A case-control study was conducted to evaluate the relation between several factors and the risk of non-insulin-dependent diabetes mellitus in a rural population of the island of Ojika, in the Goto islands, Nagasaki prefecture Japan. We selected 62 diabetes mellitus (DM) and 70 impaired glucose tolerance (IGT) cases and 168 normal controls for the study. They were diagnosed by WHO criteria using 75 gram glucose tolerance test applied to inhabitants of the island in June 1991. Obesity, expressed as body mass index (BMI, weight (kg)/height (cm)$^2$) at the time of diagnosis and BMI at the time when they had heaviest weight, was associated with increased risk for DM (odds ratio for one unit difference (OR)=1.15, 95% confidence interval (CI)=1.04-1.27 and OR=1.13, 95% CI=1.02-1.25, respectively). Occupational experience of rice growing, vegetable growing and breeding of cattle were inversely associated with the risk (OR=0.36; CI=0.17-0.76, OR=0.44; CI=0.21-0.93, OR=0.43; CI=0.21-0.93, respectively). The DM history of father was associated with the significantly high risk (OR=10.94; CI=1.18-101.14), but that of mother did not (OR=1.49; CI=0.13-17.17). The sample size of this study was not large enough to get the narrow odds ratio confidence intervals. To increase the reliability of the relative risk estimation, further intensive studies are necessary. J Epidemiol, 1994; 4 : 25-29.

Although obesity and genetic load are believed to be major risk factors of non-insulin-dependent diabetes mellitus$^{1-7}$, most evidence of the risks were reported qualitatively, with the exception of recent cohort study reports$^{8-12}$. Study populations of these cohort studies are limited to Swedish men$^{6,9}$, Mexican Americans$^{10}$, Caucasians$^{11}$ and Iowa women$^{12}$. One case-control study$^{13}$ in Japanese population was reported recently, but intensive epidemiologic studies for evaluating the magnitude of the risks in Japanese population are rare.

The purpose of this case-control study is to estimate the relative risks of diabetes mellitus attributable to obesity, parental history of DM, and occupational experience in a Japanese community.
defined by the World Health Organization\textsuperscript{14}: 1) Diabetes mellitus (DM), a fasting glucose level of 140 mg/dl or over and/or a two hours post glucose load level of 200 mg/dl or over; 2) impaired glucose tolerance (IGT), a fasting glucose level of less than 140 mg/dl and a two hours post glucose load level 140 mg/dl or over and less than 200 mg/dl; and 3) normal glucose tolerance, all other levels. Out of 86 individuals classified into DM, 62 patients who had never been diagnosed as DM previously were selected for a case series. And out of 254 individuals classified into IGT, 71 participants who had a glucose level of 170 mg/dl or over at two hours after the glucose load were selected for another case series. For a control series, 172 individuals were randomly selected from the participants who were classified normal glucose tolerance and also had a glucose level less than 110 mg/dl at fasting time and less than 120 mg/dl at two hours after the glucose load. We selected only newly diagnosed DM to avoid so-called prevalence bias as far as possible. And to evaluate the dose-response relationship, two level of abnormal glucose tolerance groups were utilized for case series. To make the difference of glucose tolerance among the comparison groups greater, more severely impaired individuals in the IGT group and better glucose tolerance individuals in the normal group were selected for comparison groups.

Information of risk factors

A self-administered questionnaire was employed to obtain the information of the exposure to possible risk factors to all the cases and controls. The factors included in the questionnaire were the past history of infectious diseases such as measles, chicken pox, rubella, and mumps, and of medications for high blood pressure, tuberculosis, contraception, constipation, other intestinal disorders, and pains. Height and weight at the time of sixth grade in primary school comparing to other classmates were asked and classified into three categories: 1) small, 2) medium and 3) large. The ever heaviest body weight in the life was also asked and used for calculation of body mass index (BMI, weight (kg)/height (m)$^2$) assuming the height is same as the current height. Current BMI were calculated in the same method using the current body measurement. Habits of smoking and alcohol drinking were asked and classified into ever and never smoked or drank. The amount of the consumed alcohol (counted in 180 ml Japanese sake unit) per a week was also evaluated. Information of the occupational works, sedentary hours and hours of working with sweat per a day and parental DM history were also obtained by the questionnaire.

Statistical methods

Logistic regression analysis was carried out for estimating the relative risks of DM and IGT. The comparison of DM cases and controls, and the comparison of IGT cases and controls were carried out separately. Variables of age and sex were controlled in all the analyses. Individuals with unknown value of analyzed variables were excluded in each analysis. These analyses were performed on a personal computer using the LOGISTIC procedure of the Statistical Analysis System\textsuperscript{15}.

RESULTS

Most of the inhabitants assigned to the case or the control responded to the questionnaires as shown in Table 1. The age distributions of participated cases and controls were almost identical as shown in Table 2. The proportions of participants who were exposed to the factors and mean values of exposure variables for each case or control series are shown in Tables 3 and 4, respectively. Variables of the history of infections and medications for several disorders did not show any considerable differences, those results are not shown in the tables. The relative risk estimated for each exposure variable controlling for age and sex are shown in Table 5. In the analyses using IGT as case series, high blood pressure medication (relative risk...
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(\text{RR})=3.42) and cattle breeding (\text{RR}=0.24) showed statistically significant relative risks. And in the analyses using DM as case series, rice growing (\text{RR}=0.36), vegetable growing (\text{RR}=0.44), cattle breeding (\text{RR}=0.43), DM history of father (\text{RR}=10.94), current BMI (\text{RR}=1.15) and maximum BMI (\text{RR}=1.13) showed significant results. The significant relative risks for DM showed greater difference from one than those for IGT with the exception of relative risk of cattle breeding.

Selecting the rice growing as a representative factor which indicate agricultural work, and present time BMI as a factor indicating obesity, and DM history of father as a familial factor, we estimated each factor's relative risk controlling for the other factors. Those relative risks shown in Table 6 were almost identical with those without controlling for the other factors shown in Table 5, although that of DM history of father was regarded to be infinite because of the limited number of subjects.

**DISCUSSION**

The subjects of this study were selected from one community members who attended a mass health examination project intending to detect diabetes mellitus patients. The diagnosis of DM and IGT were made according to the international standard. Control series were ascertainment as normal by the oral glucose tolerance test performed at the same time when the case series were ascertained. The persons who had already been known to have the disease were not included in the case series, this means that all the cases were newly diagnosed in the study. These are the substantial characteristics and the advantages of this study for avoiding the possible selection and information biases.

The relationship of obesity or genetic load and diabetes mellitus have been reported\textsuperscript{1-7}, and these factors are believed to be major risk factors. But the quantitative measure of the effects, such as relative risk or odds ratio, were rarely reported.

Yamamoto et al.\textsuperscript{13} conducted a case-control study of DM in Japanese population, and reported odds ratios of family history of diabetes to be 14.8 (\text{CI}=6.51-33.59) for getting DM and to be 2.8 (\text{CI}=0.9-8.88) for getting IGT. These values are not much different from odds ratios of DM history of father obtained in our study, although the definitions of the family history and case definition are not the same. The effect of DM history of father and mother were much different from each other in our study. It is a interesting finding which have never been reported.

Most of the cohort studies\textsuperscript{8,11,12} focused on not only total-body fat (represented by BMI) but also abdominal fat (represented by the ratio of waist to hip circumferences), and reported both factors' positive associations with the risk for DM. The highest relative risk of BMI was reported as high as 21.7 in a study of Swedish men.\textsuperscript{8} As the relative risks were calculated by tertile or quintile of BMI in those studies, and their cutpoints were different from each other, it is difficult to compare the absolute value of relative risks. But it may be possible to state that the previously reported relative risks of BMI were roughly in the range of 1.3-6.0.

The relative risk of maximum BMI for DM which was reported in Japanese population study\textsuperscript{13} (calculated from reported logistic regression coefficients by us) is 1.54, this model used the BMI as continuous variable like our analysis. The observed relative risk of current BMI for DM in our study was 1.15. The relative risk of 1.15 means that 3 kg weight gain for 173 cm height person results 1.15 times high risk to get DM for example. In other words, 15

**Table 3.** Proportion (%) of participants exposed to factors for cases and controls.

| Factor                        | Control | Case |
|-------------------------------|---------|------|
|                               | IGT     | DM   |
| High blood pressure medication| 23.2    | 35.5 |
| Intestinal disorder medication| 4.2     | 6.5  |
| Obese at 12 years old         | 5.4     | 12.9 |
| Smoking (Male)                | 81.0    | 78.8 |
| Smoking (Female)              | 6.7     | 6.9  |
| Drinking (Male)               | 70.9    | 75.8 |
| Drinking (Female)             | 7.9     | 4.5  |
| Rice growing                  | 35.7    | 19.4 |
| Vegetable growing             | 32.1    | 19.4 |
| Cattle breeding               | 29.8    | 17.7 |
| Construction work             | 18.5    | 9.7  |
| DM history of father          | 0.6     | 6.5  |
| DM history of mother          | 1.2     | 1.6  |

**Table 4.** Mean of exposure variables by sex for cases and controls.

| Factor                        | Control | Case |
|-------------------------------|---------|------|
|                               | IGT     | DM   |
| Current BMI (Male)            | 22.4    | 23.2 |
| Current BMI (Female)          | 22.7    | 24.3 |
| Maximum weight (kg) (Male)    | 65.8    | 67.8 |
| Maximum weight (kg) (Female)  | 56.5    | 59.4 |
| Maximum BMI (Male)            | 25.1    | 25.8 |
| Maximum BMI (Female)          | 24.7    | 26.2 |
| Amount of alcohol (Male)      | 9.3     | 13.5 |
| Amount of alcohol (Female)    | 4.1     | 1.5  |
| Sedentary hours a day (Male)  | 2.6     | 2.6  |
| Sedentary hours a day (Female)| 2.7     | 3.6  |
| Hours of working with sweat a day (Male) | 4.9 | 4.6 |
| Hours of working with sweat a day (Female) | 4.7 | 4.3 |
Table 5. Relative risk and its 95% confidence intervals for DM and IGT estimated by logistic regression analysis adjusting for age and sex.

| Factor                        | IGT                   | DM                   |
|-------------------------------|-----------------------|----------------------|
| High blood pressure medication| 3.42 (1.83-6.41)*     | 1.94 (1.00-3.76)     |
| Intestinal disorder medication| 1.91 (0.60-6.07)      | 1.66 (0.64-5.92)     |
| Obese at 12 years old         | 2.62 (0.97-7.09)      | 0.60 (0.13-2.88)     |
| Smoking                       | 0.81 (0.33-2.01)      | 0.85 (0.36-2.01)     |
| Drinking                      | 1.24 (0.55-2.79)      | 0.97 (0.45-2.11)     |
| Rice growing                  | 0.57 (0.29-1.10)      | 0.36 (0.17-0.76)*    |
| Vegetable growing             | 0.58 (0.29-1.14)      | 0.44 (0.21-0.93)*    |
| Cattle breeding               | 0.24 (0.10-0.57)*     | 0.43 (0.20-0.93)*    |
| Construction work             | 0.58 (0.24-1.39)      | 0.39 (0.15-1.03)     |
| DM history of father          | 6.42 (0.68-60.47)     | 10.94 (1.18-101.14)* |
| DM history of mother          | 1.30 (0.11-15.30)     | 1.49 (0.13-17.17)    |
| Current BMI*                  | 1.09 (0.99-1.21)      | 1.15 (1.04-1.27)*    |
| Maximum weight (kg)*          | 1.02 (0.98-1.06)      | 1.03 (1.00-1.07)     |
| Maximum BMI*                  | 1.09 (0.98-1.21)      | 1.13 (1.02-1.25)*    |
| Amount of alcohol*            | 1.04 (0.99-1.10)      | 1.03 (0.99-1.08)     |
| Sedentary hours a day*        | 0.99 (0.83-1.17)      | 1.07 (0.92-1.26)     |
| Hours of working with sweat a day* | 0.90 (0.78-1.04) | 0.96 (0.83-1.10)    |

*: Continuous variables. The relative risk means the risk relative to those whose values are one unit less. The other variables are dichotomous and the relative risk of the positive relative to the negatives.

Table 6. Relative risk with 95% confidence intervals for DM estimated by logistic regression analysis adjusting for the other factors, age and sex.1

| Factor                        | Relative risk       |
|-------------------------------|---------------------|
| Rice growing                  | 0.38 (0.17-0.86)*   |
| DM history of father          | &                   |
| Current BMI                   | 1.16 (1.02-1.33)*   |

*: Continuous variable. The relative risk means the risk relative to those whose values are one unit less. The other variables are dichotomous and the relative risk of the positive relative to the negatives.

ACKNOWLEDGEMENTS

This study was supported by a Research Grant for Epidemiological study of Diabetes Mellitus from Ministry of Health and Welfare of Japan and a Research Grant for Longevity Society Project from the Foundation for the Development of the Community.

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kg weight gain for him/her means fifth (15/3) power of 1.15, approximately 2 times high risk to get the disease. As much as 30 kg weight gain can give him/her 4-fold high risk. The observed effect of BMI in our study seems to be rather less than previously reported effects.

Quantitative evaluations of risk factors make it possible to compare the importances of risk factors. And such evaluations are valuable from epidemiological and public health view points. As the sample size of our study is not enough large to get precise quantitative risk estimations, further investigations will be required.
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