

Increasing incidence of type 1 diabetes in population from Santiago of Chile: trends in a period of 18 years (1986–2003)

E. Carrasco^{1*}
F. Pérez-Bravo²
J. Dorman³
A. Mondragón²
J. L. Santos²

¹*Department of Diabetes, Hospital San Juan de Dios, Faculty of Medicine, University of Chile, Santiago, Chile, South America*

²*Genetic Epidemiology Laboratory, Nutrition and Food Technology Institute (INTA), University of Chile, Santiago, Chile, South America*

³*Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, USA*

*Correspondence to: E. Carrasco, Real Audiencia 1361, San Miguel, Santiago, Chile, South America.
E-mail: ecarrasc@med.uchile.cl

Abstract

Study objective and setting The aim of this study is to determine the incidence rate of type 1 diabetes in the metropolitan region of Santiago, Chile from 1 January 1986 to 31 December 2003.

Design Population-based incidence study. Participants: A case must fulfill the following requirements to be included in this study: age at onset: 0 to 14 years, diagnosed with diabetes and placed on insulin, diagnosed within the defined time period, and to be a resident of the metropolitan region of Santiago at the time of the diagnosis. The population 'at risk' is the population less than 15 years of age.

Result The overall rate of type 1 diabetes was estimated as 4.02 cases per 100 000 children per year (95% confidence interval: 2.98–4.83).

Conclusion The incidence of type 1 diabetes in Santiago, Chile has increased during the last years. This data are concordant with the observation that the incidence of type 1 diabetes is increasing in Latin America and worldwide.

Keywords epidemiology; incidence; type 1 diabetes; Chile

Introduction

Type 1 diabetes mellitus is characterised by the autoimmune destruction of the insulin-secreting beta-cells located in the pancreas [1]. In the last years, the methodology provided by the World Health Organisation Diabetes Mondiale project [2] has definitively confirmed the existence of large geographic differences in the incidence rate of type 1 diabetes around the world. The great variation in the incidence rates of this complex disorder suggests that both genetic and environmental factors participate in the etiological process of beta-cell elimination. The highest incidence rates in the world correspond to north European countries such as Norway, Finland, Denmark, or in the island of Sardinia in Italy [3]. On the other hand, very low incidence rates were estimated in Asian countries such as regions of China and Korea [4,5].

The Chilean population constitutes a melting pot of populations arising from different groups including Europeans (predominantly from Spain) and Amerindians (mainly Mapuche and Aymara natives) [6]. It has been reported that the Aboriginal Mapuche population from Chile has a very low incidence of type 1 diabetes in subjects aged less than 15 years (0.43 per 100 000

per year) [7], while the incidence rate found in the metropolitan region of Santiago, Chile was estimated to be 2.36 per 100 000 per year, in the period 1986 to 1992. [8].

The aim of this study is to estimate the incidence rate of type 1 diabetes in the metropolitan region of Santiago, Chile from 1 January 1986 to 31 December 2003.

Methods

Area of study

The metropolitan region of Santiago is placed in the central region of the country, and it concentrates close to 40% of the total Chilean population. According to the 2002 census, the total population of the metropolitan region of Santiago was 5 257 937 [9] that lives in an area of 15 349 sq Km. More than 96% of this population lives in urban conditions. In this study, the population 'at risk' is the population less than 15 years of age (1 509 218 subjects in 2002, according to the National Institute of Statistics, Santiago, Chile).

Ascertainment of cases

A Chilean registry of type 1 diabetes was created in 1995 for the metropolitan region of Santiago in such a way that every incident case of the disease is reported to the Ministry of Health. In this report, we included incident type 1 diabetic cases diagnosed from 1 January 1986 to 31 December 2003 that were ascertained in this study. Two independent sources were used for the ascertainment of cases. Medical records in hospitals, private clinics, diabetologists, and pediatricians were collectively considered as the primary source, and the secondary source was the record of Juvenile Diabetes Foundation Members. Patients usually are recommended to join Juvenile Diabetes Foundation (JDF) by general practitioners. Most type 1 diabetes incident cases included in the primary source were also registered in JDF lists. Consequently, JDF acted mainly as a confirmatory registry for newly diagnosed cases. A case must fulfill the following requirements to be included: age at onset 0 to 14 years, diagnosed with diabetes and placed on insulin, diagnosed within the defined time period, and to be a resident of the metropolitan region of Santiago at the time of the diagnosis [10–12]. The day of the first insulin injection was considered as the date of diagnosis. In the area of study, the National System of Health population and its diagnostic ability is reliable as far as type 1 diabetes is concerned. Consequently, it is unlikely that a new case may die at the onset of the disease. Owing to the disease severity, predominant urban location, and wide access to health care, it is unlikely for a type 1 diabetic patient to be undiagnosed, unreported, or for the patient to die at onset. This research project was approved by the Ethics Committee at the University of Chile.

Statistical analyses

For each year, the midyear population aged less than 15 years, obtained from post-census projections, was used as a denominator of the incidence rate (census 1992 and their projections and census 2002 and their corrections). Incidence rate is expressed as number of cases per 100 000 inhabitants aged less than 15 years and per year. The 95% confidence intervals were calculated assuming a Poisson distribution. Taking the whole period from 1986 to 2003, incidence rates by sex and groups of age (cases aged 0–4 years, 5–9 years, and 10–14 years) were also computed. Age-standardized incidence rates were computed assuming equal population size for the three age groups considered. A simple chi-square formula was used to assess the existence of an increased number of cases across the study period [2].

Results

The total number of cases in the period of ascertainment was 1121 (561 boys and 560 girls). The mean age of cases was 8.7 years with a standard deviation of 4.0 years (257 cases aged 0–4 years, 398 aged 5–9 years, and 466 aged 10–14 years). The exam of primary and secondary sources indicates that all cases were essentially ascertained by the primary source (ascertainment of primary source = 100%), the secondary source being a subset of the primary source (ascertainment of secondary source = 99%). Therefore, the ascertainment of the registry can be considered 100% since no new cases were identified in the secondary source of ascertainment with respect to the primary source.

The overall rate of type 1 diabetes was calculated as 4.02 cases per 100 000 per year (95% confidence interval: 2.98–4.83). Table 1 shows the incidence rate of type 1 diabetes by gender and age groups. Incidence rates did not differ significantly by gender. Regarding age, there were significant differences when comparing the incidence rate for children aged 10 to 14 years compared to those aged 0 to 4 years ($p < 0.01$). The age-standardized rate was computed as 4.08 cases per 100 000 per year. Table 2 shows incidence rates for the last 18 years in Santiago, where a very low incidence was detected during the year 1987, and a higher incidence was determined for the years 1996 and 2003 ($p < 0.02$).

Discussion

The overall incidence of type 1 diabetes in the present report (4.02 cases per 100 000 per year) seems to be notably increased with respect to the last estimation of the incidence in the years 1986 to 1992 (2.36 cases per 100 000 per year). This conclusion is concordant with the observation that the incidence of type 1 diabetes is increasing worldwide [12–14]. The highest incidence rate

Table 1. Incidence rate of type 1 diabetes in the metropolitan region of Santiago, Chile (1986–2003) by sex and age groups

Gender Age groups	n	Incidence rate ^a	95% Confidence interval
Sex			
Boys	561	4.06	(3.73–4.41)
Girls	560	4.22	(3.86–4.56)
Age (years)			
0–4	257	3.16	(2.78–3.57)
5–9	398	4.32	(3.91–4.77)
10–14	466	4.75*	(4.33–5.20)

^aIncidence rates are expressed as number of cases per 100 000 aged under 15 years and per year (* $p < 0.05$, between 0–4 versus 10–14 years).

Table 2. Incidence rate of type 1 diabetes in the metropolitan region of Santiago, Chile (1986–2003)

Year	Boys	CI 95%	Girls	CI 95%
1986	2.05	1.15–3.38	3.11	1.95–4.71
1987	2.05	1.12–3.31	0.83	0.30–1.81
1988	1.83	1.01–3.08	2.57	1.54–4.02
1989	2.05	1.08–3.18	2.66	1.62–4.11
1990	1.27	0.61–2.33	2.88	1.81–4.36
1991	3.12	2.02–4.59	2.57	1.56–3.97
1992	2.93	1.88–4.36	2.57	1.53–3.89
1993	4.07	2.82–5.68	3.09	2.01–4.56
1994	3.88	2.67–5.44	4.24	2.96–5.91
1995	4.63	3.31–6.30	4.66	3.31–6.37
1996	2.93	1.91–4.30	4.43	3.13–6.09
1997	4.22	2.99–5.81	4.38	3.10–6.02
1998	3.97	2.78–5.49	4.32	3.06–5.94
1999	3.96	2.77–5.48	5.45	4.02–7.22
2000	5.08	3.23–6.11	5.80	3.25–6.19
2001	6.90	3.77–7.46	5.13	3.17–5.98
2002	6.38	3.13–7.34	4.72	3.30–6.19
2003	8.47	4.03–9.12	6.61	3.15–7.66

was estimated in the 10- to 14-year group in both sexes, with a modest excess in the number of female cases. This situation is a common feature of type 1 diabetes occurrence, especially in countries with low incidence of the disease [15]. During the year 1987, the low incidence might be explained by a low prevalence of infection diseases, especially by viruses [16].

Validated incidence rates of type 1 diabetes are still scarce in Latin America. However, there still seems to be a large geographical variation in the risk of developing type 1 diabetes in our region [17]. The differences in incidence of childhood diabetes among countries and ethnic groups can be explained by a variety of factors such as disparity in the exposure to environmental risk factors [18] or distinct frequencies of susceptible alleles in the Human Leukocyte Antigen (HLA) system [19]. The medium to low incidence of type 1 diabetes estimated in the Chilean population could represent a balance of ethnicity between the different frequencies of HLA alleles in Caucasian versus Amerindian populations [20]. The Mapuche population is the major aboriginal group in Chile, and it represents almost 5.5% of the Chilean population according the 2002 Chilean census. This aboriginal group shows a remarkably lower incidence of type 1 diabetes than Caucasian populations [7]. With respect to the environmental risk

factors, increased frequency of breast feeding duration in the Chilean population could also be a determinant in the low incidence of type 1 diabetes in the metropolitan region of Santiago [21–23]. There are numerous reports of adolescent children, usually from minority groups, who show clinical characteristics of type 2 diabetes such as obesity, acanthosis nigricans, family history of diabetes, and absence of islet cell antibodies, but with ketoacidosis. These children were initially diagnosed as having type 1 diabetes because of their clinical presentation, but were later diagnosed as having type 2 diabetes because they could develop insulin independence. Therefore, it is possible that some of the children commonly diagnosed as type 1 diabetic subjects may have a form of severe type 2 diabetes with non-autoimmune pathogenesis of their beta-cell damage and relative insulin deficiency. In our study, it was not possible to do a C-peptide test for the patients, but every characteristic of these cases led to type 1 diabetes diagnosis (most of them were lean, the beginning of the disease was abrupt, and all of them were using insulin at the time of diagnosis). In the future, it will be necessary to determine C-Peptide in the newly diagnosed cases to classify, without error, between type 1 and type 2 diabetes cases. Finally, we can conclude that the incidence of type 1 diabetes in Santiago, Chile showed a steady increase during the last 10 years.

Acknowledgements

The authors acknowledge the collaboration of the Juvenile Diabetes Foundation of Chile, hospitals, private clinics, diabetologists, and pediatricians of the metropolitan region of Santiago. This study was partially supported by Grant Fondecyt 1000944 and 1030680.

References

- Atkinson MA, McLaren NK. The pathogenesis of insulin-dependent diabetes mellitus. *N Engl J Med* 1994; **331**: 1428–1436.
- corpauWorld Health Organization DIAMOND Project Group on Epidemics. Childhood diabetes, epidemics, and epidemiology: an approach for controlling diabetes. *Am J Epidemiol* 1992; **135**: 803–816.
- Green A, Gale EAM, Patterson CC. Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE study. *Lancet* 1992; **339**: 905–909.
- Yang Z, Wang K, Li T, et al. Childhood diabetes in China. Enormous variation by place and ethnic group. *Diabetes Care* 1998; **21**: 525–529.
- Ko KW, Yang SW, Cho NH. The incidence of IDDM in Seoul from 1985 to 1988. *Diabetes Care* 1994; **17**: 1473–1475.
- Cruz-Coke R. Origen y evolución étnica de la población chilena (Ethnic origin and evolution of the Chilean population). *Rev Med Chil* 1976; **104**: 365–368.
- Larenas G, Montecinos A, Manosalva A, et al. Incidence of insulin-dependent diabetes mellitus in the IX region of Chile: ethnic differences. *Diabetes Res Clin Pract* 1996; **34**: S147–S151.
- Carrasco E, Pérez-Bravo F, Santos JL, et al. One of the lowest validated incidence of insulin dependent diabetes mellitus in the Americas: Santiago, Chile. *Diabetes Res Clin Pract* 1996; **34**: S153–S157.
- Instituto nacional de estadísticas (INE). Resultados generales. *Censo de Población y Vivienda 2002*, Santiago, Chile, 2002; <http://www.ine.cl>.

10. LaPorte RE, McCarty D, Tull E, *et al.* Beyond insulin-dependent diabetes mellitus registries: capture-recapture approaches for monitoring incidence. In *Standardization of Epidemiologic Studies of Host Susceptibility, NATO ASI Series*, Dorman J (ed). Plenum Press: New York, 1994; 7–12.
11. La Porte RE, McCarty DJ, Tull ES, Tajima N. Counting birds, bees, and NCD's. *Lancet* 1992; **339**: 18–19.
12. Onkamo P, Vaananen S, Karvonen M, Tuomilehto J. Worldwide increase in incidence of type I diabetes—the analysis of the data on published incidence trends. *Diabetologia* 1999; **42**: 1395–1403.
13. Casu A, Pascutto C, Bernardinelli L, *et al.* Type 1 diabetes among Sardinian children is increasing. *Diabetes Care* 2004; **27**: 1623–1629.
14. Newhook LA, Curtis J, Hagerty D, *et al.* High incidence of childhood type 1 diabetes in the Avalon Peninsula, Newfoundland, Canada. *Diabetes Care* 2004; **27**: 885–888.
15. Muntoni S, Muntoni S. New insights into the epidemiology of type 1 diabetes in mediterranean countries. *Diabetes Metab Res Rev* 1999; **15**: 133–140.
16. Report of morbidity in some infectious diseases (1950–1997). Ministry of Health: Santiago de Chile, 1997.
17. Serrano-Ríos M, Goday A, Martínez-Larrad T. Migrant populations and the incidence of type 1 diabetes mellitus: an overview of the literature with a focus on the Spanish-heritage countries in Latin America. *Diabetes Metab Res Rev* 1999; **15**: 113–132.
18. Fava D, Leslie RDG, Pozzilli P. Relationship between dairy product consumption and incidence of IDDM in childhood in Italy. *Diabetes Care* 1994; **17**: 1488–1490.
19. Nejentsev S, Koskinen S, Sjoroos M, *et al.* Distribution of insulin-dependent diabetes mellitus (IDDM)-related HLA alleles correlates with the difference in IDDM incidence in four populations of the Eastern Baltic region. *Tissue Antigens* 1998; **52**: 473–477.
20. Santos JL, Schaid D, Pérez-Bravo F, *et al.* Applicability of the case-parent design in the etiological research of type 1 diabetes in Chile and other genetically mixed populations. *Diabetes Res Clin Pract* 1999; **43**: 143–146.
21. Pérez-Bravo F, Carrasco E, Gutierrez-López MD, *et al.* Genetic predisposition and environmental factors leading to the development of insulin-dependent diabetes mellitus in Chilean subjects. *J Mol Med* 1996; **74**: 105–109.
22. Santos JL, Pérez-Bravo F, Carrasco E, Calvillán M, Albala C. Association between type 1 diabetes and HLA-DQ alleles in a case-parental study conducted in Santiago, Chile. *Am J Epidemiol* 2001; **153**: 794–798.
23. Pérez-Bravo F, Oyarzún A, Carrasco E, Albala C, Dorman J, Santos JL. Duration of breast feeding and bovine serum albumin antibody levels in type 1 diabetes: a case-control study. *Pediatr Diabetes* 2003; **4**: 157–161.