# Low Incidence of Type 1 Diabetes in Iran

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There is a worldwide increase in the incidence of type 1 diabetes (1–3). This increase, in conjunction with the lack of complete concordance in monozygotic twin pairs, points to the importance of environmental factors (3). Useful clues about these environmental factors may be obtained by studying geographical variation in incidence in relation to the characteristics of different countries. There is a paucity of information regarding type 1 diabetes in Iran. It was the purpose of this study to provide some baseline data regarding this disease in Iran.

The surveyed area was the southern province of Fars in the 5-year time period between 21 March 1991 and 20 March 1996. The region, which had a population of 3,800,000 in 1996, covers an area of 133,000 $km^2$ and is the largest province in southern Iran. Of the whole Iranian population, 10% live in southern Iran and 64% are residents of Fars.

## RESEARCH DESIGN AND METHODS

### Primary ascertainment procedure

In a prospective study from 21 March 1991 to 20 March 1996, all type 1 diabetic patients with age at onset of disease <30 years were selected from diabetic patients of endocrine and diabetes clinics and university hospitals of southern Iran. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus criteria (4) were used in the assessment of the diagnosis of the disease and its type, and the diagnosis was confirmed by at least one endocrinologist. Patients who first presented with diabetic ketoacidosis (DKA), had DKA as a complication of diabetes, or were severely symptomatic with significant weight loss on any therapeutic regimen except insulin were considered to have type 1 diabetes. When there were diagnostic doubts, islet cell antibodies (ICAs) (by indirect immunofluorescence) and C-peptide levels (by radioimmunoassay) were measured at the time of initial presentation, and those with strongly positive ICA and/or undetectable or very low fasting C-peptide levels were considered to have type 1 diabetes. No patients with type 2 diabetes, gestational diabetes, or secondary diabetes were included in the study. The identification data registered for each patient included first name, family name, parents' names, date of birth, and address.

### Independent second source of case ascertainment

Beginning simultaneously with the primary ascertainment procedure and using the same methods, all diabetic patients attending the diabetes classes of the region were prospectively screened for type 1 diabetes by a group of pretrained physicians, postgraduate trainees, and senior medical students under the supervision of endocrinologists. The above-mentioned identification data were registered for each type 1 diabetic patient who met the criteria of the study.

### Further validation of ascertainment

Of 120 randomly selected doctors (from a total of ~1,500 physicians in practice in Fars during the study period), none had any patient with insulin-requiring diabetes under their care who was not being simultaneously followed in endocrinology or diabetes clinics. No physician ever followed any patient who met our study criteria but was still missing from our register.

### Population data and statistical methods

The completeness of ascertainment was assessed by the capture-recapture method. The denominators of the age- and sex-specific incidence rates were defined as the average of the two 1991 and 1996 Iranian census population data, and an $\chi^2$ test was used to evaluate seasonal variation and to compare age- and sex-specific incidence rates and urban-rural differences.

**RESULTS** — There were 493 incident cases with a completeness of ascertainment of 100%. Of these, only 33 (6.7%) were less acutely symptomatic at presentation but were included in the study because of strongly positive ICAs and undetectable or very low fasting C-peptide levels. The incidence of the disease was significantly lower in male than in female subjects ($P < 0.01$). Mean annual age- and sex-specific incidence rates of the disease were 3.14/100,000 (95% CI 2.60–3.68) for male subjects and 4.37/100,000 (3.72–5.02) for female subjects (both 0–14 years of age). The same rates were 3.36/100,000 (2.92–3.8) and 4.26/100,000 (3.76–4.76) for all male and female subjects <30 years of age, respectively (Table 1). Mean annual age-specific incidence rates of the disease were 4.37/100,000 for urban dwellers and 3.27/100,000 for residents of rural regions ($P < 0.002$). This equaled a 34% higher risk for developing diabetes for the population living in urban regions. In both sexes, the disease had its peak of incidence at between 10 and 14 years of age, and in girls it was earlier than in boys. Although the highest proportions of patients had the clinical onset of disease in February (10.75%) and November (11.5%) and the lowest in May (6.5%)

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Received for publication 1 October 2004 and accepted in revised form 2 January 2005.

**Abbreviations:** DKA, diabetic ketoacidosis; ICA, islet cell antibody.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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**Table 1—*Age-specific incidence rates (mean annual number per 100,000) of type 1 diabetes in an Iranian population <30 years of age***

| Age-group (years) | No. of incident cases in 5 years | | Population at risk | | Incidence rate (95% CI) | |
|---|---|---|---|---|---|---|
| | Male | Female | Male | Female | Male | Female |
| 0–4 | 25 | 28 | 237,000 | 226,000 | 2.11 (1.28–2.94) | 2.48 (1.56–3.40) |
| 5–9 | 40 | 63 | 298,000 | 284,000 | 2.68 (1.86–3.52) | 4.44 (3.34–5.54) |
| 10–14 | 63 | 79 | 281,000 | 268,000 | 4.48 (3.38–5.60) | 5.90 (4.60–7.20) |
| 15–19 | 47 | 50 | 210,000 | 202,000 | 4.48 (1.60–3.54) | 4.95 (3.58–6.32) |
| 20–24 | 26 | 27 | 158,000 | 158,000 | 3.29 (2.02–4.56) | 3.42 (2.12–4.70) |
| 25–29 | 21 | 24 | 137,000 | 134,000 | 3.07 (1.76–4.38) | 3.58 (2.14–5.02) |
| 0–29 | 222 | 271 | 1,321,000 | 1,272,000 | 3.36 (2.92–3.80) | 4.26 (3.76–4.76) |

and July (6%), the apparent differences were not statistically significant ($P > 0.1$).

**CONCLUSIONS** — Worldwide, in populations <14 years of age, type 1 diabetes incidence varies from <1/100,000 per year to >35/100,000 per year (5,6). Scandinavia has the highest and the Pacific Rim the lowest rates. Northern Europe and the U.S. share an intermediate range (8–17/100,000 per year). Most of the information regarding type 1 diabetes incidence thus far has come from regions with a high or intermediate incidence, mostly in Europe or North America (5,6). Setting up and maintaining population-based registries in very-low-incidence areas such as South America, Africa, and Asia are extremely difficult and so the data from these regions are still sparse (5). Nonetheless, the availability of standardized rates on type 1 diabetes incidence from these low-incidence areas is particularly important to confirm that the presumed large variation in incidence exists (5). When compared with the neighboring and Asian countries, the incidence of type 1 diabetes in Iran (3.7/100,000 per year) is less than that in Israel (6/100,000 per year), Kuwait (18.3/100,000 per year), or Russia (6/100,000 per year) but more than that in Pakistan (0.7/100,000 per year), Japan (1.4–2.2/100,000 per year), or China (0.1–2.3/100,000 per year) (5).

In conclusion, in Iran, the incidence of type 1 diabetes is low but has a significant urban-rural difference. In this report, we have shown that type 1 diabetes has a female predilection but lacks significant seasonality. As the incidence of type 1 diabetes is increasing worldwide, the data produced by this study provide a baseline for assessing future changes.

**Acknowledgments**— This study would not have been possible without the contribution of the many people who helped with data collection at the different centers. Special thanks go to all the doctors, nurses, pharmacists, and medical students who provided a long-standing collaboration with this study.

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