

Population-Based Incidence of IDDM in the State of São Paulo, Brazil

SANDRA R.G. FERREIRA, MD, PHD
LAERCIO J. FRANCO, MD, PHD
MARCO A. VIVOLO, MD

CARLOS A. NEGRATO, MD
ANTONIO C.P. SIMOES, MD
CARLOS R. VENTURELI, MD

OBJECTIVE— To study the incidence of IDDM among children, infants to 14 yr of age, in the state of São Paulo, Brazil, 1987–1991.

RESEARCH DESIGN AND METHODS— A prospective population-based register was established, using physician reports of newly diagnosed IDDM patients <15 yr of age as the primary source of case identification and school surveys as the main secondary source. Data were collected according to the methods recommended by the Diabetes Epidemiology Research International group.

RESULTS— Case ascertainment was estimated at 95.0, 92.8, and 98.8% complete for each of the three cities studied. The average annual IDDM incidence was 7.6/100,000 inhabitants (95% confidence interval, 5.6–9.7). We found a higher incidence rate in girls than boys.

CONCLUSIONS— The incidence of childhood IDDM in a tropical region in South America (São Paulo, Brazil) is in the middle incidence range observed in developed countries throughout the world. Increased incidence of IDDM in girls compared with boys will be tested by the ongoing Brazilian incidence study being developed in 18 other centers across the country.

In the last decade, epidemiological studies have been recognized as an important tool in the etiological research and public health administration of diabetes. Population-based registries of IDDM have been conducted world-

wide, and large geographic variations in incidence have been observed (1). A standardized approach for data collection is necessary to compare global patterns of the disease. This standardization was one of the goals of the WHO Multi-

national Project for Childhood Diabetes, known as DIAMOND. As part of the DIAMOND project, the Brazilian incidence study has contributed to the limited data concerning epidemiology of IDDM in Spanish- and Portuguese-heritage populations (2–4). Little information has been published from countries south of the equator (5), and in South America, IDDM incidence data are scarce. Brazilian population-based reports started in a defined population from the state of São Paulo in January 1987. Herein we present data prospectively collected during a 5-yr period in three centers from São Paulo, according to the methods recommended by DERI (1).

The state of São Paulo is considered a developed area, located in the southeastern part of Brazil, crossed by the Tropic of Capricorn. Migration from Europe, Africa, and Asia made the Brazilian population ethnically heterogeneous. The population also varies greatly by region. The majority of the Brazilian population is white (54%), followed by mulatto (39%), and black (6%); <1% is of Asian origin and only 0.1% is Amerindian, according to the national census from 1980.

In São Paulo, the population is 75% white, mainly of Portuguese and Italian origin, 5% black, 18% mulatto, and 0.9% Asian (6). This Brazilian state is a particularly developed part of the country. The three cities in our study—Bauru, Botucatu, and Rio Claro—had estimated populations of 220,105; 71,139; and 129,859, respectively, in 1987. The economies of these cities are diversified, with industry, trade, agriculture, cattle raising, and aviculture as principal activities. The level of literacy in these cities is satisfactory. All three cities have universities.

RESEARCH DESIGN AND METHODS

METHODS— The estimated population of children <15 yr of age for Bauru, Botucatu, and Rio Claro in 1991 was

FROM THE DEPARTMENT OF PREVENTIVE MEDICINE, ESCOLA PAULISTA DE MEDICINA, SÃO PAULO; THE DEPARTMENT OF PEDIATRICS, UNIVERSIDADE ESTADUAL DE SÃO PAULO, BOTUCATU, BRAZIL.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO SANDRA R.G. FERREIRA, MD, PHD, ESCOLA PAULISTA DE MEDICINA, DEPARTAMENTO DE MEDICINA PREVENTIVA, RUA BOTUCATU, 740 CEP 04023-062 SÃO PAULO-SP, BRAZIL.

RECEIVED FOR PUBLICATION 2 SEPTEMBER 1992 AND ACCEPTED IN REVISED FORM 28 JANUARY 1993.

IDDM, INSULIN-DEPENDENT DIABETES MELLITUS; WHO, WORLD HEALTH ORGANIZATION; DERI, DIABETES EPIDEMIOLOGY RESEARCH INTERNATIONAL; CI, CONFIDENCE INTERVAL.

Table 1— Number of cases 0–14 yr of age from the primary and secondary sources, ascertainment and estimated incidence rates of IDDM for each city

	BAURU 1990	BOTUCATU 1991	RIO CLARO 1991
PRIMARY SOURCE CASES	17	09	12
SECONDARY SOURCE CASES	09	08	13
TOTAL CASES*	19.0 ± 2.8	11.9 ± 2.3	14.2 ± 0.9
PRIMARY SOURCE ASCERTAINMENT (%)	89.5	75.9	84.7
SECONDARY SOURCE ASCERTAINMENT (%)	47.4	67.5	91.8
TOTAL ESTIMATED ASCERTAINMENT (%)	94.7	92.8	98.8
ESTIMATED INCIDENCE RATE (× 100,000)	6.8	9.7	6.9

*Data are means ± SD.

142,974. We selected these cities because they had reasonable health-care service and Juvenile Diabetes Foundation chapters. General practitioners, endocrinologists, and pediatricians from each city were our primary source of information.

All newly diagnosed IDDM patients <15 yr of age were registered from January 1987 through December 1991, using a standardized questionnaire. Patients had lived in the survey area for at least 1 yr. We validated identification with a standardized questionnaire sent to schools. Secondary sources were new members of the local diabetic associations, participants in events organized for young diabetic patients, and reply mail from a mailing list provided by a drug company. The schools were surveyed in Bauru in 1990 and in Botucatu and Rio Claro in 1991.

To determine completeness of ascertainment and to estimate the true number of incident cases in the population, we applied the Lincoln-Peterson capture-recapture method (7), modified according to Cochi et al. (8). The cases identified through secondary sources were compared with those identified by physician reports. We analyzed incidence rates each 12-mo period with a 95% CI based on the Poisson distribution. *P* < 0.05 was significant.

RESULTS— The validation procedure showed satisfactory completeness of our

lists from the primary sources in the three cities, through matching these records with data collected from the secondary sources. Total estimated ascertainment for the case registry was 94.7, 92.8, and 98.8% for Bauru, Botucatu, and Rio Claro, respectively (Table 1). With the degree of ascertainment >90%, observed and estimated IDDM incidence rates were very close (6.4 vs. 6.8, 9.0 vs. 9.7, and 6.8 vs. 6.9/100,000/yr for each city), and the former was used in our analysis. Although validation procedures were performed only in 1990 and 1991, we extrapolated the validity of the data for the entire study period.

During the 5-yr period, 52 newly diagnosed IDDM patients (20 boys and 32 girls) were identified by the primary sources for all three cities. The mean age at diagnosis was 9.9 ± 3.4 yr for boys and 7.6 ± 3.8 yr for girls. The average incidence rate over the 5-yr period for both sexes was 7.6/100,000 (95% CI,

5.6–9.7). The overall male-to-female ratio was 0.61 (0.27–0.95). Table 2 shows the average annual incidence rates by sex and age. Considering the CIs for IDDM incidence rates, no difference was detected between boys and girls. The highest IDDM incidence rates were found in the 5- to 9-yr-old age-group for girls and the 10- to 14-yr age-group for boys.

Despite no significant temporal variation in incidence rates during the study period, we noticed two peaks in 1988 and 1991 (Fig. 1A) and a parallel trend for both sexes (Fig. 1B). Although the rates did not differ between sexes during the calendar years of the study, particularly high female rates were found in 1988, 16.7/100,000 (95% CI, 6.8–26.6), and in 1991, 12.9/100,000 (95% CI, 4.5–21.3), whereas the male incidence rates were 7.4/100,000 (95% CI, 0.9–13.9) and 8.4/100,000 (95% CI, 1.7–15.0), respectively. To some extent, this parallel trend was also observed when age-specific incidences were compared (Fig. 1C).

CONCLUSIONS— Large geographic variations in IDDM incidence have been observed in many countries (1). Environmental and genetic factors may be involved in the etiopathogenesis of IDDM. It has been proposed that population variation in the prevalence of IDDM susceptibility genes is a primary determinant of the worldwide patterns of the disease (9). Although genetic factors are associated with increased risk for IDDM (10,11), geographic location also is an

Table 2— Age-specific and age-adjusted incidence rates of IDDM from 1987–1991 by sex

AGE-GROUP (YR)	BOYS	GIRLS	TOTAL
0–4	2.4 (0.0–5.1)	7.6 (2.6–12.5)	4.9 (2.2–7.7)
5–9	5.3 (1.1–9.6)	12.7 (6.0–19.3)	9.0 (5.0–12.9)
10–14	10.1 (4.1–16.0)	8.5 (2.9–14.0)	9.3 (5.2–13.5)
0–14	5.8 (3.3–8.3)	9.5 (6.2–12.8)	7.6 (5.6–9.7)
AGE-ADJUSTED RATE	5.7	9.5	7.6

Data are per 100,000/yr (95% CI).

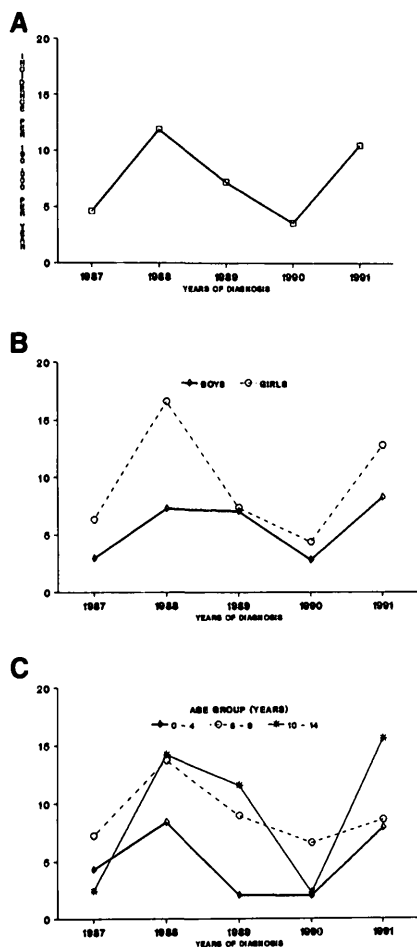


Figure 1—Annual IDDM incidence in children 0–14 yr of age in three cities from the state of São Paulo during the 5-yr study period (1987–1991). A: Age-adjusted incidence (Brazilian population, 1980 census). B: Incidence by sex. C: Incidence by age-group.

important determinant of risk (12). In general, developed countries in northern Europe and North America show higher incidence rates than those observed in developing countries (13).

We found the overall incidence rate among children 0–14 yr old in the three Brazilian cities studied for the period 1987–1991 to be 7.6/100,000/yr. This places São Paulo in the middle range of incidence, together with Italy, France, Poland, and Canada (3,14–16). The reasons for these findings are not

clear. We could speculate that the European descent, especially from Portugal and Italy, of the São Paulo population could influence IDDM incidence. In addition, the three cities studied should be seen as developed areas of Brazil. Thus, our findings are not necessarily representative of the whole Brazilian population.

A higher incidence rate for girls was verified in our study, in contrast to the excess risk for boys in populations of high incidences (13,17). On the other hand, recent data from 24 EURODIAB participating centers, a collaborative study of IDDM incidence in Europe, do not confirm the male excess, except for northern populations (3). In fact, preliminary data from western Australia, which like Brazil is a tropical country in the southern hemisphere, indicate girls were more likely than boys to be diagnosed with IDDM in the period from 1985–1989 (5). Although we observed an apparent female excess, analysis of our data does not show a statistical difference between sexes, and more information is necessary to define a sex-specific incidence pattern in Brazil.

Some fluctuations in incidence rates were found, with higher levels detected in 1988 and 1991 (Fig. 1A), but those variations did not reach statistical significance. Because the ongoing IDDM Brazilian registry was extended in 1991 to another 18 regional centers with different climatic and ethnic characteristics, our study represents, in the international context, a perspective of increasing contributions for clarifying the pattern of childhood IDDM risk in Portuguese-speaking populations. Studies have shown large incidence differences among children of Iberian heritage (2–4). Standard methods for accurate data collection, like those used in this study, are essential for geographic and racial comparisons in an attempt to identify determinants of IDDM throughout the world (18). Immunogenetic studies and the evaluation of racial admixture and local environmental factors also might provide

important data about the genetic environmental interaction.

Acknowledgments—This study was supported by the Brazilian Ministry of Health, the National Council for Scientific and Technological Development (CNPq), and the Juvenile Diabetes Associations in Brazil.

References

1. Diabetes Epidemiology Research International Group: Geographic patterns of childhood insulin-dependent diabetes mellitus. *Diabetes* 37:1113–19, 1988
2. Diabetes Epidemiology Research International Group: Evaluation of epidemiology and immunogenetics of IDDM in Spanish- and Portuguese-heritage registries. A key to understanding the etiology of IDDM? *Diabetes Care* 12:487–93, 1989
3. Green A, Gale EAM, Patterson CC: Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE Study. *Lancet* 339:905–9, 1992
4. Goday A, Castell C, Tresserras R, Canela J, Taberner JL, Lloveras G: Incidence of type 1 diabetes mellitus in Catalonia, Spain. The Catalan Epidemiology Diabetes Study. *Diabetologia* 35:267–71, 1992
5. Kelly HA, Byrne GC: Incidence of IDDM in Western Australia in children aged 0–14 yr from 1985 to 1989. *Diabetes Care* 15:515–17, 1992
6. Fundação IBGE: IX Recenseamento Geral do Brasil-1980. Rio de Janeiro, 1992, V.1, Tomo 4, p.10–11 14. Cormack RM: The statistics of capture-recapture methods. *Oceanogr Mar Biol Annu Rev* 6:455–506, 1968
7. Cormack RM: The statistics of capture-recapture methods. *Oceanogr Mar Biol Annu Rev* 6:455–506, 1968
8. Cochi SL, Edmonds LE, Dyer K, Greaves WL, Marks JS, Rovira EZ, Preblud SR, Orenstein WA: Congenital rubella syndrome in the United States, 1970–1985. On the verge of elimination. *Am J Epidemiology* 129:349–61, 1989
9. Dorman JS, Laporte RE, Stone RA, Trucco M: World differences in the inci-

- dence of type 1 diabetes are associated with amino acid variation at position 57 of the HLA-DQ β -chain. *Proc Natl Acad Sci* 87:7370–74, 1990
10. Tiwari JL, Terasaki PI: *HLA and Disease Associations*. New York, Springer-Verlag, 1985, p. 196–98
 11. Barnett AH, Eff C, Leslie RD, Pyke DA: Diabetes in identical twins. *Diabetologia* 20:87–93, 1981
 12. Diabetes Epidemiology Research International Group: Preventing insulin-dependent diabetes mellitus: the environmental challenge. *Br Med J* 295:479–81, 1987
 13. Rewers M, LaPorte R, King H, Tuomilehto J: Trends in the prevalence and incidence of diabetes: insulin-dependent diabetes mellitus in childhood. *World Health Stat Q* 41:179–89, 1988
 14. Levy-Marchal C, Papoz L, de Beaufort C, Doutreix J, Froment V, Voirin J, Czernichow P: Incidence of insulin-dependent diabetes occurring before 20 years of age in France. *Pediatric* 46:367–71, 1991
 15. Rewers M, LaPorte RE, Walczak M, Dmochowski K, Bogaczynska E: Apparent epidemic of insulin-dependent diabetes mellitus in Midwestern Poland. *Diabetes* 36:106–13, 1987
 16. Siemiatycki J, Colle E, Cambell S, Dewan R, Aubert D, Belmonte MM: Incidence of insulin-dependent (type 1) diabetes by ethnic group and by social class in Montreal, and comparisons with comparable ethnic group living elsewhere. *Diabetes* 37:1096–1102, 1988
 17. Akerblom HK, Reunanen A: The epidemiology of insulin-dependent diabetes (IDDM) in Finland and Northern Europe. *Diabetes Care* 8 (Suppl. 1):10–16, 1985
 18. The WHO Multinational Project for Childhood Diabetes Group. Familial insulin-dependent diabetes mellitus (IDDM) epidemiology: standardization of data for the DIAMOND Project. *Bull WHO* 69:767–77, 1991