Type II Diabetes Mellitus in Seattle and Tokyo

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Human diabetes mellitus is a heterogenous disorder. Both genetic and
environmental factors affect the development and the course of the disease. A
cross-cultural study in which a migrant pure Japanese population living in Seattle
is compared to a native Japanese population in Tokyo may distinguish significant
environmental influences upon the occurrence and course of diabetes from influen-
ces due to race. To examine the feasibility of mounting a cross-cultural study of
type II (non-insulin dependent) diabetes mellitus in the Japanese-American
(Nikkei) community of the greater Seattle (King County) region of Washington
State and the native Japanese population of Tokyo, a pilot study was begun in
1979 and completed in 1981. Nikkei refers to all Japanese who have become
permanent residents of the United States and includes first generation immigrants.

METHODS

Approximately 14,000 individuals of Japanese ancestry resided within the greater Seattle
(King County) area of Washington State in 19701-2). The present Washington State Nikkei
population has an age distribution curve with several distinctive peaks, each representing a
separate generation. The demographic discreteness of the generations is recognized by
Nikkei and is reflected in their use of separate labels for the members of each generational
group: first generation immigrants, Issei; second generation, Nisei; and third generation,
Sansei. In Seattle, eighteen Nisei males with diabetes volunteered for the study. Based
upon a reported prevalence of overt, clinically apparent diabetes of 9% in Japanese males
40-60 years of age living in Hawaii3) and an estimated 1600 Japanese males between the
ages of 40 and 60 years old living in the greater Seattle area4), approximately 140 diabetic
Nisei men constitute the pool from which we obtained our volunteers. Thus our study
population represented an estimated >10% sample of the total pool. The 20 Tokyo

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Subjects were recruited for the study from the Diabetes Clinic at the Institute for Adult Diseases, Asahi Life Foundation, in Tokyo.

All subjects had a medical history covering the duration of diabetes, current therapeutic regimen for diabetes, diet, physical activity, tobacco and alcohol use, history of hypertension, and history of macrovascular or microvascular disease. Duration of diabetes, admittedly difficult to accurately determine for type II diabetes, was estimated from date of onset of symptoms (polyuria, polydipsia, polyphagia, weight loss), diagnosis by a physician, or institution of therapy, depending upon the recall of the subject, but in every case using the earliest date to estimate duration. None of the subjects had been treated with insulin. Dietary intake analysis was based upon a 3-day diet diary maintained by the subject. Nutrient intake was estimated from standard tables of food consumption. The Seattle dietitian met with the Tokyo dieticians to assure comparable methodology. Before the Tokyo phase was started, diet diaries taken in Seattle were analyzed by dieticians in Seattle and Tokyo. The same was done for diet diaries taken in Tokyo.

Each subject then received a physical examination. Included in this was a dilated funduscopic examination consisting of both indirect and direct ophthalmoscopy of each eye by an ophthalmologist expert in diabetic retinal disease. An estimate of current adiposity was made from the following formula: relative weight (%) = actual weight (kg) / (height in cm − 100) x 0.9. The thickness of the skinfold in a standard area of the right triceps was obtained with a Lange skinfold caliper (Cambridge Scientific Industries, Inc., Cambridge, MA).

Laboratory investigation included a fasting plasma glucose (glucose oxidase method), total glycosylated hemoglobin (Hb A₁ by ion exchange chromatography, IsoLab, Akron, OH), and 24-hr urinary excretion of glucose (glucose oxidase method) to assess glycemic control; a lipid profile including both total and high density lipoprotein cholesterol, and total triglyceride measured by NIH Lipid Research Clinic methodology; and an assessment of kidney function by serum creatinine (alkaline picric acid method), 24-hr creatinine clearance, and 24-hr urinary total protein (sulfosalicylic acid method). A resting 12-lead electrocardiogram was done to screen for ischemic heart disease as defined by Minnesota code criteria 1.1-1.3, 4.1-4.3, 5.1-5.4, or 7.1.

To assure comparability of data between Seattle and Tokyo, a set of 10 unknown urine and plasma samples stored on dry ice for 24 hr were sent from Tokyo to Seattle. Glucose, protein, creatinine, total cholesterol, high density lipoprotein cholesterol, and triglyceride were measured in Tokyo and Seattle on these samples.

Results are presented either as mean±s.e. or as ratios. The comparison of Seattle and Tokyo laboratory procedures was done by simple linear correlation. For comparisons between the Nisei and Tokyo subjects, pairwise correlations were computed and when appropriate, were age adjusted. Fisher's exact test was used to compare prevalence data.

Results

A comparison of laboratory results on the same 10 samples from Tokyo demonstrated good agreement between Seattle and Tokyo, although requiring a correction for plasma glucose (−8 mg/100 ml) and plasma triglyceride (+21 mg/100 ml) to the Tokyo values.

Physical and certain other characteristics of the subjects are shown in Table 1. Duration of diabetes was slightly longer in Tokyo, but the difference was not significant (Nisei 5.2±1.4 years, Tokyo 8.0±1.1 years). Furthermore, since exact time of onset of type II diabetes is difficult to determine, these differences should be minimized. Mean systolic blood pressure (Nisei 137±3, Tokyo 130±4) and
TABLE 1. Physical and other characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Age</th>
<th>Age at diagnosis of diabetes</th>
<th>Relative weight (%)</th>
<th>Triceps skinfold (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nisei</td>
<td>18</td>
<td>56.9±1.6</td>
<td>51.8±1.6</td>
<td>118±3</td>
<td>11.4±0.9</td>
</tr>
<tr>
<td>Tokyo</td>
<td>20</td>
<td>50.6±1.3</td>
<td>42.7±1.4</td>
<td>103±4</td>
<td>9.5±1.0</td>
</tr>
<tr>
<td>p &lt; .001</td>
<td>p &lt; .001</td>
<td></td>
<td></td>
<td>p = .07*</td>
<td>NS*</td>
</tr>
</tbody>
</table>

*(x ± s.e.)*

* Age adjusted.

prevalence of hypertension (history of hypertension and/or blood pressure > 140/90 mmHg; Nisei 12/18, Tokyo 8/20) were not significantly different. However, diastolic blood pressure was greater among Nisei (86±2 vs. 75±3, p = 0.003). This difference was still significant when adjusted for age. Current use of tobacco was not different (Nisei 7/18, Tokyo 8/20). Physical activity levels were similar. Nutrient intake analysis demonstrated significant differences between Nisei and Tokyo subjects for the proportion of calories as fat and carbohydrate and the proportion of animal origin of fat or protein (Table 2). Biochemical measurements showed Tokyo diabetics to differ significantly from Nisei diabetics with regard to plasma cholesterol (p = 0.01) and creatinine clearance (p ≤ 0.001) (Table 3). More Nisei had plasma cholesterol ≥ 250 mg/100 ml (6/18 vs. 1/20). The data also suggest that glycemia may be greater in Tokyo. Nisei tended to have a higher prevalence of ischemic electrocardiographic changes (5/18 vs. 0/20) and lower prevalence of diabetic retinopathy (1/18 vs. 7/20).

DISCUSSION

The Nikkei population residing in the greater Seattle area represents one of the most closely characterized ethnically homogenous but economically assimilated immigrant groups in the United States. It differs from most Euro-American populations in its genetic and cultural homogeneity. However, it has attained a socioeconomic profile (education, occupation, and income) similar to that of the United States white population. It has roots in a native Japanese population with a low risk of developing diabetes and cardiovascular disease, yet has prevalence rates of both which are greater than in Japan. Because it has evolved with rapid social and cultural changes, there is a strong probability that these differences have arisen from associated environmental factors.

Deaths due to atherosclerotic cardiovascular disease are greater in Western diabetic populations than in Japan. However, the development of atherosclerotic cardiovascular disease is influenced by numerous factors, both genetic and non-genetic. Among these are serum lipid and lipoprotein levels, blood pressure, certain habits such as use of alcohol and tobacco, physical exercise, dietary content of cholesterol and saturated fat, and psychologic and social factors.

The merit of a cross-cultural study of a migrant population lies in the
TABLE 2. Nutritional intake analysis

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Calories</th>
<th>% Protein total</th>
<th>% Animal protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nisei</td>
<td>16*</td>
<td>1970±111</td>
<td>17.3±0.8</td>
<td>66.9±3.2</td>
</tr>
<tr>
<td>Tokyo</td>
<td>20</td>
<td>1984±131</td>
<td>17.9±0.9</td>
<td>54.9±2.5</td>
</tr>
</tbody>
</table>

(NS)

*(x±s.e.)*

* Data were available from 16 of the 18 subjects.

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TABLE 3. Biochemical

Glycemic control

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Fasting glucose (mg/100 ml)</th>
<th>Glycosuria 24/hr (g/24 hr)</th>
<th>Hemoglobin Al (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nisei</td>
<td>18</td>
<td>159±10</td>
<td>8.2±2.6</td>
<td>9.5±0.4</td>
</tr>
<tr>
<td>Tokyo</td>
<td>20</td>
<td>176±11</td>
<td>18.1±5.6</td>
<td>11.0±0.5</td>
</tr>
</tbody>
</table>

*(x±s.e.)*

possibility of detecting influences due to environment as opposed to heredity. Thus the present study was performed to examine the feasibility of conducting a cross-cultural study in the Seattle Nikkei community and in Tokyo. When we examined the data, certain interesting differences were found which we feel deserve presentation at this time. However, since the data reported here have been derived from a very small pilot study, they must be interpreted cautiously.

Although the Seattle subjects represent a fairly sizeable proportion of the total estimated pool of Nisei males with type II diabetes, the Tokyo group is possibly not a representative sample of the total Japanese male population with type II diabetes. Since the Tokyo subjects were individuals who had already been scheduled for evaluation of their current status at a relatively small but specialty-oriented hospital with a strong interest in diabetes and were not volunteers like the Seattle subjects, certain biases are present in their selection but the nature of the biases cannot be ascertained by this limited study. Their younger age, earlier onset of diabetes, and slightly greater glycemia may be indicative of this bias. However, since differences remained significant after correction for age, their lower mean age does not explain the lesser obesity, lower diastolic blood pressure, or lower plasma cholesterol levels of the Tokyo subjects.

Nutrient intake analysis revealed differences in agreement with other studies3), namely a lower proportion of calories consumed as carbohydrate and a greater amount as fat, and a greater consumption of animal fat or protein in Nisei. Whether this is responsible for the higher mean plasma cholesterol level among Nisei is speculative, as is the possibility of a relationship to an apparently greater
Type II diabetes in Seattle and Tokyo

Based upon a 3-day diet diary

<table>
<thead>
<tr>
<th>% Fat total</th>
<th>% Animal fat</th>
<th>% Carbohydrate</th>
<th>% Alcohol</th>
<th>Cholesterol (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>41.4 ± 1.4</td>
<td>55.1 ± 2.9</td>
<td>39.4 ± 1.7</td>
<td>2.0 ± 1.2</td>
<td>401 ± 39</td>
</tr>
<tr>
<td>24.2 ± 1.9</td>
<td>47.8 ± 2.6</td>
<td>51.0 ± 2.0</td>
<td>6.6 ± 1.9</td>
<td>449 ± 49</td>
</tr>
<tr>
<td>p = .001</td>
<td>p = .069</td>
<td>p = .001</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

measurements

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Triglyceride (mg/100 ml)</th>
<th>Cholesterol (mg/100 ml)</th>
<th>HDL cholesterol (mg/100 ml)</th>
<th>Creatinine clearance (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>199 ± 31</td>
<td>239 ± 7</td>
<td>45.7 ± 4.3</td>
<td>110 ± 4</td>
</tr>
<tr>
<td></td>
<td>204 ± 29</td>
<td>195 ± 10</td>
<td>46.1 ± 2.2</td>
<td>77 ± 3</td>
</tr>
</tbody>
</table>

proportion of subjects among Nisei with ischemic electrocardiographic abnormalities. Also to be considered is the psychosocial stress experienced by the Nisei population as it underwent tremendous socioeconomic changes. These psychosocial factors have not been considered at all in this pilot study, but will be examined in a new study which is currently under development. Nevertheless, the seemingly lower prevalence of ischemic ECG abnormalities in Tokyo agrees with previous studies\(^{16}\) documenting a lower prevalence of ischemic heart disease in Japanese diabetics and does emphasize the necessity to more carefully determine the reasons for the apparent differences between the Nisei and Tokyo subjects. Finally, our results suggest that microvascular disease (diabetic retinopathy and reduced creatinine clearance) may be more prevalent in Tokyo subjects. This could be due to the greater duration of diabetes or the greater glycemia in the Tokyo subjects.

We conclude that a more extensive study is indicated in which a larger number of Nisei males are examined longitudinally to determine whether there are subgroups within the Nisei community who have different inherent risks for developing diabetes and its associated complications. If this is the case, the characteristics of these groups would be of interest, especially in comparison to the native Japanese population. Such an investigation is now being developed.

Acknowledgments

We are grateful for the assistance provided by Judith Okamoto, Stephen Thompson, Jeanette Teague, Sharon Kemp, Kung-Yee Liang, the nursing staff of the University
Hospital Clinical Research Center, and the Core Laboratory of the Lipid Research Center in Seattle, and by Sonoe Kojima, Kaoru Ito, and the clinical and laboratory staffs of the Institute for Adult Diseases, Asahi Life Foundation, in Tokyo.

This research was supported by grants from the Kroc Foundation, the American Diabetes Association, Washington Affiliate, Inc., and the National Institute of Handicapped Research, and was performed in the General Clinical Research Center (RR-37) at the University Hospital, with assistance from the Diabetes-Endocrinology Research Center (AM 17047). Computational assistance was provided by the CLINFO system and by the University of Washington Health Sciences Center Public Health Computing Facility. Dr. Fujimoto received a long-term fellowship from the Japan Society for the Promotion of Science and was on sabbatical leave at the University of Tokyo, Faculty of Medicine, Third Department of Internal Medicine, 1979–1980.

References


