Sex Differences in Incidence of IDDM in Age-Group 15–29 Yr

Higher risk in males in Province of Turin, Italy

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OBJECTIVE — To report the incidence of IDDM in the age-group 0–29 yr in the Province of Turin, Italy (951,445 inhabitants 0–29 yr of age), over a 5-yr period (1984–1988) according to age, sex, and geographical region within the area and to identify any temporal trend.

RESEARCH DESIGN AND METHODS — The survey used as the primary data source the list of all patients attending diabetic clinics, and as secondary data source, used the list of hospital discharges for diabetes.

RESULTS — We identified 298 incident cases of IDDM in people 0–29 yr of age. Estimated completeness of ascertainment of the registry was 97%. Age-adjusted (world-standard) incidence rates were 7.40/100,000 (95% CI 6.28–8.71), 5.83 (4.95–6.86), and 6.70 (5.97–7.51), respectively, in the age-groups 0–14, 15–29, and 0–29 yr. Incidence was significantly higher in males than in females in the age-group 15–29 yr (7.36, 6.02–8.98, vs. 4.21, 3.12–5.56). An increasing incidence from rural areas to the greater Turin area (city and its industrial belt) was evident. No significant temporal trend during the study period was found, although year-to-year variability was evident, with the highest incidence in 1984.

CONCLUSIONS — This study suggests a high male-to-female ratio of incidence of IDDM after 14 yr; either sex hormones or different exposure to environmental determinants could be involved.

In recent years, the increasing interest of diabetologists in the epidemiology of IDDM has resulted in the worldwide institution of population-based registries (1). Incidence data are available in many geographical areas now, as part of either Eurodiab (2) or Diamond Projects (3), showing a striking dishomogeneous distribution of the disease. However, most available data are limited to the age-group 0–14 yr, which includes just a proportion of incident cases; in the light of the hypothesis that recently suggested (4) that determinants of IDDM could differ with age, further data in young adults are needed.

Recently, in Sweden, an area at high risk for IDDM, an increasing male-to-female ratio after puberty has been described in a survey including the age-group 15–34 yr, suggesting a role for sex hormones in the etiopathogenesis of IDDM (5). At this time, data on the incidence of IDDM in young adults in areas at lower risk, such as the Mediterranean countries, are limited (6–8).

A 3-yr survey in the age-group 0–29 yr in the city of Turin (7–8) was expanded to 5 yr (1984–1988) and to the population of the whole Province of Turin. Incidence was analyzed according to age, sex, seasonality, geographic subareas, and year of diagnosis.

RESEARCH DESIGN AND METHODS

The highly industrialized Province of Turin covers an area of 6830 km^2 in the Piedmont Region, in the northwestern part of Italy, and has 951,445 inhabitants 0–29 yr of age as of 1981 general census (city of Turin: 440,421; industrial belt: 181,720; rest of the province, mainly rural: 329,304).

Incident cases among residents of the city of Turin in 1984–1986 were identified in 1987 in a pilot survey (7,8), which showed a good validity and completeness of ascertainment of cases when the files of either diabetic clinics or hospital discharges were used. These two data sources were used to extend identification of cases to the whole Province of Turin since 1984. Inclusion criteria for rates estimates were as follows: *1*) diagnosis of IDDM from 1 January 1984 to 31 December 1988; 2) 0–29 yr of age at diagnosis; and 3) residence in the Province of Turin at onset of the disease. Criteria used for diagnosis of IDDM were those defined by National Diabetes Data Group (9). Date of onset of the disease was the start of insulin treatment.

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IDDM, INSULIN-DEPENDENT DIABETES; CI, CONFIDENCE INTERVAL.

Table 1—*Age-specific incidence rates (per 100,000 person-yr) of IDDM for residents of Province of Turin from 1984 to 1988*

Age (yr)	Males N	Males Age-specific incidence rate (95% CI)	Females N	Females Age-specific incidence rate (95% CI)	Total M/F	Total N	Total Age-specific incidence rate (95% CI)
0–4	12	4.98 (2.57–8.71)	11	4.82 (2.41–8.63)	1.03	23	4.90 (3.11–7.35)
5–9	23	7.84 (4.97–11.76)	19	6.78 (4.08–10.57)	1.16	42	7.32 (5.28–9.88)
10–14	46	11.75 (8.57–15.74)	37	9.86 (10.57–13.56)	1.19	83	10.82 (8.63–13.52)
15–19	41	9.22 (6.58–12.54)	19	4.47 (2.69–6.97)	2.06	60	6.90 (5.31–8.97)
20–24	32	6.90 (4.73–9.73)	21	4.84 (2.9959–7.41)	1.43	53	5.90 (4.38–7.79)
25–29	24	5.85 (3.75–8.72)	13	3.26 (1.73–5.57)	1.79	37	4.57 (3.22–6.28)
0–14	81	8.75 (6.98–10.94)	67	7.58 (5.87–9.74)	1.15	148	8.18 (6.94–9.63)
15–29	97	7.36 (6.02–8.98)	53	4.21 (3.12–5.56)	1.75	150	5.82 (4.94–6.85)
0–29	178	7.93 (6.84–9.20)	120	5.60 (4.66–6.72)	1.42	298	6.79 (6.06–7.61)

n, number of cases.

Statistical analysis

The estimated completeness of both the primary data source and the registry was computed with the capture-recapture method (10). Data on the age and sex composition of the population of the Province of Turin were available from the general census of 1981 and from subsequent intercensual estimates for 1984, 1985, 1986, and 1987. Incident rates for 1988 were computed from the 1987 estimates. Denominators of incidence rates over 1984–1988 were the sum of the denominators of each year (4,387,097 person-yr <30 yr of age). Rates were standardized (direct method) according to the world population. The 95% CIs were computed, assuming a Poisson distribution of observed number of cases (11). Homogeneity of rates across monthly and seasonal subgroups were tested with the Roger test for cyclic trends in incidence data (12).

RESULTS — During the study period, 298 incident cases of IDDM were identified in residents of the Province of Turin 0–29 yr of age.

The estimated number of incident cases in the study period, according to the capture-recapture method, was 306 (95% CI 299.02–312.98); therefore, the completeness of ascertainment was 97% (279 of 306). Corresponding proportions in the age-group 0–14 and 15–29 yr were, respectively, 99 (148 of 149) and 93% (150 of 161).

Table 1 and Table 2 show the sex- and age-specific incident rates for 1984–1988 in the Province of Turin and in different areas of the province. After age 5, rates were higher in males than in

Table 2—*Age-specific incidence rates (per 100,000 person-yr) of IDDM for different areas of Province of Turin from 1984 to 1988*

Age (yr)	Males N	Males Age-specific incidence rate (95% CI)	Females N	Females Age-specific incidence rate (95% CI)	Total M/F	Total N	Total Age-specific incidence rate (95% CI)
Greater Turin area (city and its industrial belt)							
0–14	58	10.07 (7.75–13.09)	50	9.16 (6.80–12.09)	1.10	108	9.62 (7.91–11.64)
15–29	56	6.74 (5.10–8.83)	37	4.70 (3.32–6.46)	1.43	93	5.75 (4.65–7.13)
0–29	114	8.10 (6.72–9.80)	87	6.53 (5.25–8.13)	1.24	201	7.34 (6.37–8.45)
Rest of the province (rural areas)							
0–14	23	6.57 (4.17–9.90)	17	5.03 (2.93–8.05)	1.30	40	5.82 (4.16–7.91)
15–29	41	8.41 (6.00–11.44)	16	3.39 (1.94–5.49)	2.48	57	5.94 (4.57–7.72)
0–29	64	7.64 (5.94–9.82)	33	4.08 (2.82–5.71)	1.87	97	5.89 (4.82–7.19)

n, number of cases.

Table 3—*Age-specific incidence rates (per 100,000 person-yr) of IDDM for residents of Province of Turin from 1984 to 1988*

	Age-Group (yr)					
	0–14		15–29		0–29	
Year	*n*	Age-specific incidence rate (95% CI)	*n*	Age-specific incidence rate (95% CI)	*n*	Age-specific incidence rate (95% CI)
1984	39	10.02 (7.15–13.63)	40	7.71 (5.40–10.49)	79	8.70 (6.93–10.87)
1985	30	8.07 (5.45–11.54)	37	7.04 (4.97–9.68)	67	7.47 (5.79–9.60)
1986	22	6.26 (3.92–9.45)	25	4.94 (3.20–7.31)	47	5.48 (4.03–7.28)
1987	30	8.95 (6.04–12.80)	24	4.68 (3.00–6.97)	54	6.37 (4.82–8.34)
1988	27	8.06 (5.31–11.77)	24	4.68 (3.00–6.97)	51	6.02 (4.47–7.95)

n, number of cases.

females, and the sex ratio tended to increase with age. Statistical significance (i.e., no overlapping between the two CIs) of the difference between sexes was attained for rates computed for ages 0–29 and 15–29. Age-adjusted (world-standard) incidence rates/100,000 were 7.40 (95% CI 6.28–8.71), 5.83 (4.95–6.86), and 6.70 (5.97–7.51), respectively, in the age-groups 0–14, 15–29, and 0–29 yr. As shown in Table 2, in both sexes <15 yr of age, rates were 1.5–2 times higher in the Greater Turin Area than in rural areas, whereas the corresponding difference after age 15 was negligible. A significantly higher incidence in males in the age-group 15–29 yr was evident just in the rural areas.

Table 3 shows the year and age-specific incidence rates from 1984 to 1988. No significant temporal trend was observed for all age-groups combined; rates were highest in 1984, although lower and upper limits of the 95% CIs slightly overlap. Our study showed no differences in monthly ($R = 0.95$, $P = 0.62$) or seasonal ($R = 1.18$, $P = 0.55$) incidence of IDDM.

CONCLUSIONS— In this survey, a significantly higher incidence of IDDM was found in males than in females in the age-group 15–29 yr. Few surveys including this age-group have been conducted in the past (13–18), mainly in high-risk areas; most of them showed a high male-to-female ratio after 14 yr. Recently in Sweden, a male predominance was described in the age-group 15–34 yr in a large population-based survey (5). The new incident data from Catalonia, Spain, shows a significantly higher incidence in males just in the age-group 15–29 yr (6), which is consistent with our data. Moreover, in Pittsburgh, a higher secondary attack rate in male than female siblings between 16 and 30 yr was described (19). These findings could suggest either an effect of sex hormones in the etiopathogenesis of IDDM or an increased male exposure to environmental determinants after 14 yr.

In this study, incidence rates in both sexes were higher in the greater Turin area than in the mainly rural remaining part of the province. The difference was limited to the age-group 0–14 yr. A significant sex difference in the age-group 15–29 yr was evident just in rural areas, suggesting that environmental factors could play a role. Urban-rural differences in incidence of IDDM were explored in some studies (15,19); however, no consistent data were found, with higher rates in rural areas in Scotland (20) but no significant difference in Wisconsin (15).

Temporal trends of incidence may help disentangle the relative roles of genetic and environmental factors. Our study shows no statistically significant increase in rates over the 5-yr survey. Nevertheless, variability was evident, with the highest incidence in 1984. This is consistent with peaks of incidence observed in the same period in Finland (21), Sweden (22), Poland (23), Allegheny County, PA (23), the Virgin Islands (24), and Jefferson County, AL (25). These might point to environmental determinants across countries.

In conclusion, our study showed an increasing male-to-female difference of IDDM incidence after age 14, suggesting either a role for sex hormones or an increased male exposure to environmental determinants after 14 yr of age.

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APPENDIX— THE PIEDMONT STUDY GROUP FOR DIABETES EPIDEMIOLOGY—Vittorio Battistini, Pierdomenico Bertello, Graziella Bruno, Valen-

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