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NUTRITION
Research Article

Evaluation of Family History, Antioxidant Intake and Activity Level as Indicators for Chronic Disease in A Healthy Young Population

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Received: April 24, 2015; **Published:** May 02, 2015

Abstract

We recruited 24 men and 26 women (18-30 y) to evaluate whether family history, activity level, or dietary intake correlated with dyslipidemias, blood pressure or blood glucose levels in this young population. The mean values for plasma triglycerides (72.5 ± 29.9 mg/dL), LDL-cholesterol (LDL-C) (75.6 ± 24.4 mg/dL) HDL-cholesterol (64.9 ± 18.9 mg/dL), glucose (92.2 ± 6.6 mg/dl), systolic (112.0 ± 12.4 mmHg) and diastolic blood pressure (72.9 ± 7.0 mmHg), body mass index (23.3 ± 3.1 kg/m^2), and waist circumference (81.3 ± 6.5 cm) were within a healthy range. However, 32% of individuals (n = 16, 11 male and 5 female) had either elevated LDL-C (> 100 mg/dL), or at least one parameter associated with metabolic syndrome. Family history indicated that 60% of the participants could be at risk for cancer, 46% for heart disease, and 38% for diabetes. For all subjects, number of active minutes per week was negatively correlated with LDL-C ($r = -0.339$, $P < 0.05$) and triglycerides ($r = -0.41$, $P < 0.01$), whereas HDL-cholesterol was positively correlated with intake of the carotenoids, lutein and zeaxanthin ($r = 0.339$, $P < 0.05$).Systolic ($r = -0.277$, $p < 0.05$) and diastolic blood pressure ($r = -0.307$, $P < 0.05$) negatively correlated with dietary lutein and zeaxanthin. These results imply that increased physical activity and a diet high in antioxidants favorably affect biomarkers for heart disease and diabetes, suggesting that lifestyle factors may protect against disease risk in this population characterized as having a family history of chronic disease.

Keywords: *Chronic disease; diet; exercise; family history; healthy population*

Abbreviations: BMI: Body Mass Index; BP: Blood Pressure; HDL-C: HDL-Cholesterol; LDL-C: LDL-Cholesterol; MetS: Metabolic Syndrome; PCSK9: Protein Convertase Subtilisin/Kexin type 9; TC: Total Cholesterol; TG: Triglycerides; WC: Waist Circumference

Introduction

It has been established that a healthy lifestyle comprised of appropriate dietary habits and adequate physical activity can counteract genetic predisposition for the development of chronic disease [1]. There are a number of useful dietary interventions to control for the development of Metabolic Syndrome (MetS) [2], a clinical condition characterized by a constellation of biomarkers, which together increase the risk for heart disease and diabetes by 2-fold and 5-fold, respectively [3]. There are also dietary interventions designed to prevent diabetes [4], heart disease [5] or cancer [6]. For example, the Mediterranean diet, which is high in olive oil, fish, whole grain, fruits and vegetables, has been demonstrated both in epidemiological studies [7,8] and clinical interventions [9] to decrease the biomarkers

for heart disease [10] and diabetes [11]. Other diets that are considered useful in decreasing the biomarkers associated with MetS and diabetes are low carbohydrate diets [12,13], diets high in dietary fiber [14], and diets high in antioxidants [15]. Recent studies have shown that certain foods, including eggs and soy, might be beneficial in individuals with MetS or type 2 diabetes by decreasing inflammatory markers [16], increasing HDL-cholesterol (HDL-C) [17], decreasing other cardiovascular risk factors [18] or have an association with reduced breast cancer incidence and mortality [19].

The role of dietary antioxidants, including carotenoids and polyphenols, in improving the biomarkers associated with non-communicable diseases [20] has been well established. Epidemiological data also support that high intake of fruits and vegetables rich in antioxidants protect against atherosclerosis, heart disease, diabetes and cancer [21-23].

The Center for Disease Control and Prevention recommends 150-300 minutes per week of low to moderate intensity exercise for health maintenance in adults. Exercise has proven to increase the quality of life in patients with chronic heart failure [24], and has also been used successfully in preventing MetS [25] and improving non-alcoholic fatty liver disease [26]. However, the strongest lifestyle factor that protects against chronic disease is the maintenance of a healthy body weight [8,27], which can be achieved by a combination of a healthy diet and increased physical activity.

In this study, we evaluated the presence of biomarkers related to chronic disease in a young healthy population, and aimed to determine the population's potential risk for developing non-communicable diseases associated with their lifestyle habits and family history. We hypothesized that dietary antioxidants and physical activity levels would be negatively correlated with biomarkers of chronic disease even in those with a strong family history of cancer, heart disease, and type 2 diabetes.

Materials and Methods

Experimental design

We recruited a healthy population (24 men and 26 women), aged 18-30 years old. The exclusion criteria were plasma total cholesterol TC) > 240 mg/dL, plasma triglycerides (TG) > 500 mg/dL; blood pressure (BP) > 145/90 mmHg, fasting blood glucose > 126 mg/dL, and body mass index (BMI) > 30 kg/m^2. Subjects were asked to fast overnight for 12 hours and blood was taken to measure plasma lipids and glucose. In addition, blood pressure (BP), body weight, and waist circumference (WC) were determined, 3-day dietary and exercise records (two non-consecutive days and one weekend day) were collected for each participant. The study protocol was approved by the University of Connecticut-Storrs Institutional Review Board, and all participants signed the written, informed consent.

Diet and physical activity assessment and family history

Participants were asked to complete3-day records to assess dietary intake. Dietary records were analyzed using the Nutrition Data System for Research (NDSR) (Nutrition Coordinating Center, University of Minnesota) nutrient analysis software. Physical activity was assessed using 3-day records targeted at evaluating number of active minutes per week. Family history was assessed by a questionnaire that asked participants if a parent, grandparent or sibling had been diagnosed with: heart disease, high blood pressure, elevated plasma cholesterol, type 2 diabetes or cancer. Subjects were considered to be at risk for any of these conditions if they responded "yes" to the disease-specific survey questions.

Anthropometrics and blood pressure

Body weight was calculated to the nearest 0.5 kg and height to the nearest centimeter to calculate BMI (kg/m^2). WC was measured on bare skin during minimal respiration at the top of the iliac crest to the nearest 0.1 cm. Blood pressure (BP) was measured using an automated BP monitor (Omron, Healthcare Inc., Bannockburn, IL) after participants were seated and rested for at least 5 minutes. The average of three separate recordings was used for both WC and BP measures.

Blood collection and processing and plasma lipids

Blood (7 ml) was drawn from participants into EDTA-coated blood collection tubes after a 12-h overnight fast and immediately centrifuged at 2000 x g for 20 minutes at 4°C for the separation of plasma. Plasma TC, HDL-C, TG, and glucose were measured using an automated clinical chemistry analyzer (Cobas C111, Roche Diagnostics, Indianapolis, IN) via enzymatic methods. Plasma LDL-C was estimated via the Friedewald equation.

Statistical Analysis

Data are presented as mean ± SD for men and women. An un-paired t test was used for comparisons between groups. Pearson correlations were performed to assess the relationship between dietary intake, parameters of MetS and physical activity levels (number of active minutes per week) and plasma lipids. $P < 0.05$ was considered to be significant. SPSS version 14 was used for statistical analysis.

Results and Discussion

Dietary Intake and Level of Activity

Baseline dietary intake is presented in Table 1. As expected, the female participants had 19% lower daily energy intake when compared to male participants ($p < 0.01$). In addition, females had a lower daily intake of total fat (g) ($p < 0.01$) and carbohydrate (g) ($p < 0.01$), while total protein intake did not differ between genders. Men consumed a more energy-dense diet overall, as indicated by the higher consumption of total sugar, higher glycemic index and glycemic load, as well as lower consumption of the carotenoids beta-carotene, cryptoxanthin and lutein and zeaxanthin (Table 1).

Parameter	Women (n =26)	Men (n = 24)
Energy (kcal)	2002 ± 538[a]	2469 ± 940[b]
Carbohydrate (%en)	43.8 ± 6.38	42.9 ± 7.3
Fat (%en)	36.1 ± 5.0	36.8 ± 6.8
Protein (%en)	17.7 ± 4.2	18.8 ± 4.4
Alcohol (%en)	2.6 ± 4.4	2.1 ± 4.6
Total Carbohydrate (g)	222.1 ± 69.9[a]	270.8 ± 114.2[b]
Total fat (g)	82.7 ± 26.9[a]	97.8 ± 43.0[b]
Total Protein (g)	109.4 ± 107.1	121.0 ± 86.7
Cholesterol (mg)	341.3 ± 190.7	433.1 ± 203.9
Saturated fatty acids (g)	27.1 ± 10.1a	39.8 ± 19.4[b]
Monounsaturated fatty acids (g)	29.8 ± 8.9	34.2 ± 11.4
Polyunsaturated fatty acids (g)	19.2 ± 9.4	17.9 ± 9.0
Total sugar (g)	83.9 ± 30.5[a]	99.0 ± 51.2[b]
Total fiber (g)	21.6 ± 9.0	19.7 ± 9.2
Insoluble fiber (g)	15.3 ± 7.1	12.4 ± 5.8
Soluble fiber (g)	6.0 ± 2.7	6.6 ± 2.8
Glycemic Index	56.8 ± 4.0[a]	58.1 ± 7.1[b]
Glycemic Load	114.9 ± 33.0[a]	144.8 ± 61.7[b]
Beta-carotene (µg)	5347 ± 5740[a]	2911 ± 2661[b]
Alpha carotene (µg)	766 ± 1428	432 ± 633
Cryptoxanthin (µg)	147 ± 178[a]	221 ± 380[b]

Parameter	Women (n =26)	Men (n = 24)
Lutein + Zeaxanthin (µg)	5700 ± 7359[a]	2633 ± 4071[b]
Lycopene (µg)	7686 ± 9938	8182 ± 8112
Minutes of Activity	306.5 ± 245.9	416.4 ± 265.6

Table 1: *Daily dietary intake as determined by 3-day diet records and number of minutes exercised as assessed by 3-day exercise dairy healthy men and women.*

Data are presented as mean ± SD for the number of subjects indicated in parentheses. Numbers in the same row with different superscripts are significantly different at P < 0.01.

Plasma Biomarkers, Anthropometrics and Family History of Chronic Disease

As a group, subjects were very healthy in terms of plasma lipids and all parameters of metabolic syndrome (Table 2). The only difference between men and women was that men had lower HDL-C ($p < 0.05$) and higher plasma glucose ($p < 0.01$). We classified the risk for chronic disease based on family history into 3 categories: cancer, heart disease and type 2 diabetes. For this population, 60% of subjects had risk for cancer, 43% for heart disease (including high blood pressure and/or elevated plasma cholesterol) and 36% for diabetes (Figure 1).

Parameter	Women (n = 26)	Men (n = 24)
BMI (kg/m^2)	22.7 ± 1.8	23.7 ± 2.4
Waist Circumference (cm)	79.9 ± 5.7	82.9 ± 7.0
Total cholesterol (mg/dL)	162.2 ± 25.9	146.8 ± 29.1
LDL-cholesterol (mg/dL)	76.0 ± 23.8	75.3 ± 25.6
HDL-cholesterol (mg/dL)	70.8 ± 22.4[a]	58.5 ± 11.6[b]
Triglycerides (mg/dL)	77.9 ± 33.3	66.5 ± 25.0
Glucose (mg/dL)	90.5 ± 4.6[a]	94.2 ± 8.0[b]
Systolic BP (mmHg)	106.0 ± 10.4	118.7 ± 11.1
Diastolic BP (mmHg)	72.0 ± 7.1	73.5 ± 7.0
CRP (mg/mL)	2.4 ± 4.1	2.5 ± 10.9

Table 2: *Anthropometrics, plasma lipids, glucose, C-reactive protein (CRP) and blood pressure (BP) for healthy men and women. Data are presented as mean ± SD for the number of subjects indicated in parentheses. Numbers in the same row with different superscripts are significantly different at P < 0.01.*

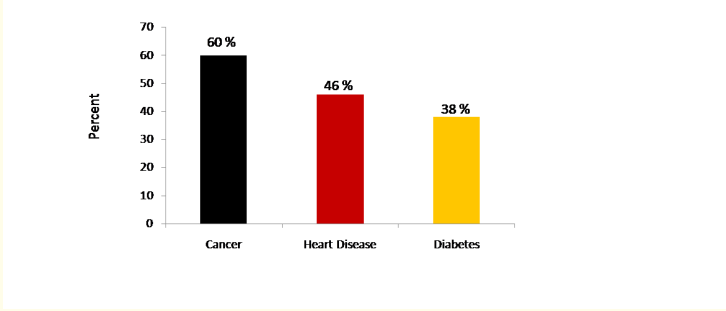

Figure 1: *Percent of family history with cancer (60%), heart disease (46%) or diabetes (38%) in a healthy population aged 18-30 years.*

When analyzed individually, there were 16 subjects who had one, or at the most, two biomarkers for heart disease (32%, 11 men and 5 women). Of these, 6 subjects had high LDL-C (> 100 mg/dL), 7 had high blood pressure (> 130 systolic or > 85 diastolic), 2 had low HDL-C (< 50 mg/dL for women and < 40 mg/dL for men), 1 had high WC (> 88 cm for women and > 102 cm for men), and 1 had high plasma triglycerides (> 150 mg/dL) (Table 3). In addition, 6 subjects had elevated fasting blood glucose (≤ 100 mg/dL), a risk factor for type 2 diabetes.

Gender Subject #	LDL-C[1]	HDL-C[2]	TG[3]	Glucose[4]	BP[5]	WC[6]	Chronic Disease		
							Cancer	Diabetes	Heart Disease
6 (M)	103								XX
7 (M)	130						XX		XX
8 (M)				101	130/83		XX		XX
10 (F)	108								
13 (M)				100	133/78				XX
16 (M)					135/73			XX	
22 (F)		38					XX		
25 (M)	120				126/85				
28 (M)				104				XX	XX
32 (F)			194		118/85		XX	XX	XX
33 (F)	150					92	XX	XX	
39 (M)				104			XX		XX
44 (F)		48					XX	XX	
47 (M)	109							XX	
48 (M)				107					
50 (M)				102	131/75		XX	XX	XX

Table 3: *Plasma biomarkers and history of chronic disease in 16 subjects with levels higher than current recommendations by National Cholesterol Education Program.*

LDL cholesterol ≥ 100 mg/dL[2] HDL cholesterol < 40 mg/dL for men and < 50 mg/dL for women; plasma triglycerides (TG) ≥ 150 mg/dL; plasma glucose ≥ 100 mg/dL; Blood pressure (BP) ≥130/85 mm Hg; waist circumference (WC) > 88 cm for women and > 102 cm for men.

Pearson Correlations between diet or exercise and biomarkers of disease

Regarding diet, a significant correlation was found between the dietary carotenoids lutein + zeaxanthin and HDL-C concentrations (Figure 2). In contrast, inverse correlations were found between systolic (Figure 3, panel A) and diastolic blood pressure (Figure 3, panel B) vs. dietary lutein + zeaxanthin.

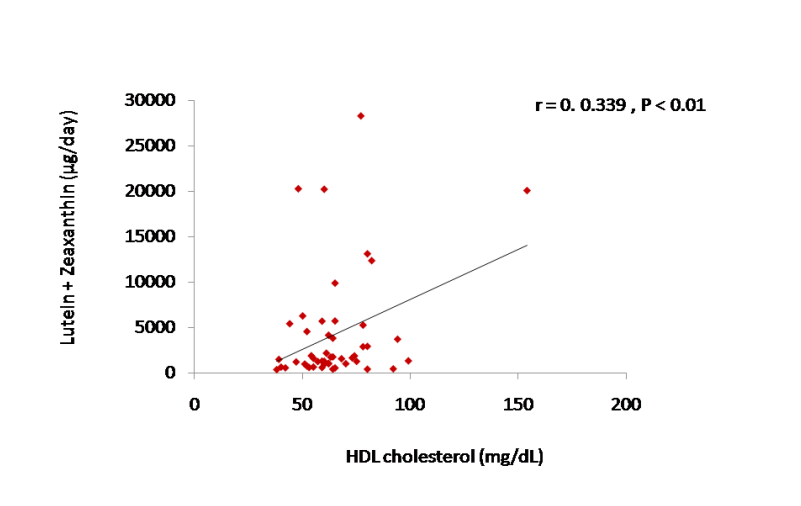

Figure 2: *Correlations between dietary intake of lutein and zeaxanthin (as assessed by 3-day dietary records) and plasma HDL-cholesterol concentrations (r = 0.339, p < 0.05).*

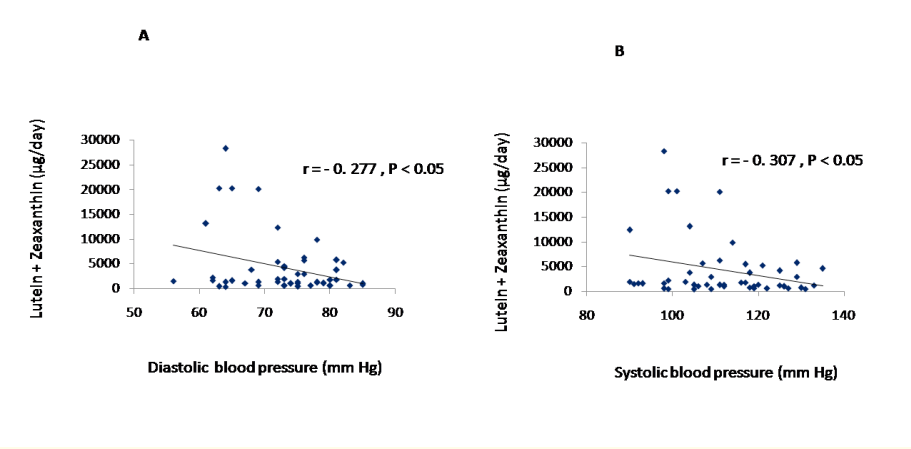

Figure 3: *Correlations between plasma lutein and zeaxanthin and systolic blood pressure (r= -0.277, P , 0.05) (Panel A) and diastolic blood pressure (r = -0.307, P < 0.05)(Panel B)*

Regarding exercise, significant negative correlations were found between the number of active minutes per week and plasma concentrations of LDLC (Figure 4, panel A). Additionally, the number of active minutes per week was negatively correlated with plasma TG concentrations (Figure 4, panel B).

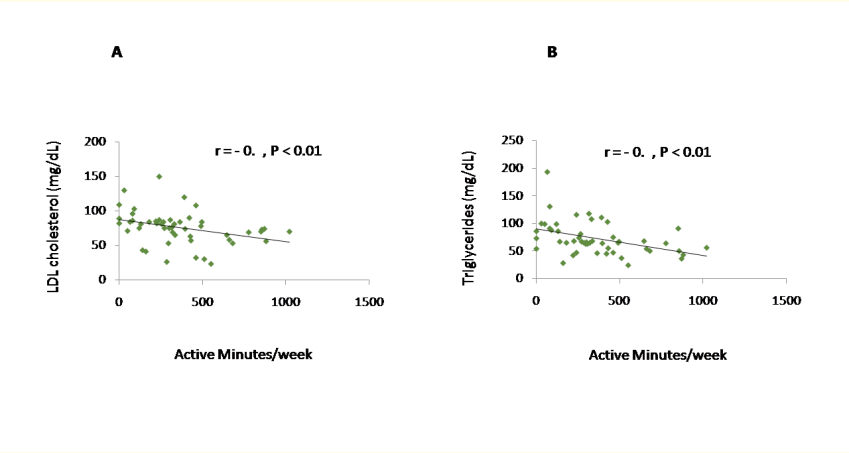

Figure 4: *Correlations between number of active minutes per week (as assessed by exercise questionnaires) and plasma LDL-cholesterol (r = - 0.3339 P < 0.05) (Panel A) and active minutes per week and plasma triglycerides (r= -0.41, P < 0.01) (Panel B).*

Discussion

In the present study, we report that 32% of individuals from this cohort of young healthy participants had one or two biomarkers associated with chronic disease risk. Surprisingly, the population under study was found to have high risk for developing cancer, heart disease or diabetes based on their self-reported family history.

Despite the fact that obesity and clinical manifestations of heart disease and type 2 diabetes were exclusion criteria for recruitment, 1/3 of these participants exhibited clinical parameters, which may place them at risk for chronic disease later in life. In terms of family history, 46% of the subjects appear to have an increased risk for heart disease, a higher proportion than the 34% of US population who has been diagnosed with cardiovascular problems [28]. Another interesting observation is that the parameters associated with heart disease risk, including high blood pressure and hypercholesterolemia, were higher in men when compared to women. There were also 6 men with high plasma glucose while all women had plasma glucose concentrations < 100 mg/dL.

Although several population studies have shown higher concentrations of plasma cholesterol in women when compared to men in their older age [29], a recent analysis of the Framingham offspring reported that after a 10 year follow up, 8.4% of the men had a cardiovascular event (i.e. ischemic heart disease, coronary event or death) while only 2.9% of women had an event in the same period of time [30]. In contrast, it has been reported that in the case of type 2 diabetes, women have more difficulty in reaching their LDL-C target. This is complicated by the fact that women are not prescribed statins as often as men, leading to a higher risk for heart disease in women with diabetes, especially as they age and disease duration lengthens [31].

The data obtained in the current study from this younger population is in agreement with the protective effect of estrogen in women in their earlier years. Protein convertase subtilisin/kexin type 9 (PCSK9) has been recently identified as a post-transcriptional regulator of the LDL receptor by promoting its degradation [32]. In a recent study, plasma levels of PCSK9 were inversely correlated with plasma estrogen [33], which provides insight into a potential mechanism as to why younger women have lower plasma cholesterol when compared to men and their post-menopausal counterparts.

Another possibility for the lower number of biomarkers in women could be that, as demonstrated in this study, women consume an overall healthier diet compared to men. For example, women had higher intake of the carotenoids lycopene, cryptoxanthin, lutein and zeaxanthin. The positive associations found between lutein and zeaxantin intake, higher HDL-C and lower blood pressure support that

fact that the healthier lifestyle in women may also contribute to the lower proportion of unfavorable biomarkers at this age. It is noteworthy to mention that 2 women in this population had low HDL-C, and both had a family history of cancer but not of heart disease.

We found strong negative correlations between number of active minutes per day and plasma TG and LDL-C. It is well known that there are multiple benefits associated with exercise, including the lowering of plasma cholesterol and TG, increases in plasma anti-inflammatory effects of HDL due to increases in paraoxonase (PON)-1 activity [34], increases in nitric oxide production, which regulates mitrochondial biogenesis [35], decreases in blood pressure [36], and improvements in the parameters of MetS, which lead to the development of heart disease and diabetes.

According to the American Cancer Society, 14.5 million individuals are living with cancer in U.S. whereas 2015 projections estimate an additional 1.5 million cancer cases and close to 600,000 deaths [37]. Thus, it is a very surprising finding that 60% of subjects in the current study reported having a parent, grandparent or sibling with cancer. This higher cancer incidence compared to national numbers could represent an anomaly associated with the random selection of individuals who were tested and interviewed for the current study.

We have identified several strengths and weakness in this study. The strengths of the study include the accuracy in the information from family history, in addition to the careful analysis of the dietary and exercise records from all of our participants, which are highly representative of their daily nutrient intake and their level of activity. The weakness of this study is that although the measured biomarkers are the most commonly analyzed in clinical laboratories, they do not provide sufficient information on chronic disease risk. Measures of biomarkers of inflammation [38], oxidative stress [39] and atherogenicity of lipoproteins [40] would have been useful to better understand the risk of these subjects. Another limitation is that we only tested 50 subjects and it is possible that the statistics for family history of chronic disease would differ with a larger sample size.

Conclusions

We conclude that young, healthy non-obese individuals who were screened for not having diabetes, cancer or heart disease could still be at risk for developing chronic disease later in life based on the biomarkers already present in 32% of the population and their self-reported family history. Intake of the dietary antioxidants lutein and zeaxanthin and physical activity levels correlated with lower values of plasma lipids, blood pressure and higher HDL-C. Thus, maintaining a healthy lifestyle appears to be protective against chronic disease in this population.

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Volume 1 Issue 4 May 2015
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