Temporal Variation in Incidence of IDDM in Canterbury, New Zealand

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OBJECTIVES — To establish the statistical significance of observed variations over the last decade in the incidence of insulin-dependent diabetes mellitus (IDDM) in the 0- to 19-yr-old age-group and to determine whether incidence has increased in Canterbury, New Zealand.

RESEARCH DESIGN AND METHODS — The Canterbury, New Zealand, Diabetes Registry has recorded all incidence cases of diabetes mellitus prospectively since 1982. All IDDM subjects aged 0–19 yr at diagnosis and using insulin are included in the study. Ascertainment is believed to be 100%. Prevalence was recorded at 1 January 1982 and 1 January 1990. Annual incidence for 1982–1990 was determined using age and sex cross-sectional census population denominators. The statistical significance of temporal, age, sex, and seasonal variations in incidence rates was ascertained by Poisson regression models (GLIM statistical software).

RESULTS — Prevalence on 1 January 1990 was 115/100,000. Incidence rates during the 9 yr were periodic, with two major peaks—one in the early 1980s, the other in 1989 continuing into 1990. The temporal variation ($P < 0.02$) was not age or sex specific. Incidence rates for boys were three- to fourfold higher during peak versus trough years, with a peak level of 20.7/100,000 in 1990. For girls, there was less variation, with a peak rate of 21.6/100,000 in 1990. There has been no significant increase in IDDM incidence over time. The mean rate of incidence across all age-groups for 1982–1990 was 12.7/100,000 person-yr. A significant seasonal association to the onset of IDDM was found only in boys, with incidence rates being significantly higher in winter than in summer ($P < 0.01$).

CONCLUSIONS — IDDM in Canterbury, New Zealand, presents in cycles of incidence peaks and troughs, each spanning 2–3 yr.

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RECEIVED FOR PUBLICATION 11 JANUARY 1991 AND ACCEPTED IN REVISED FORM 4 DECEMBER 1991.

Prospective monitoring of incidence rates of insulin-dependent diabetes mellitus (IDDM) may give important clues to determining disease etiology and preventive approaches (1–4). Environmental factors are believed to be major contributors to the onset of IDDM (5). These factors may act as a trigger in individuals who have an underlying genetic susceptibility for the β-cell destruction process. The intensity and frequency of individuals' exposure to environmental risk factors accounts for some of the variation in incidence rates observed among communities around the world, especially among populations that have genetic similarities. Incidence rates within communities would also be expected to vary in response to fluctuations in the environment. Temporal trends in the incidence of IDDM may reflect periodic increases or decreases as one or more diabetogenic factors are introduced or removed from the environment.

During the past decade, IDDM rates from numerous countries have increased (1–4). For example, in Allegheny County, Pennsylvania (6), there was a rise in incidence rates during 1982–1983 in those <10 yr. In Wielkopolska, Poland, all age-groups 0–16 yr showed an increase between 1982 and 1985 (1,6). Short-term increases in incidence rates have also been reported in Scandinavia and Canada (3,7,8), with marked cyclic variation reported from Rochester, New York (9) and Vasterbotten, Sweden (8). No changes have been reported in most studies from North America (3,6).

This study reports variation in the incidence rate of IDDM in Canterbury, New Zealand. It has been suggested that attack rates for IDDM are increasing in countries of the South Pacific (3,10). Using the database of the Canterbury Insulin-Treated Diabetes Registry (11–13), we examined: *1*) whether rates of IDDM in the 0- to 19-yr-old age-group have been stable over the last decade, *2*) whether temporal variations in incidence rates differed along age and sex lines, and *3*) whether

there are seasonal associations to the onset of IDDM in New Zealand.

RESEARCH DESIGN AND METHODS

— The Canterbury Registry of diabetic individuals is population based. The methods involved in its development and validation have been reported previously (12). The registry includes demographic data on all individuals, regardless of age, who are usually resident in Canterbury, New Zealand (population 350,000) and who are treated with insulin on a long-term basis for diabetes. New cases of IDDM are added to the registry on a prospective basis. Children and adolescents with IDDM are treated at no personal cost within this geographic area by a single hospital authority, either by the Pediatric Section or the Specialist Adult Diabetes Services. Data collected include nationwide hospital registration number, date of birth, sex, date of diagnosis (based on the first biochemical test confirming diabetes mellitus), and date of insulin initiation. Data on family history, clinical status, and immunobiochemical characterization are collected but are not included in this report.

Cases are identified through regular contact with medical and paramedical personnel of Diabetes Services and ongoing surveillance of medical records. Virtually all patients aged 0–19 yr living in the study area are treated by one of three specialists who provide diabetes care in this institution (R.S.S., M.P.M., and B.A.D.). Any missing data can be obtained by direct patient contact.

An independent check on ascertainment is made through contact with the lay Diabetes Society and through retail pharmacy surveys that monitor insulin use in the community. Ascertainment is believed to be 100%, as all eligible cases in the secondary sources had been previously identified on the registry. Since initiation of this study, no incidence case has been identified later than 6 mo after diagnosis; 95% were included on the registry within 4 wk of diagnosis.

Age and sex cross-sectional population denominators used to calculate prevalence and annual incidence rates for 1982–1990 were obtained from the New Zealand Department of Statistics. These denominators were pulled from the national censuses of 1981, 1986, and 1991. In 1982, there were 58,082 boys and 55,809 girls age 0–19 yr; these numbers fell to 53,047 and 51,392, respectively, by 1990.

Statistical methods

Prevalence data have been determined for 1 January 1982 (at the commencement of the study) and 1 January 1990. Incidence data are presented by age of onset for age-groups 0–4, 5–9, 10–14, and 15–19 yr, using population denominators for each age-group. Seasonality was defined by month of diagnosis. In New Zealand, the summer months are December through February, the winter months, June through August. Ninety-five percent confidence intervals (CI) for prevalence and incidence rates were estimated, assuming a Poisson distribution for the observed number of cases (14). χ^2 tests were used to analyze statistical significance of differences among rates.

Poisson regression models were fitted to the annual incidence data using maximum likelihood estimations in the GLIM statistical package (15). The risk of developing IDDM <20 yr of age was modeled as a function of age, sex, calendar time (yr), seasonality, and interactions among these factors. Calendar time was divided into four categorical time periods: 1982–1983, 1984–1985, 1986–1988, and 1989–1990. To determine whether there was a linear trend in incidence rates, a linear term for the time variable was fitted to the model. These statistical methods have been described previously (2,3,6). The obtained deviance is a measure of the discrepancy between observed and fitted values in the generalized linear model. A significant effect of the variables and their interactions was assessed using likelihood ratio statistics.

RESULTS

— Prevalence of IDDM in Canterbury at 1 January 1990 was 115 cases/100,000 individuals (95% CI, 96–138/100,000). There were no significant differences between the sexes (males 108/100,000 with 95% CI, 83–141/100,000; females 123/100,000 with 95% CI, 95–159/100,000). These sex-specific rates were no different from those determined for 1 January 1982—100/100,000 (95% CI, 83–120/100,000).

The mean annual incidence data for children and adolescents 0–4, 5–9, 10–14, and 15–19 yr, diagnosed as having IDDM in Canterbury during the 9-yr study period, are presented in Table 1. The highest incidence rates are among those 10- to 14-yr-old, with the age-specific rate for that group being significantly higher than for the two younger age-groups ($P < 0.01$).

Sex-specific annual incidence rates are shown in Fig. 1. These rates varied markedly over time, particularly among boys. High attack rates occurred in boys in 1984–85, followed by a decline during 1986–1987, subsequently increasing again in 1989 with a three- to fourfold difference between trough rates and peak rates. Among girls, annual rates were more stable; but peak rates also were observed in 1989 and 1990.

Incidence rates for boys were significantly higher ($P < 0.01$) in winter months (20.2/100,000 person yr with 95% CI, 13.1–29.8/100,000) than summer (incidence 6.4/100,000 person yr with 95% CI, 2.8–12.6/100,000) (Fig. 2). In contrast, incidence peaked in summer for girls (16.0/100,000 person yr with 95% CI, 9.6–25.0/100,000), but seasonal differences in incidence rates were not statistically significant.

Regression modeling

The statistical significance of age, sex, temporal, and seasonal variations in incidence rates over 1982–1990 was ascertained using Poisson regression models (Tables 2 and 3). Age was the most significant predictor of IDDM risk ($P = 0.001$; model 2; Table 2). The fit of

Table 1—*Mean annual incidence rates and case numbers for insulin-dependent diabetes mellitus, 1982–1990, in Canterbury, New Zealand*

	BOYS			GIRLS			TOTAL		
	POPULATION AT RISK*	*N*	INCIDENCE RATE†	POPULATION AT RISK*	*N*	INCIDENCE RATE†	POPULATION AT RISK*	*N*	INCIDENCE RATE†
AGE-GROUP (YR)									
0–4	11,679	7	6.6 (2.7–13.6)	11,280	10	9.9 (4.7–18.1)	22,959	17	8.2 (4.8–13.2)
5–9	12,018	9	8.3 (3.8–15.8)	11,646	10	9.5 (4.6–17.6)	23,664	19	8.9 (5.4–13.9)
10–14	14,571	24	18.3 (11.7–27.3)	14,085	27	21.3 (14.0–31.0)	28,656	51	19.8 (14.9–26.3)
15–19	16,803	23	15.2 (9.6–22.8)	15,783	13	9.1 (4.9–15.6)	32,586	36	12.3 (8.6–17.0)
TOTAL									
0–19	55,071	63	12.7 (9.8–16.3)	52,794	60	12.6 (9.8–16.3)	107,865	123	12.7 (10.5–15.1)

N, number of cases.
*Midpoint 1986 census data.
†Incidence rates expressed as cases per 100,000 of age-specific person-yr with 95% confidence intervals in parentheses.

the model was not significantly improved by the inclusion of either sex as a main effect or an age-sex interaction term (models 3 and 4). Therefore, temporal variation in IDDM risk was evaluated after adjusting for the effect of age only. Sex was retained as part of the hierarchical modeling only to investigate a possible sex-time interaction.

The significance of temporal variability was evaluated by the inclusion of the categorical time variable into the regression model (model 5). This shows that IDDM incidence rates varied significantly ($P = 0.014$) between 1982 and 1990 (Fig. 1). Instead, the incorporation of a linear term for time (trend) with one degree of freedom did not improve the fit of the model to the data (model 6), indicating that there was no significant trend for an increase in incidence over 1982–1990. The temporal variability could not be explained by differential effects over time among age-groups or sexes because incorporation of their interaction terms were not significant (models 7 and 8). The conclusions from these analyses are that IDDM rates have not increased over the past decade but there has been significant variability within this period for both sexes and for all age-groups.

The data were remodeled using the variables time, season, and sex (Table 3) to determine whether there was a seasonal component to the temporal variability (i.e., were incidence peaks and troughs related to season?). IDDM risk was found to be significantly related to season (model 11), after adjusting for significant variation in incidence among the four time periods (model 10). Inclusion of the season-sex interaction variable also significantly reduced the deviance in fit ($P = 0.048$; model 13), thus indicating that seasonal presentation of IDDM in Canterbury is significantly different between the sexes (Fig. 2). The incorporation of the interaction term season-time was not significant (model 14), demonstrating that changes over time in incidence rates have been proportional across the four seasons.

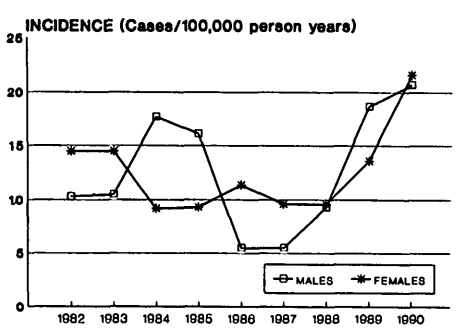

Figure 1—*Incidence of insulin-dependent diabetes mellitus, 0–19 yr of age, 1982–1990.*

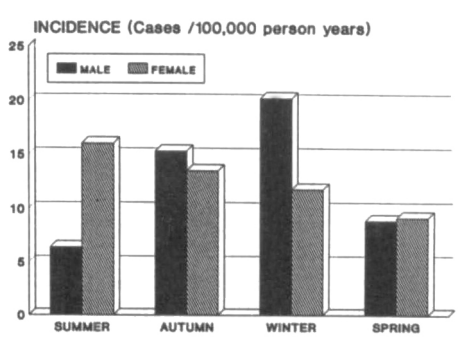

Figure 2—*Seasonal variation in insulin-dependent diabetes mellitus.*

Table 2—*Summary of regression modeling of insulin-dependent diabetes mellitus risk in the age-group 0–19 yr, 1982–1990*

Model	Deviance	df	Likelihood ratio statistics: Deviance	df	P
1. C	65.8	31			
2. C, AGE	48.7	28	17.0	3	0.001
3. C, AGE, SEX	48.7	27	0.0	1	1.000
4. C, AGE, SEX, AGE × SEX	45.4	24	3.3	3	0.348
5. C, AGE, TIME	38.1	25	10.6	3	0.014
6. C, AGE, TREND	47.4	27	1.3	1	0.254
7. C, AGE, TIME, TIME × AGE	33.5	16	4.6	9	0.868
8. C, AGE, TIME, SEX, TIME × SEX	33.5	21	4.5	4	0.343

C, constant; age, 4 age-groups: 0–4, 5–9, 10–14, 15–19 yr; time, 4-yr groups: 1982/1983, 1984/1985, 1986/1987/1988, 1989/1990; trend, linear time variable.

CONCLUSIONS— Sudden changes in incidence of IDDM have been reported in certain populations (3,6), and IDDM has been described as presenting in epidemic fashion (1). The current data derived from the Canterbury, New Zealand, Diabetes Registry are consistent with the hypothesis that incidence rates can exhibit cyclic trends and that increases and decreases in incidence are of relatively short duration.

Observers of many other populations worldwide noted an increase in IDDM incidence in the early to mid 1980s, but in Canterbury, this was followed by a fall in attack rates. Incidence rates for boys were threefold higher in 1984–1985 than 1985–86. Current data indicate that a further cycle of increased incidence is occurring in Canterbury, which commenced in 1989 and continued into 1990. Ongoing prospective monitoring will establish whether this represents a real increase or whether, as is more likely, it is simply another short-term cycle.

It has been suggested that the incidence of IDDM has been rising over the last decade in New Zealand (10) and other areas of the Pacific (3). However, this conclusion is not supported by the incidence data from Canterbury. The differences may represent racial-geographical variation, but basic epidemiological and methodological problems for primary and secondary ascertainment and determination of population denominators are more likely the explanation.

The dramatic and rapid fluctuations in incidence rates in the Canterbury area of New Zealand can be interpreted in two ways. First, environmental factor or factors act on individuals who already have β-cell damage to precipitate clinical diabetes. Second, an environmental factor that triggers IDDM is introduced or withdrawn over relatively short time periods, e.g., yearly. The latter explanation implies a brief latency period between the environmental trigger and the clinical presentation. A long time interval would tend to result in gradual changes in IDDM incidence rather than these observed patterns of cyclic increases spanning a few years. Countries that show marked incidence variability may be suitable for further investigation of environmental factors and IDDM causation.

Table 3—*Regression modeling of seasonal variation in insulin-dependent diabetes mellitus risk in the age-group 0–19 yr, 1982–1990*

Model	Deviance	df	Likelihood ratio statistics: Deviance	df	P
9. C	43.5	31			
10. C, TIME	33.2	28	10.3	3	0.016
11. C, TIME, SEAS	23.2	25	10.0	3	0.019
12. C, TIME, SEAS, SEX	23.2	24	0.0	1	1.000
13. C, TIME, SEAS, SEX, SEASON × SEX	15.3	21	7.9	3	0.048
14. C, TIME, SEAS, SEX, SEASON × SEX, SEASON × TIME	11.1	12	4.2	9	0.898

C, constant; time, 4 yr groups: 1982/1983, 1984/1985, 1986/1987/1988, 1989/1990; seas, summer (December-February), autumn (March-May), winter (June-August), spring (September-November).

Acknowledgments— This study was supported by the Health Research Council of New Zealand, the New Zealand Lottery Board, the Canterbury Medical Research Foundation, and the Mundy Trust for Diabetes.

We appreciate the assistance of Dr. R. LaPorte and colleagues participating in the Diabetes Epidemiological Research International Study Group.

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