t. y. nuo 8,4 iki 11,8 (RR = 1,40, $p < 0,001$), ir buvo didesnis vyresnio amžiaus grupėse. Moterų sergamumas I tipo cukriniu diabetu labiau augo mažuose miesteliuose ir kaime, t. y. nuo 5,8 iki 7,7 (RR = 1,33; $p = 0,003$), ir buvo didesnis jaunesnio amžiaus grupėse.

Išvada. Lietuvos miesto ir kaimo gyventojų sergamumas I tipo cukriniu diabetu buvo skirtingas. Sergamumo dinamika kito laike ir skyrėsi lyčių, gyvenamosios vietos bei amžiaus grupėse.