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Original Article

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

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Abstract

Background: Impaired glucose tolerance (IGT) is an independent risk factor of cardiovascular diseases. This increased risk can be partly explained by dyslipidemia traits, such as low levels of high-density lipoprotein-cholesterol (HDL-C) or high levels of triglyceride (TG). However, the sex-based association has been rarely reported. The study aimed to investigate the association between dietary factors and dyslipidemia traits in individuals with IGT.

Methods: The cross-sectional study included 124 female and 121 male with IGT. Demographic and biochemical parameters including body mass index, serum TG, HDL-C, and insulin resistance index were measured. Dietary intake was assessed using a food frequency questionnaire, and dietary intake was assessed.

Results: Male had significantly higher TG and lower HDL-C levels as well as higher carbohydrate intake and significantly higher daily alcohol intake than female. The multiple regression analyses showed that alcohol intake positively correlated to the TG level, although carbohydrate intake negatively correlated to the HDL-C level in male. In female, carbohydrate intake positively correlated to the TG level and alcohol intake positively correlated to the HDL-C level. The carbohydrate intake is a predictor of the HDL-C level in male and a possible predictor of the TG level in female, whereas alcohol intake is a predictor of the TG and HDL-C levels in both male and female, respectively.

Conclusions: 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

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Introduction

There is an ongoing transition from a traditional and healthy diet (i.e., low-fat and dietary fiber rich diet) to a diet characterized by increased intake of low-nutrient high-density foods [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 diabetes and cardiovascular diseases (CVD) [3]. Dyslipidemia traits such as low levels of high-density lipoprotein-cholesterol (HDL-C) and high levels of triglyceride (TG) are reported to be possible risk factors of CVD 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 Finnish Diabetes Prevention Study and Diabetes Prevention Program (DPP), have shown that dietary intervention can beneficially control the progression of IGT to type 2 diabetes mellitus (T2D) [6]. However, the relationship 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. The study was conducted with an aim to investigate the sex-based association between dietary factors and dyslipidemia traits in individuals with IGT.

Materials and Methods

Study participants and study design

The investigation was undertaken as a *post-hoc* analysis of

the Japan Diabetes Prevention Study (JDPP) [11]. Participants with IGT, aged 30 - 60 years, were recruited from collaborating study centers. We adopted a two-step strategy to identify individuals with IGT, as described previously. The study exclusion criteria were as follows: 1) T2D except gestational diabetes; 2) gastrectomy; 3) exercise therapy is contraindicated; 4) severe liver or kidney diseases; 5) autoimmune diseases; and 6) heavy alcohol consumption. Both IGT and diabetes were defined based on the criteria specified by the World Health Organization [12].

Assessments

Participants wore light clothing and removed their footwear prior to the measurements. We calculated the body mass index (BMI) as the weight in kilograms divided by the squared value of the height in meters. The waist circumference (in cm) was measured at the umbilical level in the late exhalation phase with the individual in the standing position. After a 5-min rest, the systolic and diastolic blood pressure in the sitting position was measured twice. Current smoking was defined based on a self-report of an ongoing smoking habit.

Biochemical parameters, including serum lipid (TG and HDL-C), serum insulin, fasting plasma glucose (FPG), and homeostasis model assessment of insulin resistance (HOMA-IR) [13] were measured. The dietary intake was assessed by a validated semiquantitative food frequency questionnaire (FFQ) with photographs of 122 dishes and food items [14]. Energy expenditures were assessed by self-administrated questionnaire [15].

Statistical analysis

Sex-based differences were tested using the Mann-Whitney U and Chi-square tests. The age-corrected Pearson's correlation coefficient and multiple linear regression model analyses were used. We undertook the multiple linear regression model after adjusting for confounders (age, smoking, BMI, dietary factors, and energy expenditure). The TG levels were non-normally distributed and were log (base 10)-transformed for further analyses.

The study protocol was approved by the Ethics Committee of the National Hospital Organization Kyoto Medical Center (approval number: 01-14), and was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Results

Characteristics of participants

As shown in Table 1, male patients in this study, on average, were younger than the female ones, and had a larger waist circumference. A higher proportion of male participants were current smokers and had higher FPG glucose and serum TG levels. The total energy intake, alcohol intake, and energy expenditure were higher in male than in female. Male tended to have a higher carbohydrate intake than female; 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 TG levels in male and female (Table 2). Current smoking and alcohol intake were positively associated with the TG level in male, whereas carbohydrate intake was positively associated with the TG level in female. The intake of white rice was positively associated with the waist circumference in both male and female, but was negatively associated with HDL-C levels in male. The intake of snacks was negatively associated with HDL-C levels in female. 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-TG in either male or female. Multiple linear regression analysis revealed that, in male, alcohol intake was positively associated with the TG level, whereas carbohydrate intake was negatively associated with the HDL-C level (Table 3). In female, carbohydrate and alcohol intake tended to be positively associated with the TG and HDL-C levels, respectively. Low alcohol consumption was observed in the cohort of female, although there were 10 female with $\geq$ 10 g/day of alcohol intake (moderate drinking, as 1 drink = 10 g of alcohol, in female, based on the definition by the Ministry of Health, Labour, and Welfare, Japan), and their HDL-C levels were significantly higher than in female 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 TG level in both male and female, but negatively associated with the HDL-C level in female. Current smoking and energy expenditure were not significantly correlated with TG and HDL-C levels in both male and female.

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 findings of the present study are valuable for the mitigation of CVD risk in Japanese individuals with IGT.

Daily alcohol intake was positively correlated with the serum TG level in male with IGT in this study, similar to the meta-analysis which showed that alcohol intake elevates serum TG levels [16]. In general, it is difficult to regulate the TG level [17], and these data reinforce the importance of alcohol restriction for the management of hypertriglyceridemia in male with IGT. In female with IGT, high carbohydrate intake tended to be positively correlated with the serum TG level. High intake of carbohydrate foods with a high glycemic in-

Table 1. Characteristics of Female and Male With IGT

Variables	Male (n = 124)	Female (n = 131)	P value
Demographic parameters			
Age, years	50.0 (46.0 - 56.0)	53.0 (49.3 - 57.0)	0.001
Current smoking, %	45.0	5.5	< 0.001
Statin use, %	4.0	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, mm Hg	130.0 (118.0 - 140.0)	131.5 (120.0 - 140.0)	0.570
Diastolic blood pressure, mm Hg	80.0 (74.0 - 89.9)	79.0 (72.0 - 86.0)	0.170
Dietary factors			
Total energy intake, kcal	2,429 (1,837 - 3,134)	2,104 (1,782 - 2,498)	< 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	2,290 (2,100 - 2,549)	2,149 (1,879 - 2,437)	< 0.001

Values are n (%) and median (25th - 75th percentiles).

dex are associated with higher TG levels [18]. However, the results observed in the present study did not reach statistical significance; therefore, this finding needs to be validated in a future study.

The results of the study indicated that carbohydrate intake was negatively correlated with the serum level of HDL-C in male 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 was associated with low levels of HDL-C in healthy adults. Furthermore, low-carbohydrate diets have been reported to increase serum HDL-C levels [20]. These findings might explain them.

Alcohol intake was positively correlated with the HDL-C level in female with IGT, and findings from previous studies support this relationship. Alcohol intake is correlated 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 higher HDL-C levels [23]. An association between a cardioprotective 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 [26, 27] and confirmed to have sex-related differences in the present study, serum TG 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, our study has some limitations. Firstly, the sample size in this study was relatively small. Secondly, the exact causes underlying the results cannot be determined, because this study was 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

Table 2. Correlations Between Respective Baseline Parameters

Parameters	Male				Female			
	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*	-	0.130	-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	0.020	-0.157	-0.011	0.004	-0.060	0.031	-0.027
Bread, g	-0.119	-0.091	-0.126	0.110	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

*P < 0.05.

of this study are only applicable to individuals with IGT.

Conclusions

In summary, carbohydrate intake is a predictor of HDL-C in male with IGT and may potentially be a predictor of TG level in female with IGT. Alcohol intake is a predictor of TG and HDL-C levels in male and female 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

Table 3. Multiple Regression Analysis for Dyslipidemia Traits With Explanatory Parameters

Parameters	Male				Female			
	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	0.180	0.046*	0.225	0.012*	-0.161	0.065
Dietary factors								
Protein intake	-0.532	0.215	0.490	0.227	0.272	0.280	-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	0.030	0.760	0.297	0.002*
Energy expenditure	0.098	0.327	0.087	0.355	-0.222	0.026*	-0.099	0.297

*P < 0.05.

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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Conflict of Interest

The authors declare no competing interest.

Informed Consent

Informed consents were obtained.

Author Contributions

NS and HK conceived the ideas and acquired the funding. AS analyzed the data. NS and HK wrote the article.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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