

Algae Consumption and Risk of Type 2 Diabetes: Korean National Health and Nutrition Examination Survey in 2005

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Summary The purpose of this study is to examine the relationship between dietary algae (seaweed) consumption and the risk of Type 2 diabetes mellitus in the Korean population. We analyzed data from the Korean National Health and Nutrition Examination Survey in 2005, a nationally representative survey. The study participants included 3,405 males and females aged 20–65 y. Participants were classified into four groups according to the quartiles of total algae consumption frequencies. Proportional odds models were used to assess the relationship between algae consumption and the risk of having diabetes or prediabetes, after adjustment for age, family history of diabetes, education, smoking, alcohol consumption, physical activity, body mass index, waist circumference, triglycerides, total energy intake and food group intakes. The frequency of algae consumption was positively correlated to the consumption of legumes, fruits, fish, and dairy products in both genders ($p < 0.001$). The odds ratios (95% confidence interval) for diabetes vs. prediabetes vs. normoglycemia was 0.66 (0.43–0.99) for males and 0.80 (0.51–1.24) for females in the highest quartile of algae consumption compared to the lowest quartile. Our results suggest that dietary algae consumption may decrease the risk of diabetes mellitus in Korean men. A well-designed prospective study is needed to confirm this association.

Key Words algae, diabetes mellitus, prediabetes

Type 2 diabetes is generally preceded by a ‘pre-diabetes’ phase, during which fasting glucose is slightly elevated above normal levels and/or postprandial glucose clearance is impaired (1, 2). In previous studies, increased physical activity and weight loss were found to effectively control and prevent Type 2 diabetes mellitus (3, 4). One’s diet is also considered a significant risk factor for Type 2 diabetes. Therefore, dietary recommendations can aid in the control of diabetes mellitus (5), although data on their efficacy are limited (6). Many studies have indicated that consumption of foods rich in concentrated sugars and refined flour products (7), consumption of red meat (8), low fiber intake (7), and an imbalance of polyunsaturated fatty acids (9) are associated with the development of Type 2 diabetes. In contrast, the consumption of large quantities of whole grains, fruits, vegetables, and low-fat dairy products are inversely associated with the risk of Type 2 diabetes (10). The identification of additional dietary items that can prevent diabetes is therefore of great importance.

Algae products have been shown experimentally to protect against atherosclerosis, dyslipidemia, and cancer progression (11–13). Edible algae such as purple laver (called “kim” in Korea, red alga *Porphyra yezoensis*)

and sea mustard (“miyeok”, brown alga *Undaria pinnatifida*) are also rich in biologically active substances. The remarkably high levels of dietary fiber, proteins, minerals, and vitamins in algae coupled with their non-digestible carbohydrate counterparts make algae a nutritive, low-calorie food source (14–17). Edible algae are being studied as a source of antioxidants and iron (14, 18, 19). Furthermore, the polyphenolic constituents of algae have been shown to have potential hypoglycemic properties, and algae can therefore also be used as a food supplement (20). Despite the health benefits associated with algae consumption, it is not widely consumed except in East Asian countries such as Korea, Japan and China. We evaluated the relationship between the consumption of dietary algae and the risk of Type 2 diabetes in the Korean population.

STUDY DESIGN AND METHODS

Study participants. The Korean National Health and Nutrition Examination Survey conducted in 2005 (KNHANES III) by the Korean Ministry for Health, Welfare and Family Affairs was a cross-sectional and nationally representative survey of the non-institutionalized civilian population of Korea. The sampling units were households selected through a stratified, multi-stage, probability sampling design (21). Totally 4,686 participants completed all three parts of the survey

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(health interview survey, behavior survey, and nutrition survey). We excluded subjects with a modified daily energy intake of <500 kcal or $\geq 3,500$ kcal; a history of cancer, or thyroid disease; dietary modification by the other diseases; or missing data on food items. Furthermore, participants who were taking insulin injections or oral hypoglycemic drugs for the treatment of diabetes were excluded (22). The final study participants included 1,389 males and 2,016 females.

Dietary assessment. Total habitual food consumption during the previous year was estimated using a 63-item food frequency questionnaire (FFQ). Sixty-three food items were selected as the most frequent consumed food items from 24-h recall data in KNHANES II (2001). The content validity of the FFQ was confirmed by an expert group (23). The questionnaire offers nine response options for the frequency of intake for each food item (ranging from 'never or less than once/mo' to 'three times/d') (24). Diet interviews were conducted in a standardized manner by certified interviewers who had completed intensive training. The method used in this study is not 'semi-quantitative FFQ' but 'simple FFQ.' We obtained the frequency of the consumption of food items per month. We estimated the frequency of algae consumption by adding the frequency of two items of food: purple laver (called "kim" in Korea, red alga *Porphyra yezoensis*) and sea mustard ("miyeok", brown alga *Undaria pinnatifida*). We divided the frequency of algae consumption into four quartiles ranging from the lowest algae consumption group (Quartile 1) to the highest algae consumption group (Quartile 4). To identify other food groups that could be confounding variables, we grouped the food items on the questionnaire into 11 predefined food groups (25) and classified them according to the system of the Korean Nutrient Database (Korean Nutrition Society, 2005). We excluded the alcohol and beverage groups. In this paper, the relative proportion of a specific food group (cereals, legumes, potatoes, vegetables, fruits, fish, dairy products, meat/poultry/eggs, and fast foods) was defined as the proportion of the total frequencies of food items belonging to a specific food group of the total frequencies of all food groups (26). Soybean products were included in the legume food group. The vegetable food group excluded potato, which is commonly classified as a vegetable in the United States. However, in our study, we classified the edible roots of plants (ex. sweet potato and white potato) into a potato group.

Assessment of other variables. We followed the current diabetes classification system of the American Diabetes Association (27). The normoglycemia group contained subjects with fasting blood glucose <100 mg/dL, the prediabetes group contained individuals with fasting glucose levels between 100 and 125 mg/dL, and the diabetes group contained individuals with a fasting glucose level ≥ 126 mg/dL. Body mass index (BMI) was calculated as weight divided by height squared. Waist circumference (WC) was measured halfway between the lower rib and iliac crest. Blood pressure was measured using a mercury sphygmomanometer in the sitting

position after a 5-min rest (28). Three measurements were taken from all the participants at 30-s intervals, and the average of the second and third measurements was used. Total cholesterol, triglycerides, HDL cholesterol, and fasting blood glucose were measured using an autoanalyzer (21). Self-reported questionnaires were administered to assess smoking status, education level, and physical activity. Physical activity was assessed using an adapted version of the International Physical Activity Questionnaire (IPAQ) (28). The IPAQ is a self-reported questionnaire that covers frequency and duration of several levels of planned and incidental physical activity (29). In this study, physical activity was classified into five categories: i) sedentary (inactive), ii) lightly active, iii) moderately active, iv) intensely active, and v) vigorous. We also analyzed the amount of alcohol consumption (g/d) and total energy intake (kcal/d), both of which were obtained from 24 h recall data in KNHANES III (2005).

Statistical analysis. All statistical procedures were performed using SAS software version 9.1 (SAS Institute, Cary, NC). Data was presented as a crude mean and standard deviation. To test the differences in the basic characteristics according to the fasting glucose group, we applied an analysis of covariance (ANCOVA) model with age as the covariate. The proportional odds models were used to estimate the effect of algae consumption on the risk of Type 2 diabetes after adjusting for age, demographic factors, individual metabolic parameters, and the relative proportion of each food group. Since the response categories (normoglycemia, prediabetes, and diabetes) are ordered, we first applied the proportional odds models (ordinary logistic regression model). The proportional odds model is the most popular model for ordinal logistic regression (30). The characteristics of the proportional odds models are that the odds ratios for an independent variable can be interpreted as a summary of the odds ratios obtained from a separate binary logistic regression using all possible cut points for the ordinal response categories (31). To check the assumption of proportionality, we used the score test.

Three regression models were constructed to account for potential confounders and mediators. We adjusted it for the effects of demographic variables (family history of diabetes mellitus, education level, smoking, alcohol consumption, and physical activity) known as the classic confounding factors in Model 1. In Model 2, we also adjusted for some variables which showed significance in the univariate analysis. However, we did not adjust for the intermediate variables such as SBP, DBP, and total cholesterol, because they might change according to the dependent variable. In contrast, we adjusted triglyceride, which is able to change into glucose through the metabolism in the body. Finally, we adjusted for the effect of other food groups besides algae in Model 3. We performed a separate analysis according to gender. Statistical significance was established at the level of $p < 0.05$.

Table 1. Basic characteristics according to fasting blood glucose groups.

| Variables | Male | | | Female | | | Age-adjusted p-value |
|------------------------------------|---------------------|------------------------|--------------------|---------------------|------------------------|--------------------|-------------------------|
| | Normal (n=1,044) | Prediabetes (n=277) | Diabetes (n=60) | Normal (n=1,746) | Prediabetes (n=204) | Diabetes (n=41) | |
| Age, y | 41.9±11.9 | 48.2±10.2 | 50.5±9.2 | 40.6±11.3 | 47.6±9.6 | 48.4±10.4 | |
| Body mass index, kg/m ² | 23.7±3.1 | 24.9±3.0 | 24.9±3.6 | 23.1±3.2 | 25.2±3.4 | 25.7±3.4 | <0.001 |
| Waist circumference, cm | 82.8±8.5 | 87.1±8.8 | 84.7±8.2 | 76.5±8.8 | 82.7±8.9 | 85.2±7.9 | <0.001 |
| SBP, mmHg | 119.4±14.2 | 124.4±15.0 | 129.7±16.3 | 111.1±15.4 | 121.0±16.6 | 122.9±15.9 | <0.001 |
| DBP, mmHg | 80.1±10.1 | 83.3±10.1 | 84.7±13.4 | 73.1±9.9 | 78.6±10.0 | 79.6±7.8 | <0.001 |
| Total cholesterol, mg/dL | 182.6±32.6 | 192.5±35.8 | 199.1±50.8 | 179.5±34.4 | 193.7±34.3 | 214.2±45.3 | <0.001 |
| Fasting glucose, mg/dL | 88.4±6.5 | 107.1±6.1 | 159.9±40.6 | 86.7±6.3 | 106.6±6.2 | 162.8±43.3 | <0.001 |
| HDL-cholesterol, mg/dL | 42.8±10.2 | 41.9±10.1 | 39.5±10.3 | 48.3±10.9 | 44.9±8.9 | 43.5±7.8 | <0.001 |
| Triglycerides, mg/dL | 141.9±97.2 | 194.6±165.8 | 338.0±475.2 | 102.4±67.3 | 130.8±69.7 | 175.0±102.3 | <0.001 |
| Current smoker, % | 49.9 | 43.3 | 55.6 | 4.1 | 4.4 | 2.4 | 0.943 |
| Low education (<12 y), % | 20.0 | 30.3 | 35.0 | 27.4 | 47.8 | 53.7 | <0.001 |
| Physical activity | 2.8±0.8 | 2.9±0.8 | 2.8±0.8 | 2.6±0.6 | 2.7±0.7 | 2.6±0.6 | <0.001 |
| Energy kcal/d | 2,202.7±604.4 | 2,108.2±585.8 | 2,154.0±664.9 | 1,802.7±593.1 | 1,797.5±573.6 | 1,830.1±561.3 | 0.205 |

Data are expressed as mean±SD for continuous variables.

Physical activity: five categories from sedentary to vigorous.

Table 2. Relative proportions of food groups consumed according to algae consumption quartiles.

| Food groups | Male | | | | | Female | | | | | p for trend* |
|----------------------|---------------|------------------|-------------------|-------------------|--|---------------|------------------|-------------------|-------------------|--|-----------------|
| | Q1 (0–8.5) | Q2 (8.6–21.5) | Q3 (21.6–32.8) | Q4 (over 32.9) | | Q1 (0–8.5) | Q2 (8.6–21.5) | Q3 (21.6–32.8) | Q4 (over 32.9) | | |
| n | 275 | 385 | 364 | 365 | | 377 | 545 | 482 | 612 | | |
| Cereals, % | 33.88 | 30.12 | 28.36 | 26.13 | | 32.60 | 30.82 | 28.11 | 26.33 | | <0.001 |
| Legumes, % | 5.83 | 6.69 | 6.71 | 7.69 | | 7.63 | 6.67 | 6.89 | 7.73 | | <0.001 |
| Potatoes, % | 1.42 | 1.50 | 1.86 | 1.76 | | 1.65 | 1.51 | 1.83 | 1.90 | | <0.001 |
| Vegetables, % | 35.6 | 34.28 | 34.50 | 34.7 | | 32.9 | 33.45 | 33.01 | 32.7 | | <0.001 |
| Fruits, % | 7.47 | 8.36 | 8.57 | 10.04 | | 9.67 | 9.78 | 10.72 | 11.49 | | <0.001 |
| Fish, % | 5.76 | 7.12 | 7.72 | 8.13 | | 5.31 | 6.38 | 6.83 | 7.84 | | <0.001 |
| Dairy products, % | 4.31 | 5.47 | 5.19 | 5.59 | | 5.57 | 5.92 | 6.50 | 6.29 | | <0.001 |
| Meat/poultry/eggs, % | 5.11 | 5.80 | 6.40 | 5.47 | | 4.06 | 4.81 | 5.35 | 5.14 | | <0.001 |
| Fast Foods, % | 0.60 | 0.66 | 0.69 | 0.52 | | 0.60 | 0.66 | 0.75 | 0.58 | | <0.001 |
| Energy, kcal | 2,076.3±634.5 | 2,150.5±586.5 | 2,243.9±578.7 | 2,235.2±614.8 | | 1,786.1±603.0 | 1,791.3±578.6 | 1,826.9±602.2 | 1,809.3±589.4 | | 0.038 |
| Alcohol, g/d | 11.8±30.1 | 12.3±32.1 | 15.0±30.3 | 16.8±36.9 | | 30.4±11.5 | 3.8±14.7 | 2.4±10.6 | 2.7±12.0 | | 0.270 |

* p for trend adjusted for age.

Table 3. Algae consumption and risk of abnormal glucose metabolism.

| Algae consumption | Number of people | Number of prediabetes | Number of diabetes | Odds ratio (95% CI) for diabetes vs. prediabetes vs. normoglycemia | | |
|-------------------|------------------|-----------------------|--------------------|--|--------------------------|--------------------------|
| | | | | Model 1 | Model 2 | Model 3 |
| Male | | | | | | |
| Q1 (0–8.5) | 274 | 62 | 15 | 1.000 | 1.000 | 1.00 |
| Q2 (8.6–21.5) | 383 | 77 | 10 | 0.76 (0.52–1.11) | 0.65 (0.44–0.96) | 0.64 (0.43–0.95) |
| Q3 (21.6–32.8) | 362 | 67 | 13 | 0.77 (0.53–1.12) | 0.69 (0.46–1.01) | 0.68 (0.46–1.01) |
| Q4 (over 32.9) | 362 | 71 | 22 | 0.81 (0.56–1.18) | 0.67 (0.46–0.98) | 0.66 (0.43–0.99) |
| Total | 1,381 | 277 | 60 | <i>p</i> for trend=0.351 | <i>p</i> for trend=0.086 | <i>p</i> for trend=0.088 |
| Female | | | | | | |
| Q1 (0–8.5) | 370 | 42 | 11 | 1.000 | 1.000 | 1.000 |
| Q2 (8.6–21.5) | 538 | 54 | 13 | 0.95 (0.64–1.42) | 0.94 (0.62–1.42) | 0.93 (0.60–1.39) |
| Q3 (21.6–32.8) | 477 | 49 | 6 | 0.89 (0.58–1.36) | 0.84 (0.55–1.30) | 0.77 (0.49–1.21) |
| Q4 (over 32.9) | 606 | 59 | 11 | 0.91 (0.61–1.35) | 0.92 (0.61–1.38) | 0.80 (0.51–1.24) |
| Total | 1,991 | 204 | 41 | <i>p</i> for trend=0.596 | <i>p</i> for trend=0.624 | <i>p</i> for trend=0.243 |

Model 1: adjusted for age, family history of diabetes, education, smoking, alcohol intake, and physical activity.

Model 2: adjusted for variables in Model 1+total energy intake, body mass index, waist circumference, triglycerides.

Model 3: adjusted for variables in Model 2+intakes of food groups.

RESULTS

Table 1 presents the crude mean \pm standard deviation for the basic characteristics of the study participants according to fasting blood glucose. Male and female participants in the prediabetes and diabetes groups had higher BMI, WC, blood pressure, total cholesterol, and triglyceride levels than those in the normoglycemia group, but lower HDL cholesterol levels. Overall, the percentage of participants with a level of education less than a high school graduation diploma was higher in the normal blood glucose group than the prediabetes or diabetes groups. The percentage of current male smokers was higher in the diabetes than the normoglycemia or prediabetes groups (Table 1).

Table 2 shows the relative proportions of 11 pre-defined food groups consumed according to algae consumption quartile. As algae consumption increased, so too did the consumption of proportions of legumes, fruits, fish, and dairy products ($p < 0.001$), while the relative proportions of cereals and fast foods consumed decreased significantly (Table 2).

After adjusting for the effect of the confounding variables, the summary odds ratios of disease progression were 0.66 for males and 0.80 for females (95% confidence interval (CI) 0.43–0.99, 0.51–1.24), in the highest algae intake quartile group compared with those in the lowest quartile (Model 3 in the Table 3).

The results of the trend tests showed that there was a marginally significant relationship between algae intake and the developing of diabetes in male.

DISCUSSION

Algae were used in the 4th century as a food in Japan and China (32, 33). Nowadays, these two nations and Korea are the biggest consumers of edible algae. According to KNHANES III, Koreans consume about

8.5 g of edible algae per adult person on a daily basis, with women consuming more algae than men (23).

Previous studies have shown that the consumption of algae has beneficial effects on Type 2 diabetes in vivo and in vitro (14, 20, 34). The protective effect of algae on Type 2 diabetes may involve multiple biological pathways; consumption of algae increases the level of fibers such as carageenan, agar, and alginic acid (30), and reduces the glycemic index of mixed meals (35, 36). Additionally, algae contain polyphenols, which have antioxidant effects and may protect against the progression of Type 2 diabetes (20, 37) as well as help prevent age-related degeneration. A previous study reported that dietary algae consumption affects the risk of Type 2 diabetes (38–40).

The findings show that the frequent consumption of algae may contribute to a decreased incidence of Type 2 diabetes due to the nutrient composition of algae. Possible mechanisms that may explain this could be related to the low energy density, low glycemic load, and the micronutrient content, such as Fe, Mg, and Ca. Total lipid content in algae is low, and algal fat is a negligible source of energy (41, 42). Although algal carbohydrate content is relatively high, algae cannot be considered a potential energy rich food because of the digestibility of these carbohydrates is low (42, 43). As algae also contains a large amount of micronutrients (44) that are scarce in land vegetables, algal-based supplements could not provide adults with the daily requirements of essential minerals (45). In particular, 'algae' was known to be a rich source of dietary fiber, and has been shown that dietary fiber may improve blood glucose (40, 46). In the present study, we found that after adjusting for the effect of other consumptions of food groups, algae consumption was independently associated with a decreased risk of Type 2 diabetes in Korean men.

The age-specific prevalence of diabetes and prediabetes was 25.1% for men in their fifties, while it increased to 25.7% for women in their seventies in KNHANES III (23). The age-specific prevalence of diabetes in men in their fifties was twice that of women in their fifties. We did not discover a positive relationship between algae consumption and a decreased risk of Type 2 diabetes in women. This is most likely because of the age-specific prevalence of diabetes by gender.

One limitation of this study is that it is difficult to determine a causal relationship between the consumption of algae and the decreased risk of Type 2 diabetes due to the cross-sectional nature of the study. Furthermore, FFQ has some degree of measurement error. These measurement errors could induce non-differential misclassification, and consequently relationships may be underestimated (26, 47). The true nature of these relationships would be more significant when considering the direction of bias due to non-differential misclassification of the algae consumption. In addition, we estimated the frequency of algae consumption but not the quantities, nor the type of algae consumed. We did not consider the cooking process (boiled, baked, fried, and the amount of cooking fat used) which might considerably affect the final nutrient content of algae.

In conclusion, there appears to be a significant association between the consumption of algae and a decreased risk of developing diabetes in Korean men. Further prospective studies are required to uncover the mechanisms underlying this relationship, if any.

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