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Research Article

Dietary Factors Associated with Dyslipidemia Traits in Individuals with Impaired Glucose Tolerance

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Abstract

Impaired Glucose Tolerance (IGT) is associated with a higher risk of cardiovascular diseases. This increased risk can be partly attributed to dyslipidemia traits, such as high levels of triglycerides or low levels of High-Density Lipoprotein-Cholesterol (HDL-C). However, this association has been rarely reported. Therefore, this study aimed to investigate the association between dietary factors and dyslipidemia traits in individuals with IGT. This cross-sectional study included 121 men and 124 women with IGT who were diagnosed on the basis of the 75-g oral glucose tolerance test. Demographic and biochemical parameters including body mass index, serum triglyceride, HDL-C, and insulin resistance index were measured. Dietary intake was assessed using a food frequency questionnaire. Men had significantly higher triglyceride and lower HDL-C levels as well as higher carbohydrate intake and significantly higher daily alcohol intake than women. The multiple regression analyses showed that alcohol intake positively correlated to the triglyceride level and carbohydrate intake negatively correlated to the HDL-C level in men, whereas carbohydrate intake positively correlated to the triglyceride level and alcohol intake positively correlated to the HDL-C level in women. The carbohydrate intake is a predictor of the HDL-C level in men and a possible predictor of the triglyceride level in women, whereas alcohol intake is a predictor of the triglyceride and HDL-C levels in men and women, respectively. These findings may facilitate the development of a sex-specific dietary strategy to improve dyslipidemia traits among individuals with IGT.

Keywords: Alcohol; Carbohydrate; Diabetes; Dyslipidemia

Abbreviations

IGT: Impaired Glucose Tolerance; HDL-C: High-Density Lipoprotein-Cholesterol; CVD: Cardiovascular Diseases; T2D: Type 2 Diabetes Mellitus; DPP: Diabetes Prevention Program; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; FFQ: Food Frequency Questionnaire

Introduction

There is an ongoing transition from a healthy, traditional, high-fiber, low-fat, and low-energy diet to a diet characterized by increased intake of high-energy foods containing refined carbohydrates, fats, red meats, and low fiber [1]. Developing countries are undergoing a rapid transition in nutritional trends that is concurrent with the increased incidence of metabolic disorders, such as obesity, glucose metabolic disorders, and dyslipidemia [2]. Dysregulated glucose metabolism increases the risk of Cardiovascular Diseases (CVD) [3]. Dyslipidemia traits such as high levels of triglycerides and low levels of High-Density Lipoprotein-Cholesterol (HDL-C) are reported to be a possible CVD risk factor in individuals with dysregulated glucose metabolism [4]. Dyslipidemia traits are generally associated with lifestyle factors, including smoking habit, exercise, alcohol consumption, and diet [5]. Thus, the regulation of dyslipidemia can be a crucial strategy for the mitigation of CVD risk in such individuals.

Impaired Glucose Tolerance (IGT) has been identified as a target state for preventing and/or delaying diabetes mellitus. Several clinical trials, such as the Diabetes Prevention Program (DPP) and the Finnish Diabetes Prevention Study, have shown that dietary intervention can beneficially control the progression of IGT to Type 2 Diabetes Mellitus (T2D) [6]. However, the association between specific dietary factors and dyslipidemia traits has rarely been explored in specific populations with IGT. Information on the possible association between the aforementioned factors may potentially facilitate in the reduction of CVD risk in individuals with dysregulation of glucose metabolism.

The cardiometabolic effects of carbohydrate intake, besides the influence of fat intake, have been debated [7,8]. Reports indicate that carbohydrate intake is potentially associated with dyslipidemia traits [9] and may increase the risk for CVD [10]. A relationship between dyslipidemia and specific dietary factors, including carbohydrates, is of great concern in the Japanese population, for whom rice is a staple food. This study was conducted with an aim to investigate the sex-based association between dyslipidemia traits, such as high levels of triglyceride and low levels of HDL-C, and dietary factors, by sex in Japanese study participants with IGT.

Materials and Methods

Study participants and study design

This investigation was undertaken as a part of the Japan Diabetes Prevention Study [11]. The study protocol was approved by the Ethics Committee of the National Hospital Organization Kyoto Medical

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Table 1: Population characteristics of men and women with impaired glucose tolerance in the Japan Diabetes Prevention Study.

Variables	Men (n=124)	Women (n=131)	*P*-value
Demographic parameters			
Age, years	50.0 (46.0– 56.0)	53.0 (49.3–57.0)	0.001
Current smoking, %	45	5.5	<0.001
Statin use, %	4	7.6	0.222
Body mass index, kg/m^2	24.8 (23.2–26.7)	23.3 (22.0–26.2)	0.161
Waist circumference, cm	88.5 (83.1–92.0)	80.5 (74.5–89.0)	<0.001
Metabolic parameters			
Fasting plasma glucose, mmol/L	6.1 (5.7–6.5)	5.8 (5.4–6.3)	<0.001
HOMA-IR	2.0 (1.4–2.6)	1.5 (1.1–2.2)	0.002
Triglyceride, mmol/L	1.6 (1.3–2.2)	1.0 (0.7–1.5)	<0.001
HDL-C, mmol/L	1.3 (1.2–1.6)	1.5 (1.3–1.8)	<0.001
Systolic blood pressure, mmHg	130.0 (118.0–140.0)	131.5 (120.0–140.0)	0.57
Diastolic blood pressure, mmHg	80.0 (74.0–89.9)	79.0 (72.0–86.0)	0.17
Dietary factors			
Total energy intake, kcal	2429(1837–3134)	2104 (1782–2498)	<0.001
Protein intake, g	86.5 (65.0–122.5)	89.0 (69.0–110.0)	0.344
Fat intake, g	66.5 (44.3–95.8)	64.0 (53.0–84.0)	0.379
Carbohydrate intake, g	304.0 (241.8–368.5)	280.0 (233.0–326.0)	0.018
Alcohol intake, g	15.9 (0.0–37.6)	0.3 (0.0–2.4)	<0.001
Energy expenditure, kcal	2290 (2100–2549)	2149 (1879–2437)	<0.001

Values are n (%) and median (25th–75th percentiles).
HOMA-IR: Homeostasis Model Assessment Insulin Resistance; HDL-C: High-Density Lipoprotein-Cholesterol

Center, and all participants provided written informed consent prior to study participation.

Participants with IGT, in the age range of 30-60 years, were recruited on the basis of health checkups conducted at each collaborating study center. A two-step strategy was adopted to identify participants with IGT, as described previously. The study exclusion criteria were as follows: 1) previous diagnosis of diabetes mellitus other than gestational diabetes, 2) history of gastrectomy, 3) physical ailments such as ischemic heart disease, heart failure, exercise-induced asthma, and orthopedic problems where exercise was contraindicated by a doctor, 4) liver or kidney diseases, 5) autoimmune diseases, and 6) heavy habitual alcohol consumption (≥69 g of ethanol per day). Heavy drinkers were excluded from this study because of the possible resistance that alcoholism confers against lifestyle intervention. Individuals who were on statin treatment were excluded as well. Both diabetes and IGT were diagnosed on the basis of the diagnostic criteria specified by the World Health Organization [12].

Assessments

Participants wore light clothing and removed their footwear prior to the measurements. Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. The Body Mass Index (BMI) was calculated as the weight in kilograms divided by the squared value of the height in meters. The waist circumference (in cm) at the umbilical level was measured with a non-stretchable tape in the late exhalation phase with the individual in the standing position. The blood pressure was measured twice in the sitting position after a 5-min rest, using a standard 12.5-cm cuff mercury sphygmomanometer. Current smoking was defined based on a self-report of an ongoing smoking habit.

Biochemical parameters, including serum triglyceride, HDL-C, plasma glucose, and insulin levels, were measured at a single central laboratory (SRL Co., Ltd., Tokyo, Japan) and were included in the study analyses. Insulin resistance was assessed by using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) [13]. The dietary intake of each participant was ascertained by using a validated semi quantitative Food Frequency Questionnaire (FFQ) [14], which had photographs of 122 dishes and food items; each item was depicted with a real portion size. Self-reported energy expenditures were assessed by using a physical activities questionnaire [15].

Statistical analysis

Data were analyzed using SPSS version 20.0 (IBM, Armonk, NY, USA). Sex-based differences were tested using the Mann–Whitney U and chi-square tests for categorical variables. The age-corrected Pearson's correlation coefficient and multiple linear regression model analyses were used to determine the correlation between the specified study parameters. The analyses in the multiple linear regression model was undertaken after adjusting for confounders, including age, smoking, BMI, dietary factors, and energy expenditure. The triglyceride levels were non-normally distributed and were log (base 10)-transformed for further analyses. Cases with missing data were omitted in the relevant analysis. A two-tailed P-value of less than 0.05 was considered statistically significant.

Results

Characteristics of participants

As shown in Table 1, men in this study, on average, were younger than the women and had a larger waist circumference. A higher proportion of male participants were current smokers and had higher fasting plasma glucose and serum triglyceride levels. The total energy intake, alcohol intake, and energy expenditure were higher in men than in women. Men tended to have a higher carbohydrate intake than women; however, there was no significant difference in protein and fat intake between the sexes.

Dietary factors and dyslipidemia

Both BMI and waist circumference were positively associated with serum triglyceride levels in men and women (Table 2). Current smoking and alcohol intake were positively associated with the triglyceride level in men, whereas carbohydrate intake was positively associated with the triglyceride level in women. The intake of white rice was positively associated with the waist circumference in both men and women, but was negatively associated with HDL-C levels in men. The intake of snacks was negatively associated with HDL-C levels in women. The prevalence of statin use was low among both sexes in this study population, but was positively associated with HDL-C levels; however, statin use was not associated with log-triglyceride in either men or women. Multiple linear regression analysis revealed that, in men, alcohol intake was positively associated with the triglyceride level, whereas carbohydrate intake was negatively associated with the

Table 2: Correlations between respective baseline parameters.

Parameters	Men				Women			
	BMI	WC	Log-TG	HDL-C	BMI	WC	Log-TG	HDL-C
Demographic parameters								
Current smoking, Yes	0.129	0.137	0.154	−0.244*	0.696	0.121	0.064	−0.102
Statin use, %	−0.004	−0.032	0.166	0.180*	0.009	0.039	−0.161	0.225*
BMI, kg/m^2		0.850*	0.127	−0.363*		0.797*	0.165	−0.252*
Waist circumference, cm	0.850*		0.220*	−0.408*	0.797*		0.13	−0.0137
Dietary factors								
Total energy intake, kcal	0.214*	0.158	−0.041	−0.092	0.075	−0.029	−0.039	0.013
Protein intake, g	0.175	0.112	−0.122	−0.059	−0.004	−0.102	−0.002	−0.012
Fat intake, g	0.166	0.105	−0.116	−0.091	0.045	−0.082	−0.031	−0.027
Carbohydrate intake, g	0.247*	0.194*	−0.072	−0.236*	0.13	0.063	−0.028	−0.014
Alcohol intake, g	0.104	0.092	0.202*	0.149	0.12	0.151	0.038	0.193*
Main source of complex carbohydrate								
White rice, g	0.126	0.204*	0.119	−0.226*	0.128	0.201*	−0.152	−0.095
Noodle, g	0.049	0.02	−0.157	−0.011	0.004	−0.060	0.031	−0.027
Bread, g	−0.119	−0.091	−0.126	0.11	0.013	−0.136	−0.020	−0.009
Fruit, g	−0.101	−0.146	−0.089	0.062	−0.007	−0.067	0.137	−0.100
Milk, g	0.086	−0.062	−0.074	0.026	−0.148	0.018	0.049	0.007
Snack, g	−0.002	0.051	−0.098	−0.088	0.189	0.069	0.085	−0.240*
Energy expenditure, kcal	0.357*	0.287*	0.087	−0.094	0.353*	0.262*	−0.123	−0.115

BMI: Body Mass Index; WC: Waist Circumference; TG: Triglyceride; HDL-C: High-Density Lipoprotein-Cholesterol

Table 3: Multiple regression analysis for dyslipidemia traits with explanatory parameters.

Parameters	Men				Women			
	log-TG		HDL-C		log-TG		HDL-C	
	β	*P*-value	β	*P*-value	β	*P*-value	β	*P*-value
Age	−0.062	0.551	0.044	0.657	0.114	0.252	−0.017	0.862
Body mass index	0.097	0.334	−0.318	0.001*	0.287	0.006*	−0.224	0.025*
Current smoking	0.139	0.154	−0.158	0.087	0.025	0.791	−0.131	0.146
Statin use, %	0.166	0.068	0.18	0.046*	0.225	0.012*	−0.161	0.065
Dietary factors								
Protein intake	−0.532	0.215	0.49	0.227	0.272	0.28	−0.152	0.529
Fat intake	0.262	0.517	−0.336	0.379	−0.198	0.398	0.178	0.429
Carbohydrate intake	0.084	0.585	−0.281	0.055	−0.084	0.551	−0.149	0.269
Alcohol intake	0.223	0.026*	0.137	0.146	0.03	0.76	0.297	0.002*
Energy expenditure	0.098	0.327	0.087	0.355	−0.222	0.026*	−0.099	0.297

TG: Triglyceride; HDL-C: High-Density Lipoprotein-Cholesterol.
β is the standardized coefficient. *P<0.05.

HDL-C level (Table 3). In women, carbohydrate and alcohol intake tended to be positively associated with the triglyceride and HDL-C levels, respectively. Low alcohol consumption was observed in the cohort of women, although there were 10 women with ≥10 g/day of alcohol intake (moderate drinking, as 1 drink=10 g of alcohol, in women, based on the definition by the Ministry of Health, Labour, and Welfare, Japan) and their HDL-C levels were significantly higher than in women with <10 g/day of alcohol intake (1.82±0.31 *vs*. 1.54±0.38, P=0.022). In addition, BMI was positively associated with the triglyceride level in both men and women, but negatively associated with the HDL-C level in women. Current smoking and energy expenditure were not significantly correlated with triglyceride and HDL-C levels in both men and women.

Discussion

Individuals with IGT are at risk for CVD [3]. However, the association between dyslipidemia traits and dietary factors in specific populations with IGT has been rarely examined. Given the scarce information on the dietary characteristics of CVD risk in relation to dyslipidemia in individuals with IGT, the results of the present study are valuable for the mitigation of CVD risk in Japanese individuals with IGT.

Daily alcohol intake was positively associated with the serum triglyceride level in men with IGT in this study, similar to the meta-analysis which showed that alcohol intake elevates serum triglyceride levels [16]. In general, it is difficult to regulate the triglyceride level [17], and these data reinforce the importance of alcohol restriction for the management of hypertriglyceridemia in men with IGT. In women with IGT, carbohydrate intake tended to be positively associated with the serum triglyceride level. High carbohydrate intake and consumption of foods with a high glycemic index are associated with higher triglyceride levels [18]. However, the results observed in the present study did not reach statistical significance for the association between carbohydrate intake and triglyceride levels; therefore, this finding needs to be validated in a future study.

The results of this study showed that carbohydrate intake was negatively associated with the serum level of HDL-C in men with IGT. This finding is supported by reports from previous studies [19], although the studied populations were not always similar across studies. High carbohydrate intake has been associated with low serum levels of HDL-C in healthy adults. Furthermore, low-carbohydrate diets have been reported to increase serum HDL-C levels [20].

Alcohol intake was positively associated with the HDL-C level in women with IGT, and findings from previous studies support this relationship. Alcohol consumption is associated with increased serum HDL-C levels [21], and moderate alcohol consumption has been reported to increase serum HDL-C levels [22]. In the DPP study, higher alcohol consumption tended to be associated with a higher HDL-C levels [23]. An association between a cardio protective effect with increased levels of HDL-C and alcohol consumption has been debated. A U-shaped relationship between alcohol consumption and incident myocardial infarction was identified in obese participants [24]. However, the clinical implications of the results of this study (a positive association between alcohol intake and the HDL-C level) need to be verified in follow-up studies. The significant relationships between dyslipidemia traits and dietary factors varied by sex in the present study. Sex-related differences in lipid levels are well-known [25] and this was also confirmed in the present study. Besides lifestyle factors, including smoking and alcohol intake that were previously reported [27] and confirmed to have sex-related differences in the present study, serum triglyceride and HDL-C levels are modulated by sex-oriented, intrinsic factors such as estrogen [28]. These factors may have partly led to the relative differences in the sex-related variations in the relationships between dyslipidemia traits and dietary factors in the present study.

A major strength of our study was the use of a community-based sample of Japanese adults with IGT. However, this study has some limitations. Firstly, the sample size was small. Secondly, the exact causes underlying the results cannot be determined because of the cross-sectional study design. To the best of our knowledge, no high-quality data have been reported from randomized controlled clinical trials of dietary intervention, with a focus on dyslipidemia traits, for the prevention of T2D and CVD among participants with IGT [29]. Large observational trials or randomized controlled trials are required to confirm these above-reported results. Thirdly, the data on macronutrient intake and alcohol consumption were self-reported, which could have led to the possibility of misclassification of exposure (e.g., underreporting). Fourthly, lipid traits can partially be affected by ethnicity and cultural factors. The generalization of these results to other populations must be prudently undertaken. Finally, the results of this study are only applicable to individuals with IGT.

Conclusion

In summary, carbohydrate intake is a predictor of HDL-C in men with IGT and may potentially be a predictor of triglyceride level in women with IGT. Alcohol intake is a predictor of triglyceride and HDL-C levels in men and women with IGT, respectively. The findings of this study may facilitate the development of sex-specific dietary strategies to improve dyslipidemia traits in individuals with IGT. However, the association of the findings of the present study with regard to the development of CVD in individuals with IGT needs to be ascertained in future research.

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