The Incidence of Insulin-dependent Diabetes Mellitus in Israeli Children and Adolescents 0–20 Years of Age: A Retrospective Study, 1975–1980

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A survey of the entire population of Israel revealed 392 newly diagnosed type I diabetic children and adolescents aged 0–20 for the period of 1975–80. The mean annual age specific incidence of type I (insulin-dependent) diabetes mellitus was $3.8/10^5$ for the age group 0–14 yr and $4.2/10^5$ for the age group 0–20 yr. The incidence among the Jews of Ashkenazi origin was 6.8×10^5 and that for Jews of non-Ashkenazi origin was 4.3×10^5, whereas that for the Arabs was 1.2×10^5. The overall incidence is lower than that reported for similar populations in most European countries, the USA, Canada, and New Zealand; similar to that reported for Arabs in Kuwait; and higher than only that found in Japan. The relative importance of environmental and genetic factors in the interpopulation differences in incidence of type I diabetes remains to be established. DIABETES CARE 1985; 8 (SUPPL. 1):24–28.

Due to a lack of registration of cases with diabetes mellitus and the difficulty in obtaining full ascertainment in many places in the world, there have been only a few epidemiologic studies of the incidence of type I (insulin-dependent) diabetes mellitus (IDDM) in childhood and adolescence.

Available data demonstrate wide differences between regions, countries, and populations.[1] It was therefore thought to be of particular interest to carry out a survey of the incidence of type I diabetes in the age groups 0–20 yr in Israel, which has a population comprising a number of genetically distinct ethnic groups with divergent life-styles as well as a health system enabling full nationwide accrual of newly diagnosed cases.

SUBJECTS AND METHODS

Type I diabetic individuals are defined as patients who require insulin therapy immediately upon diagnosis of the disease.

Data collection. All patients newly diagnosed as type I diabetes during the years 1975–80 were identified by reviewing the diagnostic files in all diabetic specialty clinics, institutes of endocrinology, and acute care hospitals in Israel. The medical records were abstracted for sex, date of birth, ethnic origin determined by country of birth of parents preceding generations, as well as date and age at which the diabetes-related symptoms became evident.

Statistical analysis. The mean annual incidence was calculated on the basis of the mean population for the study period. The population data were obtained from the publication by the Central Bureau of Statistics.[2] The incidence was expressed as number of patients per 100,000 of the population in the same ethnic and age group. Ninety-five percent confidence limits for the rates were calculated on the basis of Poisson distribution. Statistical comparison of the men/women ratio in the total population as well as between years was done by χ^2 test. The significance of the excess of cases in one-half the year was tested by comparing the observed proportion with 0.5.

RESULTS

Incidence. During the 6-yr period, 392 newly diagnosed IDDM subjects aged 0–20 yr were registered in Israel (Table 1). The mean annual incidence for the study period was 3.8 (95% confidence limits 3.3–4.2) for the 0–14-yr and 4.2 (95% confidence limits 3.8–4.6) for the 0–20-yr groups. There were nonsignificant fluctuations in incidence over the years, the lowest incidence rates for both age groups being observed in 1975 (3.0 and 3.8, respectively) and 1980 (3.3 and 4.2) and the highest in 1978 (4.5 and 4.8) (Table 2).

Age at diagnosis. The distribution of the patients according to age at diagnosis is shown in Table 3. The highest proportion was registered between ages 10–14 yr and the lowest at 0–4. This trend was similar in the three ethnic groups. In age group 0–4 yr, a significantly higher rate was observed among females ($P = 0.02$), while in the other age groups, rates were similar in both sexes.

TABLE 1
Distribution of type I diabetic subjects in Israel (aged 0–20 yr at diagnosis, by sex and year of diagnosis)

Year	No. of cases	Male	Female
1975	56	25	31
1976	70	36	34
1977	63	44	19
1978	74	36	38
1979	73	27	46
1980	56	24	32
Total	392	192	200

Seasonal variation. Among the 294 patients for whom the month of onset could be established with credibility, there appeared to be a seasonal variation: 170 cases, a significantly higher proportion ($P < 0.01$), had their onset in the months from November to March, as compared with 124 cases in the months from April to October.

Ethnic origin. Significant differences in incidence of type I diabetes in ages 0–20 yr were noted between the two main Jewish ethnic groups in Israel as well as between each of the two groups and the Arabs (Table 4). In the Jewish population, the children of Ashkenazi parents have a 1.6-times-higher incidence of diabetes than those of nonAshkenazi parents ($6.8–4.3/10^5$, respectively). The offspring of the Arab population had the lowest incidence ($1.2/10^5$), which was less than one-third that of the nonAshkenazi Jews and less than one-fifth that of the Ashkenazi Jews.

DISCUSSION

The results of this survey show that the overall incidence of type I diabetes in both the Jewish and Arab populations in Israel is one of the lowest in the world, much lower than that reported for Caucasian populations in Europe, North America, and New Zealand (Table 5); similar to that reported for Kuwait;[13] and higher than only that found in Japan.[15] These findings are consistent with previous studies carried out in Israel in 1963 and 1968 by Cohen, which showed a low prevalence of type I diabetes in children aged 2–16 yr.[16]

The low rate of IDDM in Israel does not seem to be due to incomplete ascertainment of cases. While in Israel there is no central registry, due to the continuous educational program started by us 20 yr ago and the resulting greater awareness of the problem of diabetes in children, most juvenile patients are diagnosed at an early stage of the disease.[17,18] Newly diagnosed diabetic children and adolescents are invariably referred at diagnosis to hospital emergency wards or regional diabetes clinics, including our institute. Since our institute serves the most densely populated region in Israel and is also a national reference center for complicated cases, from 50% to 60% of the type I diabetic children and adolescents in Israel are referred to our clinic. Treatment solely by a private physician is unlikely because everyone is a member of a health insurance institution with complete lifetime coverage of all expenses without difference in any of the ethnic groups. Thus, while for routine purposes a patient may be seen privately, every affected individual will be under long-term follow-up in a regional endocrinology-diabetes service. It thus seems that case ascertainment was practically complete.

Of particular interest is the marked difference found between the three major ethnic groups in Israel, with decreasing incidence from the Ashkenazi through the nonAshkenazi Jews, with the lowest rate in the Arab population. It is of note that the age-specific onset pattern is nevertheless similar in the three ethnic groups. The ancestry of Ashkenazi Jews lived among Caucasian populations in Europe for hundreds of years, while the nonAshkenazi came from Mediterranean and Mid-Eastern countries. This resembles the pattern that emerges from the currently available, worldwide studies (Table 5), namely highest incidence of type I diabetes in Northern Europe, decreasing toward the Mediterranean and still further in Eastern Asia. It should be noted that the surveys from North America and New Zealand covering populations of Anglo-Saxon origin, present an intermediate rate similar to that of England. The low incidence reported from France, so different from that of its neighbors, can perhaps be explained by vicinity to the Mediterranean region or by inclusion of many patients of North African origin, a group that may have an incidence as low as that of the Israeli or Kuwaiti Arabs, if it is not due to incomplete ascertainment. The interethnic group differences in Israel cannot be explained on the basis of differences in socioeconomic conditions because almost all patients belong to what is considered the middle class.

It is of note that type II diabetes in the Jewish population of all origins in Israel presents one of the highest prevalence rates in the world and the trend regarding interethnic differ-

TABLE 2
Incidence of newly diagnosed type I diabetic subjects in Israel according to age and year of diagnosis

	0–14 yr		0–20 yr	
Year	No. of cases	Incidence per 10^5	No. of cases	Incidence per 10^5
1975	35	3.0	56	3.8
1976	41	3.6	70	4.8
1977	48	4.1	63	4.2
1978	55	4.5	74	4.8
1979	56	4.4	73	4.6
1980	42	3.3	56	3.4*
Total	277		392	
Mean annual incidence		3.8		4.2
(95% Confidence limits)		(3.3–4.2)		(3.8–4.6)

*In 1980 a few patients, aged 18–20 yr, might have been inadvertently omitted due to misplacement of some of the medical records in three medical centers.

TABLE 3
Incidence of newly diagnosed insulin-dependent diabetic subjects in Israel, 1975–80, according to age and sex

Age (yr)	N	Rate/10^5	No. of men	Rate/10^5	No. of women	Rate/10^5
0–4	44	1.6	15	1.0	29	2.1
5–9	107	4.5	56	4.6	51	4.4
10–14	145	6.9	71	6.6	74	7.2
15–20	96	4.7	50	4.7	46	4.6
Total	392	4.2	192	4.0	200	4.4

ences is reversed—the prevalence rate for ages 40–70 yr in the nonAshkenazi as compared with the Ashkenazi group being 15.7 versus 11.9, respectively.[19]

The challenge with which we are faced lies in finding the reason for these differences. Once the answer is obtained, it will not only provide a better understanding of the etiology of diabetes but may pave the way for preventive intervention programs.

The knowledge accumulated up to now indicates that type I diabetes results from an interaction between a genetic predisposition, possibly marked by specific HLA antigens[20] and environmental factors linked to virus infection,[21] which together initiate immunogenic reactions,[22] which in turn lead to a progressive destruction of the pancreatic beta cells. Still to be clarified are the genetic and environmental factors that cause the regional differences in incidence, and the relative importance of each. In Japan, which has the lowest incidence, 83% of these patients have HLA MT3 and DR8 antigens.[23] In Caucasian populations, in contrast, approximately 90% of patients carry HLA antigens DR3 and DR4.[20] However, in the Jewish population of Israel (both Ashkenazi and non-Ashkenazi), which has a much lower incidence, type I diabetes is also associated with DR3 and DR4 HLA types.[24] Thus, these data again indicate that the presence of the HLA antigens associated with a high risk of type I diabetes is insufficient, and that other genetic and environmental factors will have to be found to account for the marked geographic differences. The significantly increased rate in females below age 5 yr in our population is unexplained.

Some countries have reported finding an increasing prevalence of diabetes in childhood in recent years.[25] In our data, the difference in incidence between the years 1975–76 and 1977–80 may also indicate such a trend but this remains to be verified in the future.

There can be no doubt that additional epidemiologic studies should be undertaken whenever possible in the world, and particularly in countries having migrant populations. Environmental factors such as nutrition and infections should also be studied in greater detail. A worldwide effort and the continuing accumulation of data should further our progress in solving the riddle of diabetes.

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TABLE 4
Mean annual incidence of type I diabetes 0–20 yr of age, in Israel (1975–80) according to ethnic group and sex

Ethnic group	No. of patients	Rate (10^5)	95% Confidence limits	Women:men ratio
Jews				
Ashkenazi	183	6.8	5.8–7.8	1:1.10
NonAshkenazi	185	4.3	3.7–5.0	1:1.09
Arabs	24	1.2	0.6–1.6	1:0.71
Intergroup statistical significance			$P < 0.01$	NS

TABLE 5
Comparative incidence of type I diabetes in childhood and adolescence in various countries

Location	Period of study	No. of subjects	Incidence/10^5 children of same age groups (yr)			Reference no.
			0–14	0–16	0–20	
North America						
Allegheny County	1965–76	1176			14.6	3
Erie County, N.Y.	1948–72	366		6.1–11.0		4
Michigan	1958–72	2816		20†		5
Montreal	1971–77	522		8.8		6
Toronto	1976–78	132		9.0		7
Europe						
Finland	1970–79	3011	28.6		27.3‡	8
Sweden	1977–80	369	22.6			9
Norway	1973–77	845	17.6			10
Denmark	1970–76	390	14.0			11
France	1975	465	3.7			1
England	1973–74	2274	7.7*			12
Asia						
Kuwait	1980–81	38	3.96		5.6‡	13
New Zealand	1968–72	578	8.9		10.5	14
Tokyo	1974–78	35		0.63§		15
Israel	1975–80	392	3.8		4.3	

*0–15 yr; †4–17 yr; ‡0–19 yr; §7–15 yr.

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