REVIEW

Trends of childhood diabetes incidence in Slovakia 1985–2000: Accelerated increase in the years 1990–2000

Michalkova D, Mikulecky M, Hlava P

1st Department of Pediatrics, Faculty of Medicine, Comenius University, Bratislava, Slovakia. **michalko.dfnsp@pobox.sk**

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 increaseed 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 attraacted 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.

1st Department of Pediatrics, Faculty of Mecicine, Comenius University, Bratislava, Department of Epidemiology and Biometrics, Institute of Preventive and Clinical Medicine, Bratislava, and Institute of Health Information and Statistics, Bratislava, Slovakia

Address for correspondence: D. Michalkova, MD, DSc, Dept of Pediatrics, Children's University Hospital, Limbova 1, SK-833 40 Bratislava 37, Slovakia.
Phone/Fax: +421.2.54792315
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 – by the "Epidemiology Study Group". The incidence and prevalence of diabetes type 1 in Slovakian children have been followed since 1980. By 1985 the information was complete. The completeness of ascertainment was based on the model that assumes an independent ascertainment of the same population by two alternative sources, the capture – a recapture procedure. The first source of the data were announcements in special forms 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).

Tab. 1. Juvenile diabetics (Slovakia 1985—2000).

Years	Annual incidence rates/100 000				95 % confidence intervals			
Group	0–4	5–9	10–14	0–14	0–4	5–9	10–14	0–14
1985	2.89	7.73	9.68	6.01	1.32;4.45	5.24;10.21	6.75;12.61	5.37;8.13
1986	2.47	7.16	7.11	5.62	1.01;3.93	4.75;9.57	4.65;9.57	4.36;6.87
1987	3.88	6.61	9.69	6.78	2.03;5.72	4.28;8.94	6.86;12.53	5.40;8.16
1988	2.32	6.46	10.77	6.65	0.88;3.76	4.15;8.77	7.82;13.73	5.28;8.02
1989	3.09	7.92	10.88	7.46	1.41;4.76	5.33;10.51	7.92;13.84	6.01;8.91
1990	2.91	5.13	9.21	5.90	1.27;4.56	3.03;7.23	6.49;11.93	4.60;7.21
1991	6.54	8.85	10.81	8.85	4.02;9.05	6.07;11.63	7.85;13.78	7.24;10.47
1992	6.54	10.65	9.43	8.92	4.03;9.06	7.50;13.80	6.58;12.29	7.27;10.57
1993	8.22	10.88	13.24	10.88	5.37;11.07	7.66;14.09	9.83;16.65	9.04;12.72
1994	8.86	7.92	11.07	9.35	5.84;11.88	5.22;10.62	8.00;14.13	7.65;11.05
1995	10.04	9.11	13.90	11.15	6.76;13.32	6.17;12.04	10.44;17.36	9.27;13.03
1996	5.57	10.80	10.20	9.06	3.06;8.07	7.57;14.03	7.22;13.18	7.35;10.78
1997	9.54	14.08	10.82	11.57	6.18;12.90	10.36;17.80	7.73;13.91	9.60;13.53
1998	6.46	11.24	15.25	11.44	3.63;9.29	7.88;14.59	11.54;18.96	9.46;13.43
1999	11.45	16.10	15.12	14.46	7.60;15.30	12.03;20.18	11.39;18.86	12.19;16.72
2000	9.77	12.08	17.52	13.53	6.21;13.32	8.55;15.60	13.50;21.54	11.35;15.72

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

Gender	Age (years)	1985–1990		1990–2000		Trend difference (95 %CI) (cases/100 000/year)
		b	100b/a	b	100b/a	
Male	0–4	+0.30	+15%	+0.66*	+13%*	+0.36 (-0.39; +1.11)
	5–9	-0.19	-3%	+0.76**	+12%**	+0.95** (+0.34;+1.55)
	10–14	+0.42	+5%	+0.86**	+10%**	+0.44 (-0.22;+1.10)
Female	0–4	-0.29	-7%	+0.29	+5%	+0.58 (-0.06;+1.22)
	5–9	-0.43	-5%	+0.60	+7%	+1.03* (+0.05;+2.02)
	10–14	+0.14	+2%	+0.41	+4%	+0.27 (-1.29;+1.83)
Total	0–14	+0.03	+1%	+0.63***	+9%***	+0.60* (+0.12;+1.08)

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. * $p<0.05$; ** $p<0.01$; *** $p<0.001$.

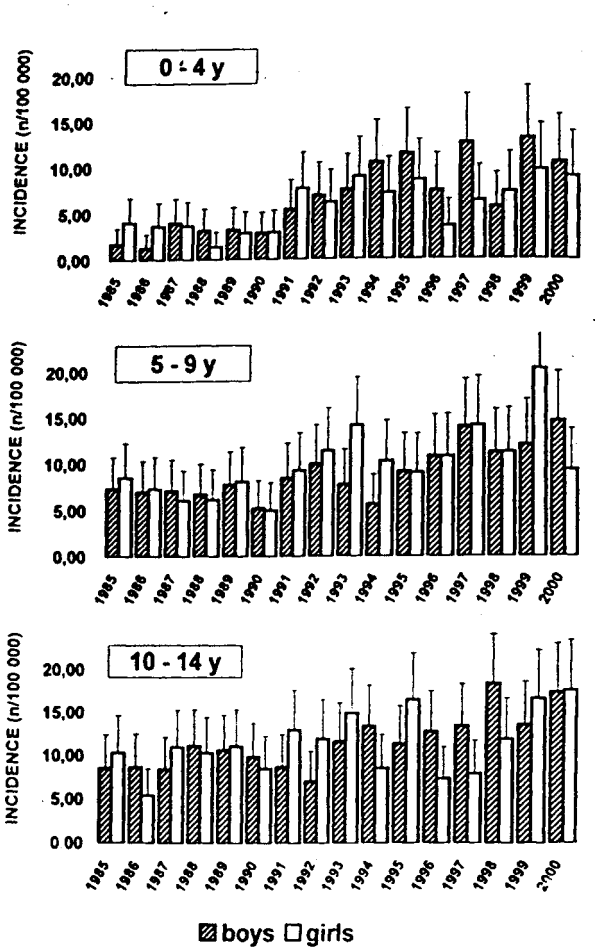

Fig. 1. Incidence rates (cases per 100 000 children per year) of diabetes mellitus type 1, in 0–4 (a), 5–9 (b) and 10–14 (c) old Slovak boys (empty bars) and girls (lined bars) during 16 years in Slovakia.

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.

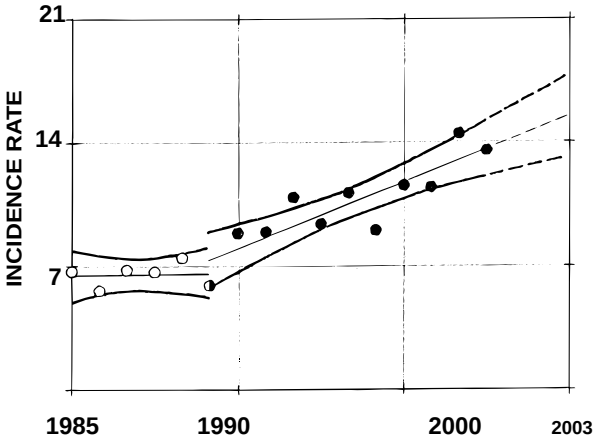

Fig. 2. Evolution trends of childhood diabetes (dots) in Slovakia 1985–2000. Linear regression was calculated separately for 1985–1990 and 1990–2000. Estimates of the linear function (straight line) are accompanied by the 95 % confidence corridor.

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 ($p<0.001$).

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 contribution confirms this trend for the time interval extended by eight 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: Ľ. Barák (Bratislava), M. Baštrnáková (Komárno), A. Čaradská (Topoľčany), M. Debreová (Poprad), K. Hálová (Trnava), Ľ. Hunák (Nitra), E. Jančová (Bratislava), J. Javorková (Martin), V. Karvaj (Nové Zámky), M. Kecerová (Dolný Kubín), M. Kúseková (Košice), M. Lukačovič (Čadca), J. Marčok (Trenčín), V. Mátheová (Rimavská Sobota), D. Michalková (Bratislava), M. Pašková (Košice), G. Nagyová (Spišská Nová Ves), S. Niňajová (Bratislava), M. Repková (Galanta), D. Reptišová (Prešov), V. Šajdíková (Považská Bystrica), A. Šarišská (Humenné), Z. Šimeková (Žilina), E. Špánitzová (Levice), E. Trézová (Košice), B. Milošovičová, J. Strnová (Bratislava).

References

1. Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, La Porte R, Tuomilehto J, for the DiaMont Project Group. Incidence of childhood Type 1 Diabetes worldwide. Diabetes Care 2000; 23: 1516—1526.

2. Karvonen M, Tuomilehto J, Libman I, La Porte R, for the WHO DiaMond Project Group. A review of the recent epidemiological data on the worldwide incidence of type 1 (insulin dependent) diabetes mellitus. Diabetologia 1993; 36: 883—892.

3. Onkamo P, Väänänen S, Karvonen M, Tuomilehto J. Worldwide increase in incidence of type 1 diabetes — the analysis of the date on published incidence trends. Diabetologia 1999; 42: 1395—1403.

4. EURODIAB ACE Study Group. Variation and trends in incidence of childhood diabetes in Europe. The Lancet 2000; 355: 873—876.

5. Green A. Recent trends in the epidemiology of type 1 diabetes. In: Marshall SM, Home PD, Rizza R (Ed). Diabetes Annual 10. 1996; Elsevier Science, Rotterdam, p. 51—64.

6. Green A. EURODIAB TIGER. Europe and Diabetes — Type 1 Genetic Epidemiology Resource. In: Summary final report. University of Aarhus, Aarhus, 1999, 1—38.

7. WHO Multinational Project for Childhood Diabetes, Methods of Operation: 1991.

8. Rewers M, Stone RA, La Porte RE et al. Poisson regression modeling of temporal variation in incidence of childhood insulin-dependent diabetes mellitus in Allegheny County, Pennsylvania and Wielkopolska, Poland. Amer J Epidemiol 1989; 129: 569—581.

9. Tuomilehto J, Karvonen M, Pitkäniemi J, Virtala E, Kohtameki K, Toivanen L et al. Record-high incidence of type 1 (insulin dependent) diabetes mellitus in Finnish children. Diabetologia 1999; 42: 655—660.

10. Kocova M, Trucco M, Konstantinova M, Dorman JS. A could spot of IDDM incidence in Europe. Diabetes Care 1993; 16: 1236—1240.

11. Dorman JS, O'Leary LA, Koehler AN. Epidemiology of childhood diabetes. In: Kelnar CJH (Ed). Childhood and Adolescent Diabetes. Chapman and Hall, London, 1994, 139—159.

12. Cínek O, Lánská V, Kolouśková S, Šumník Z, Šnajderová M, R•nningen KS. Types 1 diabetes mellitus in Czech children diagnosed in 1990—1997: a significant increase in incidence and male predominence in the age group 0—4 years. Diabetic Medicine 2000; 17: 64—69.

13. Soltész G, Madácsy L, Békefi D, Dankó I. Rising incidence of type 1 diabetes in Hungarian children (1978—1987). Diab Med 1990; 7: 111—114.

14. Gyürus E, Gyürkö M, Patterson C, Green A, Soltész G. Twenty year incidence of type 1 diabetes in Hungarian children (1978—1997). Diab Res Clin Pract 1999; 44 (Suppl): S1/01.

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

Upper Silesia children, 1989—1997 (Poland). Diabetologia 1999; 42 (Suppl 1): 309/A85.

16. Schober E, Frisch H. Incidence of childhood diabetes mellitus in Austria 1979—1984. Acta Paediat Scand 1998; 77: 299—302.

17. Schober E, Schneider E, Waldhör T, Tuomilehto J and Austrian Diabetes Incidence Study Group. Increasing incidence of IDDM in Austrian children a nationwide study 1979—1993. Diabetes Care 1995; 18: 1280—1283.

18. Gardner SG, Bingley PJ, Sarwell PA, Weeks S, Gale AM, the Bart's Oxford Study Group. Rising incidence of insulin dependent diabetes in children aged under 5 years in the Oxford region: time trend analysis. Brit Med J 1997; 315: 713—717.

19. Rosenbauer J, Herzig P, Von Kries R, Neu A, Giani G. Temporal seasonal and geographical incidence paterns of Type 1 diabetes mellitus in children under 5 years of age in Germany. Diabetologia 1999; 42: 1055—1059.

20. Karvonen M, Pitkäniemi M, Pitkäniemi J, Kohtamaki K, Tajima N, Tuomilehto J. Sex difference in the incidence of insulin-dependent diabetes mellitus: An analisys of the recent epidemiological data. Diabet Metab Rev 1997; 13: 275—291.

21. Michalková D, Černay J, Danková A, Rusnák M, Fandáková K. Incidence and prevalence of childhood diabetes in Slovakia (1985—1992). Diabet Care 1995; 18: 315—320.

22. Tull E, Tajiman N, Podar T, Dorman J, Moy C, La Porte R. Epidemics, Migrants and the Death of the Pancreas. In: Levy-Marchal C, Czernichow P (Eds). Epidemiology and Etiology of Insulin-dependent Diabetes in the Young. Pediat Adolesc Endocrinol. Karger, Basel, 1992, Vol 21, 56—65.

23. Diabetes Epidemiology Research International Group. Secular Trends in Incidence of Childhood IDDM in 10 Countries. Diabetes 1990; 39; 858—864.

24. Mikulecký M, Michalková D, Petrovičová A. Coxsackie Infection and Births of Future Diabetic Children: Year, Seasonality and Secularity. J Pediat Endocrinol Metab 2000; 13: 523—527.

25. Battelino T, Krzisnik C. Incidence of type 1 diabetes mellitus in children in Slovenia during years 1988—1995. Acta Diabetol 1998; 35: 112—114.

26. Bruno G, Merletti F, Biggeri A et al. Increasing trend of type 1 diabetes in children and young adults in the province of Turin (Italy). Diabetologia 2001; 44: 22—25.

27. Schoenle EJ, Lang-Muritano M, Gschwend S et al. Epidemiology of type 1 diabetes mellitus in Switzerland: steep rise in incidence in under 5 year old children in the past decade. Diabetologia 2001; 44: 286—289.

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