

Is Dietary Phytochemical Index in Association with the Occurrence of Hypertriglyceridemic Waist Phenotype and Changes in Lipid Accumulation Product Index? A Prospective Approach in Tehran Lipid and Glucose Study

Mottaghi A.¹, Bahadoran Z.¹, Mirmiran P.^{1*}, Mirzaei S.¹, Azizi F.²

¹Nutrition and Endocrine Research Center, and Obesity Research Center, Research Institute of Endocrine Sciences, Shahid Beheshti University of Medical Sciences, P.O. Box 193-4763, Tehran, Iran

²Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran, P.O. Box: 193-4763

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ABSTRACT

Background: The present study aimed to determine effect of the phytochemical index (PI) score on the incidence of hypertriglyceridemic waist (HTW) phenotype and lipid accumulation product (LAP) index in adults. **Materials and Methods:** This study was conducted within the framework of the Tehran Lipid and Glucose Study (TLGS). Biochemical and anthropometric measurements were assessed at baseline and after 3 years. A food frequency questionnaire (FFQ) was used to assess food intake at baseline. Dietary PI was calculated based on the modified method developed by McCarty. **Results:** After adjustment for potential confounders, dietary PI were inversely associated with changes in waist circumference ($\beta = -0.08$, $P < 0.01$), serum triglycerides ($\beta = -0.07$, $P < 0.01$) and LAP ($\beta = -0.09$, $P < 0.01$) after 3 years. Risk for occurrence of HTW phenotype in participants with highest compared to lowest dietary PI was significantly reduced (OR=0.5, 95% CI= 0.26-0.96). **Conclusion:** Higher phytochemical intake is associated with lower occurrence of HTW phenotype.

Keywords: Phytochemical, Hypertriglyceridemic waist, Lipid accumulation product, phytochemical index

INTRODUCTION

Many metabolic abnormalities, associated with central obesity and intra-abdominal adipose tissue could be more harmful than subcutaneous obesity¹. Waist circumference (WC) is related to visceral adipose tissue². The hypertriglyceridemic waist (HTW) phenotype, proposed as a diagnostic tool for visceral obesity³, is defined as the simultaneous presence of elevated serum triglyceride (TG) and increased waist circumference. High and low prevalences of HTW have been reported in Chinese women (33.6%)⁴ and Spanish women (10.8%), respectively⁵. The prevalence of HTW in Iranian women is 23.6%⁶. Evidence indicates that the HTW phenotype can put people at risk of cardiovascular diseases⁷. HTW is an excellent phenotype for prediction of diabetes mellitus (DM) and is closely associated with fasting glucose⁸. Lipid accumulation product (LAP) is a simple index for lipid over-accumulation in adults and was initially proposed by Kahn⁹; it reflects the combined anatomic and physiologic changes associated with lipid over-accumulation and is based on two measurements (WC and TG) that are safe and inexpensive to obtain; WC and circulating triglycerides are strongly associated with metabolic insulin resistance¹⁰, daylong TG¹¹, and with cardiovascular risk^{12,13}. Some prospective studies have

shown that the abdominal obesity and elevated circulating TG is associated with death from myocardial infarction and all cause and cardiovascular mortality, as well as the annual progression rate of aortic calcification^{14,15}.

Phytochemicals are bioactive nonnutrient plant chemicals found in high amount in fruits, vegetables, grains, nuts and legumes, may provide desirable health benefits and reduce risk of major chronic diseases¹⁶. Phenolic compounds are entitled as phytochemicals. Phytochemical provide protection against cardiovascular disease, inflammation and oxidative stress¹⁷, vascular dysfunction¹⁸ and type 2 diabetes^{16,19}. Monitoring phytochemical intakes in a population-based study is expensive, laborious and impractical. McCarty²⁰ proposed a simple and practical method for quantification of phytochemical intakes. The phytochemical index (PI), is defined as the percent of dietary calories derived from foods rich in phytochemicals. Calories derived from fruits, vegetables (except for potatoes), legumes, whole grains, nuts, seeds, fruit/vegetable juices, soy products, wine, beer, and cider are enumerated in this index. According to the PI, the vegan diet (excluding potato products, hard liquors and refined sugar) has the highest score 100, whereas

Table 1. Characteristics of participants by quartile categories of dietary phytochemical index: Tehran Lipid and Glucose Study

	(n = 1552)				P ¹
	Q1 n=387	Q2 n=388	Q3 n=388	Q4 n=388	
Dietary phytochemical index					
Range	<43.5	43.5-53.6	53.6-64.0	>64.0	
Mean	33.8±0.3	48.6±0.3	58.4±0.3	72.1±0.3	0.05
Age at baseline (yr)	33.9±0.6	38.3±0.6	41.2±0.7	44.1±0.7	0.01
Physical activity at baseline (Met-h/week)	35.7±2.7	37.3±2.7	32.1±2.7	35.9±2.7	0.51
Smoker at baseline (%)	13.3	9.0	8.8	13.9	0.88
Men (%)	52	40	34	35	0.01
Weight (kg)					
Baseline	71.7±0.7	72.4±0.7	71.3±0.7	71.5±0.7	0.52
After 3 years	73.0±0.3	72.6±0.3	72.7±0.3	71.9±0.3	0.03
3-year weight gain (kg)	2.2±0.2	1.8±0.2	1.8±0.2	1.1±0.2	0.03
Waist circumference (cm)					
Baseline	87.8±0.6	88.6±0.6	87.6±0.6	87.5±0.6	0.57
After 3 years	93.1±0.5	92.2±0.5	91.6±0.5	90.4±0.5	0.01
Serum triglycerides (mg/dl)					
Baseline	112±2.6	116±2.5	115±2.5	109±2.5	0.15
After 3 years	118±2.7	119±2.7	114±2.7	109±2.7	0.04
Lipid accumulation product					
Baseline	35.3±0.9	35.4±0.9	34.1±0.9	31.6±0.9	0.01
After 3 years	42.6±1.2	42.4±1.2	41.1±1.2	38.5±1.2	0.07

¹ Data are adjusted mean ± SEM. General linear model with adjustment for age and gender was employed.

Table 2. Mean dietary intake of participants by categories of dietary phytochemical index at baseline (2006-2008): Tehran Lipid and Glucose Study

	(n = 1938)				P ¹
	Q1	Q2	Q3	Q4	
Dietary phytochemical index					
Range	<43.5	43.5-53.6	53.6-64.0	>64.0	
Mean	33.9±0.6	38.3±0.6	41.2±0.7	44.1±0.7	0.01
Energy intake (kcal/d)	2790±27	2436±27	2130±27	1789±27	0.01
Carbohydrate (% of total energy)	56.6±0.4	56.9±0.4	58.1±0.4	58.8±0.4	0.01
Fat (% of total energy)	31.5±0.3	31.6±0.3	31.1±0.3	31.1±0.3	0.59
Protein (% of total energy)	13.9±0.1	13.7±0.1	13.6±0.1	13.2±0.1	0.01
Total fiber (g/d)	33.6±0.8	36.5±0.8	39.6±0.8	39.8±0.8	0.01
Total carotenoids (mg/d)	6.1±0.3	9.2±0.3	11.0±0.3	12.4±0.3	0.01
Vitamin E (mg/d)	10.1±0.3	11.2±0.3	12.2±0.3	13.1±0.3	0.01
Vitamin C (mg/d)	75±4	134±4	169±4	191±4	0.01
Whole grains (g/d)	94±4	88±4	91±4	87±4	0.60
Fruits (g/d)	171±12	333±11	438±11	524±11	0.01
Vegetables (g/d)	182±8	273±8	312±8	342±8	0.01
Legumes (g/d)	13.5±0.9	13.4±0.9	16.1±0.9	16.1±0.9	0.01
Seeds (g/d)	1.3±0.2	1.8±0.2	1.9±0.2	2.0±0.2	0.02
Nuts (g/d)	4.9±0.4	7.3±0.4	7.7±0.4	8.4±0.4	0.01

Data are adjusted mean ± SEM. general linear model with adjustment for age, gender, and energy intake was used.

unhealthy dietary patterns such as Western diets have scores below 20. Since it is not known whether the PI score affects the incidence of HTW phenotype and LAP index, the present study aimed to determine effect of PI scores on the incidence of the HTW phenotype and the LAP index in Iranian adults.

MATERIALS AND METHODS

Study population

This study was conducted within the framework of the Tehran Lipid and Glucose Study (TLGS). In brief, TLGS is a community-based prospective study conducted to investigate non-communicable diseases, in a representative sample of residents, aged ≥ 3y, from district

13 of Tehran, the capital city of Iran. The first phase of the TLGS began in March 1999 and data collection, at three-year intervals, is ongoing²¹.

Table 3. The association of dietary phytochemical index with 3-year changes of waist circumference, serum triglycerides and lipid accumulation product

	β	<i>P</i> value
Waist circumference	-0.08	0.01
Serum triglycerides	-0.07	0.01
Lipid accumulation product	-0.09	0.01

Linear regression model was used with adjustment for age, weight at baseline and dietary energy intake.

Baseline examination of our study included 2799 adults (1129 men and 1438 women), aged 19-70 years who participated in the third phase of TLGS (2006-2008), and had complete data, including demographics, anthropometrics, biochemical and dietary assessments²². Participants were excluded from the final analysis if they reported implausible energy intake (<800 kcal/d or \geq 4200 kcal/d) or were on specific diets (n=262), had no follow-up information on anthropometrics and biochemical measurements at the second examination (2009-2011) (n=629), or were consistent with the definition of HTW phenotype at baseline (n=386). Finally, 1552 participants were included in the analysis. The mean duration of the follow-up was approximately 3 years.

Written consents were obtained from all participants and the study protocol was approved by the ethics research council of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences.

Data collection

Baseline characteristics of the participants including age, smoking status, physical activity levels and anthropometric measurements were determined. Smoking status was obtained using face-to-face interviews; subjects who smoked daily or occasionally were considered as current smokers, whereas non-smokers included those who had never smoked or those who had quit smoking. Weight was measured to the nearest 100g using digital scales, while the subjects were minimally clothed, without shoes. Height was measured to the nearest 0.5 cm, in a standing position without shoes, using a tape meter. Body mass index was calculated as weight (kg) divided by square of the height (m²). Physical activity level was assessed based on the frequency and time spent on light, moderate, high and very high intensity activities according to the list of common activities of daily life over the past year. Physical activity levels were expressed as metabolic equivalent hours per week (METs h/wk).

Waist circumference was measured to the nearest 0.1 cm (at anatomical landmarks), at the widest portion, over light clothing, using a soft, tape meter, without any pressure to the body.

For serum triglyceride measurement, fasting blood samples were taken after 12-14 h, from all study participants at baseline and after the 3-year follow-up. TG level was measured by enzymatic colorimetric analysis

with glycerol phosphate oxides. Analyses were performed using Pars Azmoon kits (Pars Azmoon Inc., Tehran, Iran) and a Selectra 2 auto-analyzer (Vital Scientific, Spankeren, Netherlands). Inter- and intra-assay coefficients of variation of all assays were both < 5%.

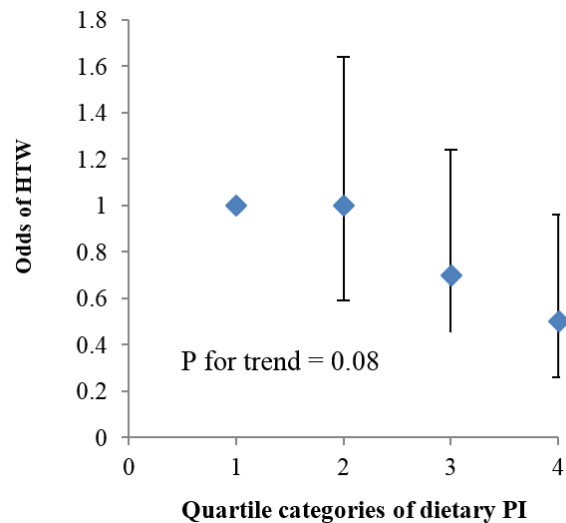


Figure 1. The occurrence of HTW phenotype across quartile categories of dietary PI, after a 3-years follow-up among Tehranian adults.

The principal dietary exposure of interest in the current study was dietary phytochemical index at baseline examination. A 168-item food frequency questionnaire (FFQ) was used to assess typical food intakes over the previous year. The validity of the food frequency questionnaire was previously evaluated by comparing food groups and nutrient values determined from the questionnaire with values estimated from the average of twelve 24-h dietary recall surveys²³. Trained dietitians, with at least 5 years of experience in the TLGS survey, asked participants to designate their intake frequency for each food item consumed during the past year on a daily, weekly, or monthly basis; portion sizes of consumed foods reported in household measures were then converted to grams²³. Because the Iranian Food Composition Table is incomplete, and has limited data on nutrient content of raw foods and beverages, to analyze foods and beverages for their energy and nutrient content, we used the US Department of Agriculture FCT.

Dietary phytochemical index was calculated based on the modified method developed by McCarty, as follows: $PI = [\text{daily intake of phytochemical-rich foods (g/d)} / \text{total daily food intake (g/d)}] \times 100$ ²⁰. Dietary PI index was residually adjusted for energy intake. Foods included in the phytochemical-rich category were fruits and vegetables, legumes, whole grains, nuts, soy products, tea, olives and olive oil. Potatoes were not considered as vegetables because they are often consumed as a starch component rather than as vegetables. Natural fruit and vegetable juices as well as tomato sauces were included in the fruit and vegetable groups because these are also considered as rich sources of phytochemicals.

Definition of terms

HTW phenotype was defined as waist circumference ≥ 90 cm and triglycerides ≥ 177 mg/dl for men and as waist circumference ≥ 85 cm and triglycerides ≥ 133 mg/dl for women²⁴.

LAP index, a novel central lipid accumulation and predictor of metabolic syndrome, cardiovascular disease, was calculated as follows: [waist circumference (cm) - 65] \times [triglycerides (mmol)] in men, and [waist circumference (cm) - 58] \times [triglycerides (mmol)] in women^{25,26}.

Statistical methods

All statistical analysis were conducted using SPSS (Version 16.0; Chicago, IL), and *P* values < 0.05 were considered significant. Dietary PI at baseline was divided into quartiles, and participant characteristics were compared across quartile categories of PI using the general linear model with adjustment for age (year, continuous) and gender, or the Chi-square test. Mean dietary intakes of participants were also compared across quartile categories of PI using the general linear model with adjustment for age (year, continuous), gender and energy intake (kcal/d). Three-year changes of waist circumference, serum triglycerides and lipid accumulation product were calculated as: [(follow-up measure - baseline measure) / baseline measure] $\times 100$. To estimate the association of dietary PI with 3-year changes of waist circumference, serum triglycerides and lipid accumulation product, linear regression models with adjustment for age, weight at baseline and dietary energy intake.

To estimate the odds ratio of HTW at the second examination in each quartile category of dietary PI, logistic regression model was used with adjustment for gender, age (y, continuous), and waist circumference (cm) and serum triglyceride (mg/dl) at baseline, and total energy intake (kcal/d). To assess the overall trends of the odds ratio of HTW across quartile categories of dietary PI, the median of PI in each quartile was used as a continuous variable in the logistic regression model.

Results

The mean age of participants at baseline was 38.9 ± 13.6 years. Forty percent of participants were men. Mean weight gain was 1.70 ± 5.1 kg (1.9 ± 5.4 kg in men and 1.5 ± 4.9 kg in women) after 3 years. Mean WC at baseline and 3-year changes in WC were 87.2 ± 13.2 cm (92.7 ± 11.1 in men, and 83.4 ± 13.0 in women), and 4.9 ± 7.1 cm (2.1 ± 4.9 in men, and 6.9 ± 7.7 in women), respectively. Mean LAP was 34.6 ± 22.6 (38.2 ± 22.1 in men, and 32.3 ± 22.7 in women) at baseline, and 43.2 ± 29.9 at second examination (44.8 ± 30.1 in men, and 42.1 ± 29.7 in women). The mean PI was 53.3 ± 15.2 (50.5 ± 15.9 in men, and 55.2 ± 14.3 in women). Dietary PI was associated with several characteristics of participants (Table 1); participants in the highest PI quartile category were more likely to be women than men (65 vs. 35%, $P < 0.01$), and were older (44.1 vs. 33.9 years, $P < 0.01$). There was no significant difference in body weight and WC at baseline across quartile categories of PI but after 3-years of follow-up, participants in the highest PI quartile category had lower body weight (71.9 vs. 73.0 kg, $P < 0.01$) and waist circumference (90.4 vs. 93.1 cm, $P < 0.01$); they also had lower weight gain (1.1 vs. 2.2 kg, $P < 0.05$). The mean

dietary intake of participants across dietary PI quartile categories is presented in Table 2. Dietary energy and protein intake decreased significantly across quartiles of PI (P for trend < 0.01), while dietary intake of carbohydrate, fiber, vitamin E and vitamin C significantly increased (P for trend < 0.01). After adjustment for potential confounding variables, dietary PI were inversely associated with 3-year changes in waist circumference ($\beta = -0.08$, $P < 0.01$), serum triglycerides ($\beta = -0.07$, $P < 0.01$) and LAP ($\beta = -0.09$, $P < 0.01$) (Table 3). The odds and 95% CI for the occurrence of HTW phenotype in each quartile category of PI after 3-year follow-up are presented in Fig.1. After adjustment for potential confounders, the occurrence risk of HTW phenotype in participants with highest compared to lowest dietary PI was significantly lower (OR=0.5, 95% CI= 0.26-0.96).

DISCUSSION

The current study, conducted in Tehranian adults, showed favorable inverse associations of PI score with LAP index and odds of occurrence of HTW phenotype. To our knowledge, this is the first study reporting the association of PI score with HTW phenotype and LAP index.

In the present study, mean PI index was 53.3 ± 15.2 and it was higher in women and older individuals, findings indicating that women and older people are more attentive to their health and may use more vegetables and phytochemical rich foods in their diet; in agreement with our findings, Schroder et al. found that diet quality improved with age²⁷. Results of this study showed that participants in the highest quartile categories of PI had lower body weight and lower weight gain after 3 years of follow-up. In one study, the PI score was inversely related to weight gain, body fat percentage and BMI²⁸. In another cohort study, adherence to the traditional Mediterranean diet, rich in vegetables, fruits and nuts was inversely associated with lower BMI²⁹. Phytochemicals via blocking pancreatic lipase and α -amylase, prevent absorption of dietary carbohydrates and/or lipids and help in controlling body weight³⁰. One in vitro study has shown that polyphenols found in fruits and vegetable such as quercetin, naringenin, hesperidine and resveratrol inhibit proliferation and induce apoptosis of preadipocytes. Some flavonoids also reduce adipogenesis and stimulate lipolysis in adiposities³¹. Our findings suggest overall diet quality was improved across quartiles of PI. Dietary energy and protein intakes decreased while intakes of carbohydrate, fiber, vitamin E, vitamin C, total carotenoids increased significantly. Reduction in energy and protein intake across quartiles of PI and increased vitamin C, vitamin E and fiber intake may be due to increase in consumption of vegetables, fruits, legumes and seeds, all of which contain high fiber and low energy. In a longitudinal study, researchers found that energy intakes, over 37% of energy, from phytochemical rich foods could prevent weight gain and reduction in adipose tissue³².

We also found that PI score was inversely related to serum TG, WC and LAP in adults. These findings demonstrate that whatever intakes of phytochemical rich foods increase serum TG, WC and LAP index decrease. In accordance

with our results, Esmailzadeh et al. showed that prevalence and odds of HTW phenotype were lower in subjects with higher intakes of whole-grain foods that contain high amounts of phytoestrogens and antioxidants³³ one of the causes of reduction in WC and serum TG following the consumption of phytochemical rich foods may be these foods low in calories. Fewer calorie intakes prevent weight gain and abdominal obesity. Fat accumulated in center of body can release fatty acid into circulation and result in increased blood lipid levels. A previous study reported that PI index is inversely associated with body weight and body fat mass in adults²⁸. There are several mechanisms to discuss benefit effects of phytochemical in obesity prevention. Some human studies indicate that phytochemicals play a pivotal role in appetite regulation, carbohydrate and lipid metabolism adjustment and the direct regulation of proliferation, differentiation and metabolism of adipocytes²⁸. Whole grains and nuts and also legumes are rich sources of phytoosterols and stanols and intakes of these can reduce absorption of dietary and biliary cholesterol from the gut and increase the enterohepatic cycle of biliary cholesterol, as a result of serum cholesterol decreases³⁴.

Several clinical studies have reported that flavonoids, such as quercetin, have a role in serum lipid reduction^{35,36} a quercetin concentration at 5nM in the human intestinal CaCo-2 cell line can inhibit TG synthesis, which in turn causes inhibition of the secretion of both apoB-100 and apo B-48³⁷. Galangin, as a flavonol glycoside, can prevent increase of body weight, energy intake and parametrial adipose tissue weight, induced by cafeteria diet in female rats. In addition, galangin produced a significant decrease in serum lipids, liver weight, lipid peroxidation and accumulation of hepatic TGs³⁸.

There are several limitations for this study. First, we used the McCarty PI score that has not considered tea, coffee and spices as sources of phytochemicals; had these values been added to the data obtained, stronger relationships would probably have been found. Second, the design of this study is cross-sectional, and longitudinally designed studies are needed to determine any relationship between the incidence of HTW phenotype and LAP index with phytochemical intakes.

The greatest strength of this study is using a population that is demographically representative of the population of Tehran. In this study we used the logistic regression model to show the relationship between the incidence of the HTW phenotype and phytochemical intakes.

The point of strength of this method is taking into account the confounding variables.

It can be concluded that the higher phytochemical intake is associated with the lower occurrence of HTW phenotype. We recommend that adults eat more fruits and vegetables and other sources of phytochemicals because increase in serum TG and WC, which are directly associated with cardiovascular diseases.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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