Incidence of IDDM During 1984–1986 in Population Aged <30 Yr

Residents of Turin, Italy

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The goal of this study was to measure the incidence of insulin-dependent diabetes mellitus (IDDM) during 1984–1986 in residents of Turin, Italy, aged <30 yr. The primary data source was the list of all subjects diagnosed with IDDM who attended diabetes clinics in Turin. Other data sources were the general register of death certificates, the list of hospital discharges, and the computerized data base of insulin prescriptions. Eighty incident cases of IDDM were identified during the study in 1,130,284 person-yr for those <30 yr of age. Age-adjusted (world standard) incidence rates were 8.05, 8.10, and 6.96/100,000 in the age-groups 0–14, 0–19, and 0–29 yr, respectively. Estimated completeness of the primary data source compared with all other data sources was 91%, whereas the estimated completeness of ascertainment of the registry was 99%. Incidence rates of IDDM in northern Italy compare with those of European countries with low-medium incidence. A population-based register is being established for the province of Turin (951,445 inhabitants aged 0–29 yr) for the collection of incident cases since 1984. *Diabetes Care* 13:1051–56, 1990

Epidemiological studies in various parts of the world have provided evidence that the incidence of insulin-dependent diabetes mellitus (IDDM) differs widely among populations (1–8). Among the countries for which reliable estimates have been made, it appears that rates are relatively high in the Nordic countries of Europe, somewhat lower in Great Britain and North America, and lowest in Japan (9,10). The age-adjusted rates showed a 17-fold difference between the highest and the lowest rates of Finland (29.5/100,000) and Japan (1.7/100,000) (9).

The causes of these differences in the incidence of IDDM, e.g., genetic factors, environmental agents, and their possible interaction, remain unknown. Although genetic factors have been suggested by family and HLA studies (11,12), correlations of IDDM incidence with geographic patterns might reflect the presence of underlying environmental factors (9). These studies provide insight into the etiology of diabetes.

In the past few years, the World Health Organization has identified the development of population-based registries as one of the essential tools in diabetes research (13). The significance and the methodology of international collaboration have been reviewed during two workshops on IDDM registries held in Philadelphia in 1983 (14) and in Madrid in 1985 (15). Following the recommendations derived from those workshops, IDDM registries have been established worldwide. Currently, few studies are available for the Italian population (16–18).

The aim of this study was to measure the incidence of IDDM among residents <30 yr of age in the city of Turin (an industrial city in northern Italy) during 1984–1986.

RESEARCH DESIGN AND METHODS

This study focused on identifying all residents of Turin <30 yr of age with a diagnosis of IDDM from 1 January 1984 to 31 December 1986. Criteria used for diagnosis

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of IDDM were those defined by the National Diabetes Data Group (19). Serum or urine C-peptide levels were available for 80% of the subjects included in the study. The dependence on insulin treatment after years from the time of diagnosis was verified by examining in 1989 the clinical records of each subject included in the study.

Date of diagnosis was the start of insulin treatment. For each subject, the following information at diagnosis was collected: address, age, sex, height, weight, date of diagnosis, blood glucose, glycosuria, ketonuria, and dose of insulin at start of treatment. Serum or urine C-peptide levels after stabilization were also included (when available).

Four sources of data were used to ensure a case ascertainment as complete as possible, to identify prevalent cases to be excluded, and to evaluate the completeness of the primary data source (20). The primary data source was the list of all patients with a diagnosis of IDDM who attended 1 of 11 diabetes clinics from 1984 to 1986 in Turin, where people with diabetes are referred after diagnosis.

The study in the diabetes clinics was conducted by one person (G.B.). A random sample of 20% of the records was verified by duplicate collection of information by another person trained by us. No omission of cases or major errors in the collected information were found.

The second data source was the general register of death certificates for Turin. All certificates mentioning diabetes mellitus as the primary or contributory cause of death were abstracted for the years 1984–1986.

The third data source was the list of hospital discharges in the 0- to 29-yr-old age-group from the 35 public and private hospitals in Turin. Records were available for 1982–1984 from all public and private hospitals of the city, including the regional pediatric hospital, and for 1980–1981 and 1985–1986 in 5 public nonpediatric hospitals. The files of hospital discharges covered >80% of discharges of residents of Turin during 1984–1986, although the absence of records from the regional pediatric hospital in 1985–1986 was damaging to the completeness of this source in the 0- to 14-yr-old age-group.

The fourth data source was the computerized data base of insulin prescriptions (recorded in 3 nonconsecutive mo/yr) for 1984–1986. The data base includes the National Health Service identification number for both the patient and family physician. After a linkage with hospital records before 1984, we obtained a list of potential incidence cases for 1984–1986. A letter was sent to the family physician of each of the 96 patients appearing on the list in 1986 to verify the diagnosis of IDDM and the year of onset. All of the physicians replied, and one new incident case was identified. Due to the information needing to be supplied by the family physician and the fact that incident cases of 1984 and 1985 were probably on the insulin prescriptions data base in 1986, we decided not to write to physicians of insulin users from 1984 to 1985. The estimated completeness of the primary data source was computed with the capture-recapture method according to the Chapman estimator (21–23). The estimated completeness of the registry was computed as the proportion between the observed and the estimated number of incident cases (Table 1)

$$N = \frac{(M + 1)(n + 1)}{(m + 1)} - 1 = \frac{75 \times 70}{64} - 1 = 81$$

$$\text{variance } (N) = \frac{(M + 1)(n + 1)(M - m)(n - m)}{(m + 1)^2(m + 2)} = 1.30$$

where N is the estimated number of cases in the target population; M is the number of cases identified in the primary source, 74; n is the number of cases identified in any secondary source, 69; and m is the number of cases identified in both the primary and any secondary sources, 63. The 95% confidence intervals (CIs) of point estimate of $N = N \pm 1.96$. Variance $\sqrt{N} = 78.7, 83.2$. Estimated completeness of primary source, 74 of 81 = 91%. Estimated completeness of registry, 80 of 81 = 99%. Denominators of incidence rates were from the 1984, 1985, and 1986 population demographic files of residents, broken down by age (6 classes) and sex. De-

TABLE 1
Incidence cases of insulin-dependent diabetes mellitus for residents of Turin, aged 0–29 yr, from 1984 to 1986 by source of ascertainment

		Source			
	Cases (*n*)	Diabetes clinics (primary)	Hospital discharges (secondary)	Insulin prescriptions (secondary)	Death certificates (secondary)
	28	X	X	X	
	5	X	X		
	30	X		X	
	11	X			
	4		X	X	
	1		X		
	1			X	
Cases (*n*)	80	74	38	63	0

nominators of incidence rates over 1984–1986 were the sum of the denominators of the 3 yr (1,130,284 person-yr <30 yr of age). Rates were standardized (direct method) according to the world population to avoid spurious differences due to the age structure in the populations and to make all rates comparable (24). The 95% CIs, assuming a Poisson distribution of observed number of cases, were computed (25). Homogeneity of rates across monthly and seasonal subgroups were tested with the Roger test for cyclic trends in incidence data (26).

RESULTS

Eighty (32 in 1984, 24 in 1985, 24 in 1986) incident cases of IDDM in Turin were identified in the study in people aged 0–29 yr. Seventy-four cases were identified in the primary data source (patients attending diabetes clinics). No cases were identified from the general register of death certificates.

Three hundred seventeen subjects were identified from the list of the hospital discharge records from the 35 public and private hospitals of the city. Of these, 216 were recognized as prevalent by comparing the admission list of the study period (1984–1986) with the lists of the previous years. The medical records of the 101 remaining patients were examined to determine the year of diagnosis of diabetes. Fifty-five were recognized as prevalent, and 8 had coding errors in residence or disease classification. The remaining 38 were incident cases of the study period; only 5 had not been previously identified from the diabetes clinics.

Sixty-three incident cases were identified from the computerized data base of insulin prescriptions; only 1 had not been previously identified from diabetes clinics and hospital discharge records. The list of subjects included in the insulin prescription data base was verified by writing to the family physician only in 1986. Nevertheless, incident cases of 1984 and 1985 should have been on the insulin prescriptions data base in 1986 as well.

Table 1 shows cases by source of ascertainment. Seventy-four cases were identified by the primary data source, 69 by any secondary source, and 63 by primary and secondary sources. With regard to the completeness of the primary data source, we applied the capture-recapture method with the use of the Chapman estimator (21–23). The estimated number of incident cases in the target population in the study period was 81 (95% CI 78.7–83.2) when cases identified by any secondary source were matched to cases identified by the primary source. Therefore, the estimated completeness of the primary data source was 74 of 81 (91%), whereas the estimated completeness of the registry was 80 of 81 (99%).

Table 2 shows the year and age-specific incidence rates for 1984–1986. There are no differences in annual rates, as shown by the overlap of the CIs. Table 3 shows sex- and age-specific incidence rates for 1984–1986. Age-adjusted (world standard) incidence rates (for both sexes combined) per 100,000 were 8.05, 8.10, and 6.96 for the age-groups 0–14, 0–19, and 0–29 yr, respectively. The male-female ratio was ~1 for all age-groups, except in age-groups 5–9 and 20–24 yr. Our study showed no differences in monthly (R = 1.04, P = 0.59) or seasonal (R = 0.67, P = 0.72) incidence of IDDM.

DISCUSSION

A worldwide effort to improve and standardize methods of ascertainment of occurrence of IDDM has been underway in 24 registries because of the large geographic differences in the incidence of the disease. A limited comparison is possible in southern Europe because of the absence of registries in this area (9).

In Italy, few population studies have been conducted that used different sources of data (16–18). In Lombardy (a region of northern Italy), an estimate of incidence rate of IDDM based only on data from hospital admissions showed rates of 4.2 and 3.9/100,000 in the age-groups 0–14 yr and 15–34 yr, respectively (16). Another Italian study conducted in Vicenza, with case ascertainment based on insulin prescription and hospital discharge records, showed an incidence rate of 10.9/

TABLE 2
Age-specific incidence rates (per 100,000 person-yr) of insulin-dependent diabetes mellitus for residents of Turin from 1984 to 1986

	1984		1985		1986	
Age (yr)	Cases (*n*)	Age-specific incidence rate (95% CI)	Cases (*n*)	Age-specific incidence rate (95% CI)	Cases (*n*)	Age-specific incidence rate (95% CI)
0–14	17	10.18 (5.93–16.29)	12	7.61 (3.93–13.32)	14	9.84 (5.37–16.53)
0–19	23	9.36 (5.93–14.04)	20	8.50 (5.19–13.09)	19	8.81 (5.30–13.74)
0–29	32	8.13 (5.58–11.46)	24	6.27 (4.02–9.34)	24	6.78 (4.35–10.10)

95% CI, 95% confidence interval.

TABLE 3
Age-specific and age-adjusted (world standard) incidence rates (per 100,000 person-yr) of insulin-dependent diabetes mellitus for residents of Turin from 1984 to 1986

	Males		Females		Total		
Age (yr)	Cases (*n*)	Age-specific incidence rate (95% CI)	Cases (*n*)	Age-specific incidence rate (95% CI)	Cases (*n*)	Age-specific incidence rate (95% CI)	Age-adjusted world standard (95% CI)
0–4	3	4.84 (0.997–14.13)	3	5.11 (1.05–14.92)	6	4.97 (1.82–10.83)	
0–14	21	8.74 (5.41–13.37)	22	9.70 (6.08–14.65)	43	9.21 (6.65–12.43)	8.05 (5.81–10.87)
0–19	32	8.95 (6.14–12.62)	30	8.85 (5.97–12.66)	62	8.90 (6.88–11.50)	8.10 (6.27–10.47)
0–29	45	7.73 (5.64–10.36)	35	6.38 (4.45–8.87)	80	7.08 (5.65–8.85)	6.96 (5.55–8.70)
5–9	3	3.98 (0.82–11.62)	7	9.87 (3.96–20.33)	10	6.83 (3.28–12.57)	
10–14	15	14.59 (8.17–24.07)	12	12.35 (6.39–21.61)	27	13.50 (8.90–19.71)	
15–19	11	9.38 (4.68–16.79)	8	7.13 (3.07–14.05)	19	8.28 (4.98–12.92)	
20–24	9	7.67 (3.51–14.58)	2	1.85 (0.22–6.68)	11	4.89 (2.44–8.75)	
25–29	4	3.74 (1.02–9.57)	3	2.96 (0.80–7.58)	7	3.36 (1.35–6.92)	

95% CI, 95% confidence interval.

100,000 in the 0- to 29-yr-old age-group based on 11 patients in 1 yr (17).

A third study was based on notification of new cases of IDDM in 1981 by diabetologists from the Piedmont and Valle d'Aosta regions (18). After publication, the data were further validated (18). Of the subjects living in Turin, 12 were in the 0- to 14-yr-old age-group, 18 were in the 0- to 19-yr-old age-group, and 22 were in the 0- to 29-yr-old age-group, which provided incidence rates, respectively, of 5.95, 6.36, and 4.99/100,000.

This study, based on four independent data sources, provided incidence rates that were *1*) higher than in Lombardy, where only hospital admissions were used; *2*) lower than in Vicenza, where data sources similar to ours were used for 100,485 population-yr at risk vs. 1,148,220 in Turin; and *3*) higher than the data of the previous study in Turin, where only data from diabetes clinics were used.

Completeness of ascertainment was due to the high quality of the primary data source, as shown with multiple independent sources. In our region, it is unusual that a person with IDDM is not hospitalized at the time of the diagnosis and/or referred to a diabetes clinic. To estimate the small number of these cases, we used the computerized insulin prescriptions data base. In 1986, prevalent cases were distinguished from incident cases by writing to family physicians; therefore, the incident cases during 1984 and 1985 should have been on insulin in 1986. The only case exclusively identified by the insulin prescriptions data base was a diabetic patient who had been admitted to a hospital whose list of discharges was not available for the year of diagnosis.

No cases were identified through death certificates. Therefore, this source did not improve the registry completeness and is probably not worth including in future studies.

The capture-recapture method used to estimate completeness of ascertainment (21–23) assumes independence of the data sources, i.e., each subject must have an equal chance of being reported as a case of diabetes in the secondary sources, regardless of whether he/she was identified as a case by the diabetes clinic. This assumption was not completely met in our study, at least not for hospitalized people, who are more likely to go to a diabetes clinic. On the other hand, this assumption should be met for the insulin prescriptions data base. Any lack of independence of the data sources would bias our estimate and underestimate the real number of incident cases. In the study of new cases of IDDM in Turin in 1981, incidence rates were lower than the 1984–1986 rates (18). In the 1981 study, only one data source (notification of new cases by diabetologists with no exhaustive survey in the diabetes clinics) was used, and underreporting might have occurred.

Diagnostic criteria for IDDM are less problematic and easier to use in the 0- to 14-yr-old age-group. Nevertheless, we believe it is important to include at least the 0- to 29-yr-old age-group in a registry to avoid focusing only on part of the disease, which could be caused by different determinants in different age-groups. In our data, validity of diagnosis, i.e., the percentage of patients reported as having IDDM who actually had the disease (20), was confirmed by meeting two criteria: *1*) serum or urine C-peptide levels, available for 80% of cases, included in the study and *2*) the persistent dependence on insulin therapy, confirmed by the examination in 1989 of clinical records of all cases.

The difference in age-specific rates in 1984, 1985, and 1986 (8.1 vs. 6.3 vs. 6.8 for the 0- to 29-yr-old age-group) is, in our opinion, due to random instability of rates. Overreporting of prevalence cases in 1984 is unlikely in our study because of the procedures described herein for data collection.

The annual age-adjusted (world standard) incidence

for those <15 yr of age in Turin from 1984 to 1986 (8.05/100,000 person-yr) compares with the 1980 rates of European countries with low-medium incidence (Netherlands 9.7; GDR 7.0; Wielkopolska, Poland 4.5; Rhône, France 4.4) (9). The absence of previously validated data about our population does not exclude the possibility of rapid changes in the incidence rate of IDDM as observed in some populations (4,7–10,27). Nevertheless, there is no evidence that the same occurred in Turin from 1980 to our study period (1984–1986). The absence of significant differences in yearly (1984–1986) rates adds likelihood to the stability of rates. The comparison with European countries is not consistent with the previous observation of a strong gradient of incidence from north to south (9), because our rate is slightly higher than in France, Poland, and Germany, although the large range of our CIs must be taken into account. The cause of these geographic differences, e.g., a genetic factor, an environmental agent, or both, remain unknown, although specific environmental factors have been explored by analytical studies (28–32). The incidence rate observed in the Italian ethnic group living in Montreal is similar to ours and could be the result of genetic or environmental causes (life-style habits) shared by the original and migrant populations (3). Age of onset of IDDM and its peak in adolescence confirm data from other registries and studies (2–8,10). Our data show a male-female ratio of ~1 in every age-group except 5–9 yr and 20–24 yr. These results are in agreement with the Swedish register, which showed an excess of females in the 5- to 9-yr-old age-group (27), whereas no difference was shown in Montreal (33) and Pittsburgh (34); in Japan a male-female ratio of 0.7 was described (5). However, when CIs of incidence rates are compared, the difference is not statistically significant for any age and sex group of our study. Similarly, international comparison of CIs of incidence rates in the 0- to 14-yr-old age-group showed a statistically significant excess of males only in Hokkaido (Japan) and Finland (10). The absence of statistically significant differences in monthly or seasonal rates shown in our survey may be caused by the small numbers used in comparison of single months or seasons.

Finally, this study was useful in validating case ascertainment by different data sources and can be seen as the first step toward the establishment, according to the recommendations from the International Workshop of Philadelphia in 1983 (14), of a population-based (951,445 inhabitants aged 0–29 yr) register of IDDM in the province of Turin, a geographic area lacking information concerning the epidemiology of IDDM.

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