

## Increasing incidence of childhood-onset Type I diabetes in 3 Baltic countries and Finland 1983–1998

T. Podar<sup>1</sup>, A. Solntsev<sup>1</sup>, M. Karvonen<sup>2</sup>, Z. Padaiga<sup>3</sup>, G. Brigis<sup>4</sup>, B. Urbonaite<sup>3</sup>, M. Viik-Kajander<sup>4</sup>, A. Reunanen<sup>2</sup>, J. Tuomilehto<sup>2</sup>

<sup>1</sup> Department of Endocrinology, Tartu University Clinics, Tartu, Estonia

<sup>2</sup> Diabetes and Genetic Epidemiology Unit, Department of Epidemiology and Health Promotion, Department of Health and Disability, National Public Health Institute, Helsinki, Finland

<sup>3</sup> Institute of Endocrinology, Kaunas Medical Academy, Kaunas, Lithuania

<sup>4</sup> Department of Public Health and Epidemiology, Latvian Medical Academy, Riga, Latvia

### Abstract

*Aims/hypothesis.* We aimed to study the incidence of Type I diabetes in 4 countries, Estonia, Latvia, Lithuania and Finland, during 1983–1998, focusing on the two separate periods of 1983–1990 and 1991–1998.

*Methods.* Population-based incidence data from nationwide diabetes registries were used. Crude and age-standardized incidence rates using the proportions of 39%, 32% and 29% for 5-year age groups (0–4, 5–9 and 10–14 years) were calculated. Yearly incidence was evaluated and the means between the two periods compared.

*Results.* Between 1983–1990 and 1991–1998 there was a statistically significant incidence increase in all 4 countries of Estonia, Latvia, Lithuania and Finland (relative risk 1.15, 95%-Confidence interval 1.10–1.19) and as well as in the 3 Baltic states of Estonia, Latvia, Lithuania (relative risk 1.13, 95% Confidence interval 1.04–1.22). The crude incidence in-

creased in Estonia from 10.1 (95%-Confidence interval 8.9–11.4) to 12.3 (11.0–13.8), in Latvia from 6.6 (5.8–7.3) to 7.4 (6.6–8.2) and in Lithuania from 6.8 (6.2–7.5) to 7.8 (7.1–8.5). In Finland the incidence rose from 34.6 (33.3–36.0) in 1983–1990 to 40.8 (39.4–42.2) in 1991–1998. In children under 5 years of a age a statistically important increase was seen in Estonia and Finland. The highest incidence for a single year was recorded for all participating countries in the late 1990 s. The highest annual incidence rate of childhood onset Type I diabetes in the world ever known was recorded in Finland in 1998 with 48.5 cases per 100 000 person-years.

*Conclusion/hypothesis.* The incidence of Type I diabetes has increased since 1983 in the three Baltic states as well as in Finland. Long-term monitoring is needed for a better detection in changes in incidence. [Diabetologia (2001) 44 [Suppl 3]: B17–B20]

**Keywords** Type I diabetes, incidence, epidemiology.

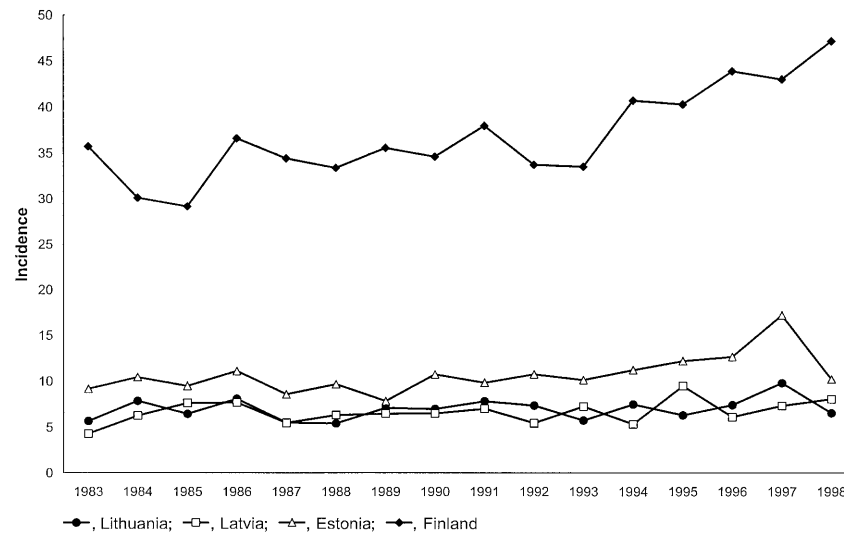
The large gradient in the morbidity of childhood-onset Type I (insulin-dependent) diabetes mellitus in the 3 Baltic states and Finland has been known for many years [1–4]. Much of the data has been obtained within the framework of EURODIAB ACE [2] and DIABALT studies [3, 4]. Long-term data indicated that the incidence of Type I diabetes is increasing in most populations [5–7]. The incidence of Type I diabetes in Finland in the 1950s was slightly higher than in the 3 Baltic states during the 1980 s and has in-

creased linearly after that [8, 9]. The cause of Type I diabetes, especially the environmental triggers, remains to be explained. Many studies have focused on the influence of socio-economic factors in the causation of Type I diabetes [10–14]. Estonia, Latvia and Lithuania have experienced major social and economic changes during the past two decades since they regained independence in 1991 and changed their path of development.

Our previous report on morbidity and Type I diabetes in the Baltic region during 1983–1992 revealed no major important temporal changes apart from the increase in the 0–4 year age group in Finland [4]. The purpose of this analysis was to investigate the incidence of childhood-onset Type I diabetes in the 3

*Corresponding author:* Toomas Podar, Department of Endocrinology, Pikk Str 64, Tartu 50603, Estonia

*Abbreviations:* CI, Confidence interval; RR, relative risk.



**Fig. 1.** Age-standardized incidence of childhood-onset Type I diabetes in Estonia, Latvia, Lithuania and Finland, 1983–1998

Baltic countries and Finland during a longer period, from 1983 to 1998, focusing on the two periods of 1983–1990 and 1991–1998. For the Baltic states these two periods coincide with a time of dependence on the former Soviet Union and independence. Special attention was paid to the change in the incidence in children under 5 years of age.

## Subjects and methods

Case ascertainment and validation procedures in the diabetes registries in these countries have been previously described in detail [3]. Annual population statistics by sex and age group were available for Estonia, Latvia and Finland for the whole study period. Reliable annual population data was obtained for Lithuania for 1983–1997 and for 1998 the 1997 data was used.

**Statistical methods.** The incidence was calculated per 100 000 persons at risk per year in a population. The 95 %-Confidence interval (CI) for the incidence was assessed assuming the Poisson distribution of the cases. For purposes of comparison, incidence of childhood-onset Type I diabetes was age standardized by using the world standard population, i.e. proportions of 39 %, 32 % and 29 % for 0–4, 5–9 and 10–14 year age groups, respectively [15]. The differences in incidence between sexes, three age groups (0–4, 5–9, 10–14 years) and two periods (1983–1990 versus 1991–1998) were estimated by 95 %-CI. Mantel-Haenszel tests were performed to evaluate the differences in incidence between the two periods, two sexes and among the four countries.

## Results

The mean incidence during the entire study period was 11.2 (95 %-CI 10.3–12.1) for Estonia, 6.9

(6.4–7.5) for Latvia, 7.3 (6.9–7.8) for Lithuania and 37.7 (36.7–38.7) for Finland. There was a male excess in incidence in Estonia and Finland and a female excess in Latvia and Lithuania but the sex difference reached statistical significance only in Finland ( $p < 0.001$ ). The annual age-standardized incidence of Type I diabetes in the four populations for the entire period is given in Figure 1. Overall, between 1983–1990 and 1991–1998 there was a statistically significant increase in all countries taken together (relative risk (RR) 1.15, 95 % CI 1.10–1.19) and in the 3 Baltic countries alone (RR 1.13, 95 %-CI 1.04–1.22). The increase was seen in the 3 Baltic states when pooled together although in individual countries separately the trend did not reach statistical significance. The crude incidence increased in Estonia from 10.1 (8.9–11.4) to 12.3 (11.0–13.8); in Latvia from 6.6 (5.8–7.3) to 7.4 (6.6–8.2); and in Lithuania from 6.8 (6.2–7.5) to 7.8 (7.1–8.5). In Finland the incidence rose from 34.6 (33.3–36.0) in 1983–1990 to 40.8 (39.4–42.2) in 1991–1998. The relative increase in the crude incidence between the two periods, on average eight years apart, was the highest in Estonia at 21.7%. In Finland the increase was 17.9%, in Lithuania 14.7% and in Latvia 12.1%. The absolute increase in incidence was 6.2 cases per 100 000 person-years in Finland, 2.2 cases in Estonia, 1.0 cases in Lithuania and 0.8 cases in Latvia. The incidence increased in both males and females in all 4 countries (Table 1).

The highest incidence for a single year ever recorded for all participating countries were seen in the late 1990 s. The highest annual incidence rate of childhood-onset Type I diabetes ever known in the world was recorded in Finland in 1998 at 48.5 per 100 000 person-years. In Estonia, the all-time high was seen in 1997 when it reached 19.0 per 100 000 person-years. Lithuania also experienced the highest ever incidence 10.3 per 100 000 person-years during 1997. In Latvia the peak in annual incidence of 9.7

**Table 1.** Mean age-specific incidence of Type I diabetes per 100 000 persons at risk per year, (number of cases) and 95 %-Confidence interval by country, sex and age group, 1983–1990 compares with 1991–1998

Period	Age group	Latvia		Lithuania		Estonia		Finland	
		Males	Females	Males	Females	Males	Females	Males	Females
1983–1990	0–4	3.5 (28) [2.3–5.0]	3.4 (26) [2.2–5.0]	4.6 (54) [3.4–6.0]	3.4 (38) [2.4–4.6]	3.5 (17) [2.1–5.7]	4.2 (19) [2.5–6.5]	24.8 (323) [22.2–27.7]	21.9 (273) [19.4–24.7]
	5–9	5.2 (39) [3.7–7.1]	7.2 (51) [5.4–9.5]	7.6 (85) [6.1–9.4]	8.5 (91) [6.8–10.4]	10.4 (48) [7.6–13.7]	12.7 (56) [9.6–16.4]	40.7 (539) [37.4–44.3]	37.4 (473) [34.1–40.9]
	10–14	11.3 (82) [9.0–14.0]	9.4 (65) [7.2–11.9]	8.2 (90) [6.6–10.0]	9.1 (98) [7.4–11.1]	17.3 (78) [13.7–21.6]	13.2 (57) [10.0–17.1]	45.6 (585) [42.0–49.5]	36.9 (452) [33.6–40.5]
	0–14 <sup>a</sup>	6.3 (149) [5.3–7.4]	6.3 (142) [5.3–7.5]	6.6 (229) [5.8–7.5]	6.7 (227) [5.8–7.6]	9.7 (143) [8.2–11.4]	9.5 (132) [7.9–11.3]	35.9 (1447) [34.1–37.8]	31.2 (1198) [29.5–33.0]
1991–1998	0–4	4.3 (28) [2.9–6.3]	4.3 (26) [2.8–6.3]	4.2 (42) [3.0–5.6]	3.6 (35) [2.5–5.1]	10.3 (36) [7.2–14.2]	7.5 (25) [4.9–11.1]	31.3 (408) [28.3–34.4]	32.4 (406) [29.3–35.7]
	5–9	6.7 (52) [5.0–8.9]	8.7 (64) [6.7–11.1]	5.7 (67) [4.4–7.2]	9.5 (107) [7.8–11.5]	11.7 (52) [8.7–15.3]	9.6 (41) [6.9–13.0]	45.1 (591) [41.5–48.9]	47.1 (591) [43.4–51.1]
	10–14	9.8 (73) [7.7–12.4]	9.3 (67) [7.2–11.9]	11.9 (133) [9.9–14.1]	11.2 (121) [9.3–13.4]	16.5 (74) [12.9–20.7]	16.8 (73) [13.2–21.1]	49.2 (655) [45.5–53.1]	39.3 (500) [35.9–42.9]
	0–14 <sup>a</sup>	6.7 (153) [5.7–7.9]	7.2 (157) [6.1–8.4]	6.9 (242) [6.0–7.8]	7.7 (263) [6.8–8.7]	12.5 (162) [10.7–14.6]	10.9 (139) [9.1–12.8]	40.9 (1654) [38.9–42.9]	39.1 (1497) [37.1–41.1]

<sup>a</sup> age-standardized population

per 100 000 person-years was documented in 1995, and it was almost equally high in 1998.

In the youngest children under five years of age, the incidence change was not uniform in the four countries (chi-square = 11.408, DF = 3,  $p < 0.01$ ). A statistically significant increase for both sexes pooled was observed in Estonia (RR 2.32, 95 %-CI 1.56–3.46) and Finland (RR 1.36, 95 %-CI 1.22–1.51). The relative increase in the youngest age group was the highest in Estonia with 189 % increase in males, 83 % in females. The increasing pattern in the 0–4 year age group was even clearer when data on complete birth cohorts of 1983–1987 and 1991–1995 were compared (data not shown). In Latvia a similar, but not significant trend, was observed. The incidence did not change much for either sex in Lithuania.

## Discussion

This study reports the incidence of Type I diabetes in four population-based cohorts from the Baltic region during a 16-year period from 1983 to 1998. In all countries the highest ever incidence of childhood diabetes was documented in the latter part of the 1990 s, around 1997–1998. A new world record high incidence of Type I diabetes was documented in Finland in 1998, with close to 50 cases per 100 000 person-years. The absolute increase in incidence in Finland between the two study periods of 6.2 per 100 000 person-years is close to the current level of incidence in Latvia and Lithuania. Empirical data of our study for Finland (17.9 % increase over 8 years) agrees well with a modelling approach from another study covering a longer period [7]. The increase, however,

was largest in Estonian children of four years of age or under.

We show increases in the incidence of Type I diabetes in these four populations by comparing the periods 1991–1998 and 1983–1990. The increase cannot be attributed to improvements in case ascertainment. In the three Baltic states the registration of new cases of childhood-onset Type I diabetes has become more difficult because of the decentralization of the health-care system since 1991. Furthermore, the laws governing access to personal data have posed obstacles to finding new patients. Maintaining the population-based registries has thus become more difficult. If anything, the incidence estimates obtained during the most recent years could be underestimates when compared with the data from the 1980 s. The nature of the socio-economic changes in the Baltic states since 1991 is manifold. The living standard has improved for some and deteriorated for other segments of the population. Considerable emigration from the Baltic states has taken place since 1991. Most of the emigrants have been non-native inhabitants. In Estonia for example, the population decreased from 1.6 million in 1990 to 1.4 million in 1998. We have previously shown that in Estonia, the non-Estonians have a lower risk of Type I diabetes compared with Estonians [16]. Selective emigration could have contributed to the increase in the overall incidence in Estonia and in the other 2 Baltic states.

Changes in incidence might not be due to socio-economic changes but to other temporally coinciding factors leading to ecological (temporal) fallacy. At the present we do not know whether the increase in morbidity of Type I diabetes seen in the 3 Baltic states is the result of having more power to detect significant differences over a larger range of years start-

ing already in 1980 s or due to drastic changes in the society in the 1990 s.

A clear change was seen in the youngest age group when the distinct mutually exclusive periods 1983–1990 and 1991–1998 were compared. We cannot say that the incidence has changed in the older age groups due to the same exposures because they also experienced the pre-1991 influences. Until now the evidence has suggested that the increase in the incidence in the younger age group has been accompanied by an increase in the overall incidence of childhood-onset Type I diabetes as in Finland [9]. During our study period the highest relative increase in the youngest age group was seen in Estonia. These findings need to be compared with the incidence of Type I diabetes in adults to detect the differences in the lifetime risk for the birth cohorts. It is not known whether the lifetime risk of Type I diabetes is levelling off at a certain level or not. The increase in the incidence of Type I diabetes in the youngest age groups still remains an important concern as it increases the number of years exposed to hyperglycaemia and hence the risk of late complications.

Incidence increased more in Estonia than in Latvia and Lithuania and the gap in the incidence among the 3 newly independent Baltic states could be widening. Differences, documented in our first comparative paper on the Baltic region, have become more manifest [3]. Despite some earlier contradictory reports on the temporal variation in morbidity in Estonia in 1980s, the incidence has increased in all 3 Baltic states [1, 17].

In conclusion, the incidence of Type I diabetes has increased since 1983 in the 3 Baltic states as in Finland. Long-term monitoring is needed to improve the detection of changes in incidence in the future.

*Acknowledgements.* This study was supported by the European Community contract BMH1 CT92 0043 and Estonian Science Foundation's grant 4325. The authors acknowledge the help of the Finnish Childhood Type I diabetes Registry group. The Finnish Childhood IDDM Registry group: A. Fagerlund, M. Flittner, P. Floman, B. Gustafsson, H. Haavisto, T. Huupponen, P. Hiltunen, M. Hyttinen, R. Jokisalo, U. Kaski, J. Komulainen, P. Korpela, M.-L. Käär, J. Lappalainen, P. Lautala, P. Lehtinen, E. Lehtokoski-Lehtiniemi, M. Lipsanen-Nyman, K. Niemi, A. Nuuja, P. Ojajärvi, J. Ollikainen, A. Putto-Laurila, S. Pöntynen, J. Sankala, T. Sillanpää, I. Sipilä, P. Tapanainen, A. Tomminen, T. Uotila, P. Varimo, P. Vuolukka, M. Väre

## References

1. Tuomilehto J, Podar T, Reunanen A et al. (1991) Comparison of incidence of IDDM in childhood between Estonia and Finland, 1980–1988. *Diabetes Care* 14: 982–988
2. Green A, Gale EA, Patterson CC (1992) Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE Study. *Lancet* 339: 905–909
3. Tuomilehto J, Podar T, Brigis G et al. (1992) Comparison of the incidence of insulin-dependent diabetes mellitus in childhood among five Baltic populations during 1983–1988. *Int J Epidemiol* 21: 518–527
4. Padaiga Z, Tuomilehto J, Karvonen M et al. (1997) Incidence trends in childhood onset IDDM in four countries around the Baltic sea during 1983–1992. *Diabetologia* 40: 187–192
5. Green A, Andersen PK, Svendsen AJ, Mortensen K (1992) Increasing incidence of early onset Type I (insulin-dependent) diabetes mellitus: a study of Danish male birth cohorts. *Diabetologia* 35: 178–182
6. Diabetes Epidemiology Research International Group (1990) Secular trends in incidence of childhood IDDM in 10 countries. *Diabetes* 39: 858–864
7. Onkamo P, Vaananen S, Karvonen M, Tuomilehto J (1999) Worldwide increase in incidence of Type I diabetes – the analysis of the data on published incidence trends. *Diabetologia* 42: 1395–1403
8. Somersalo O (1955) Studies of childhood diabetes I. Incidence in Finland. *Ann Paediatr Fenn* 1: 239–249
9. Tuomilehto J, Karvonen M, Pitkaniemi J et al. (1999) Record-high incidence of Type I (insulin-dependent) diabetes mellitus in Finnish children. The Finnish Childhood Type I Diabetes Registry Group. *Diabetologia* 42: 655–660
10. Colle E, Siemiatycki J, West R et al. (1981) Incidence of juvenile onset diabetes in Montreal-demonstration of ethnic differences and socio-economic class differences. *J Chron Dis* 34: 611–616
11. Telahun M, Abdulkadir J, Kebede E (1994) The relation of early nutrition, infections and socio-economic factors to the development of childhood diabetes. *Ethiop Med J* 32: 239–244
12. Meadows P (1995) Variation of diabetes mellitus prevalence in general practice and its relation to deprivation. *Diabet Med* 12: 696–700
13. Wadsworth EJ, Shield JP, Hunt LP, Baum JD (1997) A case-control study of environmental factors associated with diabetes in the under 5 s. *Diab Med* 14: 390–396
14. Parslow RC, McKinney PA, Law GR, Staines A, Williams R, Bodansky HJ (1997) Incidence of childhood diabetes mellitus in Yorkshire, northern England, is associated with nitrate in drinking water: an ecological analysis. *Diabetologia* 40: 550–556
15. Parkin DM, Muir CS, Whelan SL, Gao YT (1992) Cancer incidence in five continents. VI IARC No 120. IARC, Lyon
16. Podar T, Tuomilehto-Wolf E, Tuomilehto J, LaPorte RE, Adojaan B (1992) Insulin-dependent diabetes mellitus in native Estonians and immigrants to Estonia. *Am J Epidemiol* 135: 1231–1236
17. Podar T, Laporte RE (1993) Incidence of childhood diabetes did not increase in Estonia during 1980–89. *Diabetes Metab* 19: 361–363